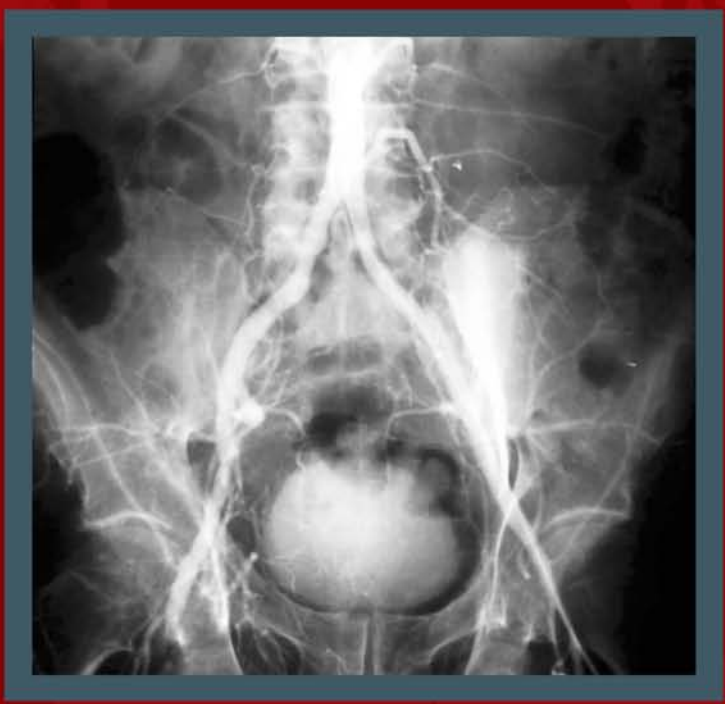
Complications in PERIPHERAL VASCULAR INTERVENTIONS



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Foreword

With the aging population in industrialized countries, increased body weight among many Western countries, resulting in a pandemic of diabetes mellitus, and continued tobacco abuse, it is of no surprise that peripheral arterial disease is occurring with increased frequency. Primarily due to atherosclerosis, arterial occlusive disease of the lower extremity, renal, mesenteric, brachiocephalic, and carotid arteries presents significant challenges to practicing physicians. In addition, aneurysmal disease of the thoracic and abdominal aorta represents significant risk to life.

Due to the advances in techniques and technology, endovascular approaches now represent the initial strategy for management of these complex patients. As devices become more flexible, lower profile, and more precise, percutaneous transluminal angioplasty, stents, covered stents, atherectomy, laser, cryotherapy, and other modalities will continue to be used in difficult anatomic situations.

Undoubtedly, due to the challenging nature of atherosclerotic vascular disease, complications will become part and parcel of the interventionists' practice. The key, of course, will be early recognition with prompt and appropriate management.

This textbook is a welcome addition to the library of any physician involved in the diagnosis and management of vascular disease. Recognized experts in the field, representing multiple specialties, cover the broad spectrum of vascular complications. Each author methodically evaluates the specific complications of each vascular bed, discussing important tips to manage the complications, as well as methods to avoid them initially.

Congratulations to Professors Schillinger and Minar who provide key insights into the diagnosis and management of iatrogenic vascular complications, along with management strategies.

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Preface

Minimal invasive endovascular treatment of peripheral arteries is one of the most rapidly evolving techniques in interventional therapies. Advanced technologies enable treatment of more complex lesions in severely diseased patients. Increasing evidence suggests that, particularly in high-risk patients, endovascular solutions offer substantial advantages compared to vascular surgical procedures. Nevertheless, growing numbers of procedures are associated with an increased incidence of complications. Knowledge of specific complications in different vessel areas will support the interventionist in preventing such adverse events and, if necessary, provide considerable reassurance if such complications need to be resolved. The present book aims to systematically cover specific complications in peripheral vascular interventions. Typical and atypical complications are described for major peripheral vessel areas and methods to handle these events are outlined.

The book is divided in two parts: Part I reviews general aspects on complications in peripheral interventions, Part II covers the specific vessel areas. Each chapter on the specific vessel areas includes

- Introduction to the frequency and type of complications in this vessel area
- Factors identifying patients at high-risk for complications
- Complications of specific interventional steps and tools
- Methods to detect potential complications – which diagnostic steps are needed routinely to rule out or identify complications
- Endovascular, surgical, and medical techniques to resolve complications
- Methods to avoid complications
- Summary
- Check list for emergency equipment for interventions in this specific vessel area.

We intended to focus on practical tips for the interventionist in the cath lab, to review complicated cases and outline different strategies in real-life cases, and thus to share the experience of high-volume interventionists with the reader. We hope that this book is a practical guide for quality improvement which will help to improve the safety of our patients undergoing peripheral vascular interventions.

Martin Schillinger
Erich Minar

Part I

Complications – general considerations

1

Introduction to complications in peripheral vascular interventions – frequency of complications and worst scenarios

Martin Schillinger

Introduction • Frequency and impact of complications • Classification of complications • Worst scenarios

INTRODUCTION

Endovascular therapy emerged as one of the most rapidly evolving fields in medicine during the last decade. In 1964 Dotter and Judkins reported the first angioplasties performed in the femoropopliteal vessel area using coaxial catheter systems up to 12 French gauge in diameter. It soon became apparent that the concept of vessel-sized dilators was not suitable, however it took another 10 years until Grüntzig and Hopff described a coaxial balloon catheter that inflated to a fixed diameter and thus initiated the era of balloon angioplasty. The equipment was continuously miniaturized and thus could be used in virtually any vessel segment. Currently, endovascular therapy has replaced vascular surgery for many indications. The use of stents has improved the durability of the results, and advanced technologies now enable the treatment of complex lesions in patients who otherwise could not have been revascularized.

Despite major advances during recent years, complications in peripheral vascular interventions remain a major issue. Because angioplasty for most entities of peripheral vascular disease does not generally have a more durable result than surgical reconstruction, its use is justified mainly by its reduced risk combined with a reasonable likelihood for success. The latter can be achieved in the vast majority of cases; technical success rates usually range between 95 and almost 100%. In contrast, complications increase morbidity and mortality, prolong the hospital stay, and increase the costs for healthcare providers. Strategies for prevention and management of complications therefore are a major goal in education and training of interventionists. The present book gives an overview about complications in peripheral vascular interventions, describes how to recognize risk factors for pitfalls, and reports strategies to prevent and handle critical situations.

FREQUENCY AND IMPACT OF COMPLICATIONS

The frequency of complications mainly depends on the clinical setting in which the interventions are performed. Emergency interventions for ruptured aortic aneurysm still carry a high mortality risk of between 15 and 50%. In contrast, elective peripheral angioplasties can be done with complication rates below 1%. Table 1.1 gives an overview on the frequency of complications after elective angioplasty procedures.[1]

Table 1.1 Complications of elective angioplasty

Complication	*Incidence (%)*
Puncture site (total)	4.0
Bleeding	3.4
False aneurysm	0.5
Arteriovenous fistula	0.1
Angioplasty site (total)	3.5
Thrombus	3.2
Rupture	0.3
Distal vessel (total)	2.7
Dissection	0.4
Embolization	2.3
Systemic (total)	0.4
Renal failure	0.2
Myocardial infarction (fatal)	0.2
Cerebrovascular accident (fatal)	0.6
Consequences	
Surgical repair	2.0
Limb loss	0.2
Mortality	0.2

The frequency and characteristics of complications differ for specific vessel areas; details are given in the relevant chapters. The major principles of complications, however, unequivocally apply to all vascular segments. Table 1.2 gives an overview on reported frequencies of complications for interventions in different vessels areas.[2–23] Quantitatively, the frequencies of complications in different vessel areas seem comparable; the impact of complications, however, differs widely for the specific vessel areas. For example, embolization is usually a relatively benign complication in peripheral arteries, but remains a major concern during carotid stenting. Principles of complications are briefly discussed below.

Table 1.2 Frequencies of complications for elective angioplasty and stenting procedures in different vessel areas

Intervention	*Incidence (%)*
Carotid arteries	6–10
Subclavian and vertebral arteries	6–10
Aortic stent graft implantation	8–12
Renal and mesenteric arteries	4–10
Iliac arteries	4–8
Femoral arteries	4–6
Below the knee arteries	4–8
Venous interventions	2–6

The most frequent complications involve the *vascular access site*.[24,25] On the one hand, the rates of access site complications can be substantially reduced due to decreasing diameters of sheaths, low-traumatic puncture techniques, adequate preinterventional imaging modalities, and modern closure devices. On the other hand, aggressive anticoagulant therapies in high-risk patients increase the likelihood for puncture site complications. Therefore, a frequency of 2 to 4% for puncture-related complications remains the most frequent clinical problem after endovascular procedures (Figures 1.1 and 1.2).

Complications at the site of angioplasty usually are rare and most of these complications can be resolved by endovascular techniques.

- The formation of clots during the intervention at the site of angioplasty hardly ever occurs in patients under adequate antiplatelet therapy

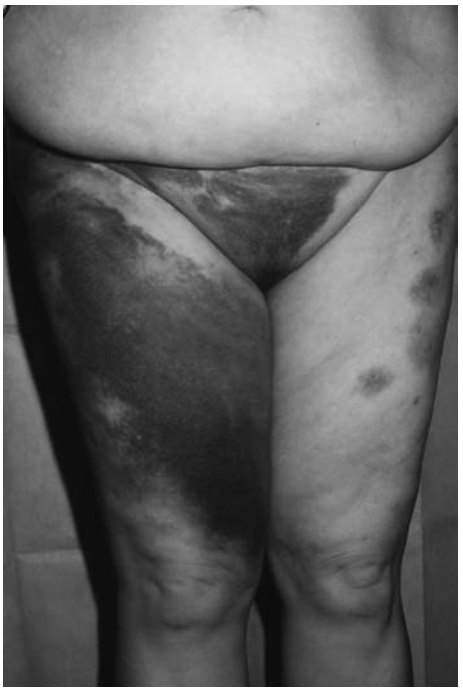

Figure 1.1 Large hematoma after inguinal arterial puncture.

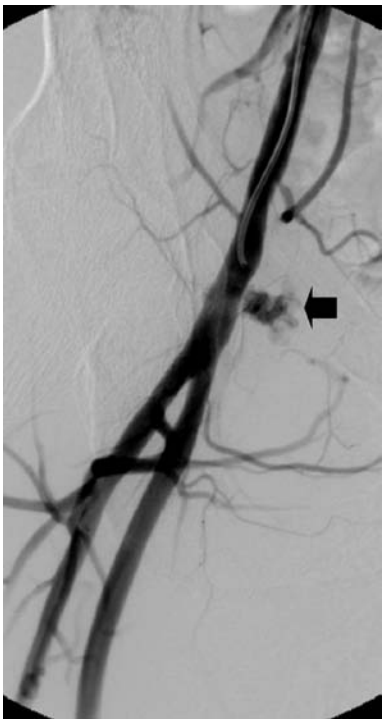

Figure 1.2 Pseudoaneurysm in the right groin 24 hours after removal of a 7 French sheath.

and when heparin or bivalirudin is used with adequate dosage and monitoring during the intervention. The incidence of early stent thrombosis in peripheral interventions could be dramatically reduced by the introduction of dual antiplatelet therapy combining aspirin and thienopyridines and is encountered in less than 2% of the cases (Figure 1.3).[22]

- Dissection is a common problem after balloon angioplasty (Figure 1.4). Its frequency varies with the anatomy of the target vessel site and the length of the treated segment, and is strongly correlated with the balloon-to-artery ratio.
- Similarly, arterio-venous (AV) fistulas are common after revascularization of long segment occlusion, especially in the case of subintimal angioplasty (Figure 1.5). Nevertheless, the use of stents has virtually eliminated the problems associated with dissection or AV fistulas at the treated segment, as long as a wire can be successfully passed to the true vessel lumen.
- Bleeding and rupture are rare but sometimes dramatic clinical problems. Perforation may occur due to improper manipulation with the wire (Figure 1.6), particularly when stiff

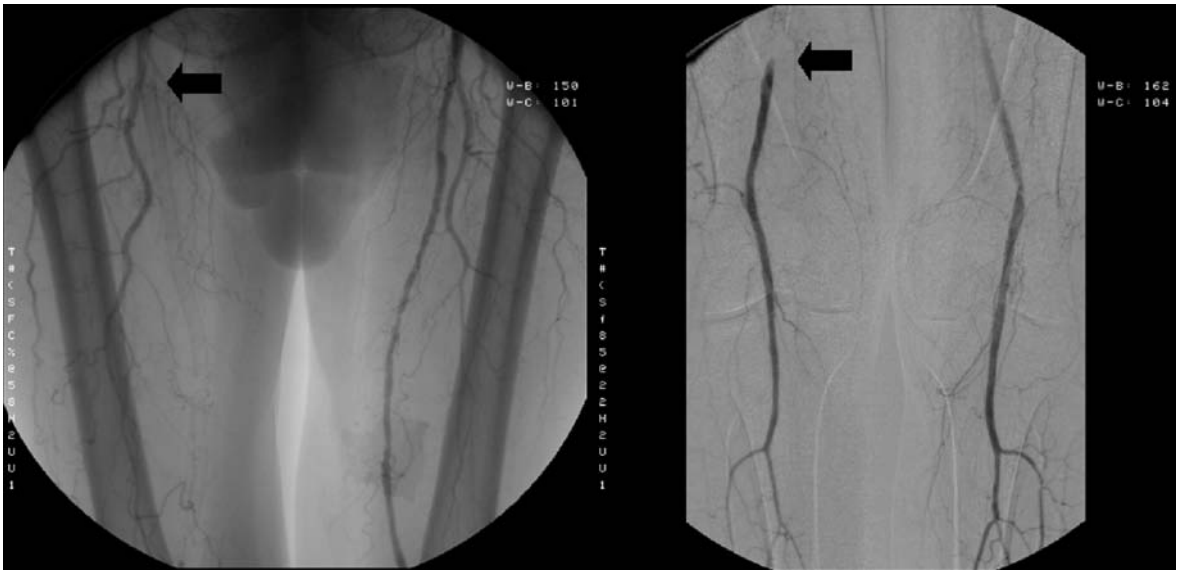

Figure 1.3 Acute stent thrombosis 24 hours after long segment stenting of the superficial femoral artery in a patient under aspirin monotherapy.

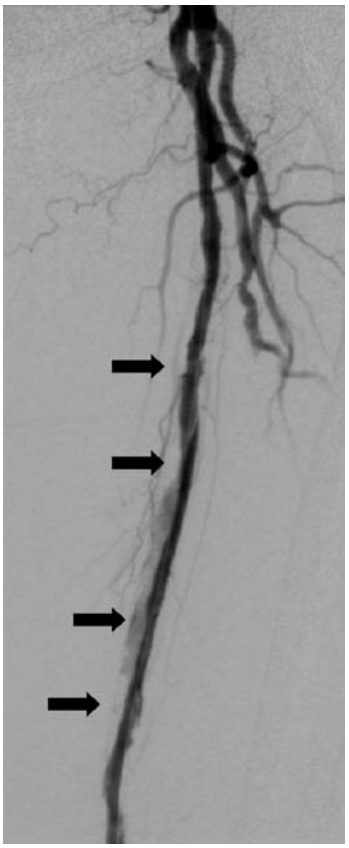

Figure 1.4 Long segment flow-limiting dissection after balloon angioplasty of a superficial femoral artery.

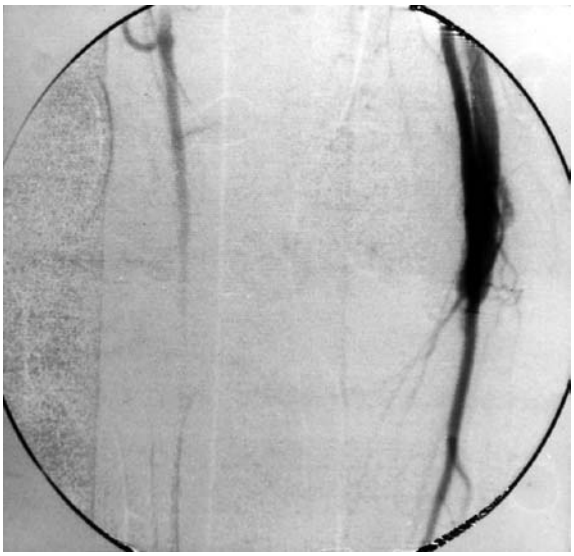

Figure 1.5 AV fistula of the left popliteal artery.

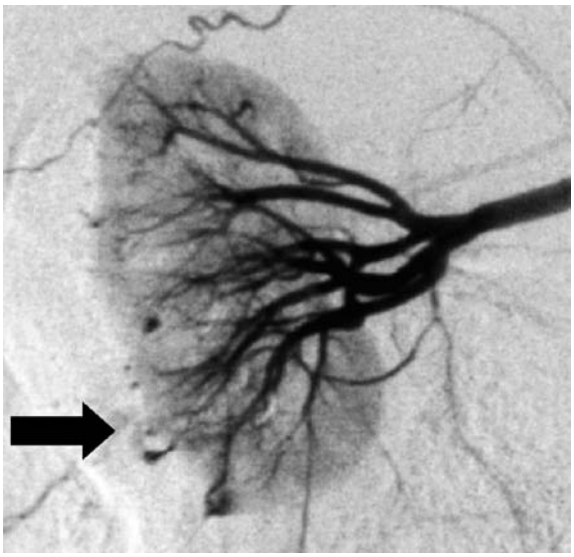

Figure 1.6 Perforation with the tip of the guidewire in the subsegmental renal arteries during renal artery stenting.

hydrophilic guidewires are used. Rupture may occur during balloon angioplasty of rigid obstructions (Figure 1.7), or due to vast oversizing of balloons. Typical settings for ruptures are the origin of calcified visceral arteries, heavily calcified lesions in the aorta, and the external iliac artery.

Complications at vessel segments distal to the target site

- Distal dissections can be mostly avoided by cautious handling of the guidewire. Keeping an eye on the tip of the guidewire always has to be considered, especially when long over-the-wire (OTW) guidewires are used, e.g. for over-the-bifurcation procedures. During changing maneuvers of catheter material with long OTW guidewires the tip of the wire always should be visualized by fluoroscopy.
- Peripheral embolization is a problem mainly in fresh thrombotic lesions. Nevertheless, particularly in case of long chronic total occlusions, the risk for peripheral macroembolization

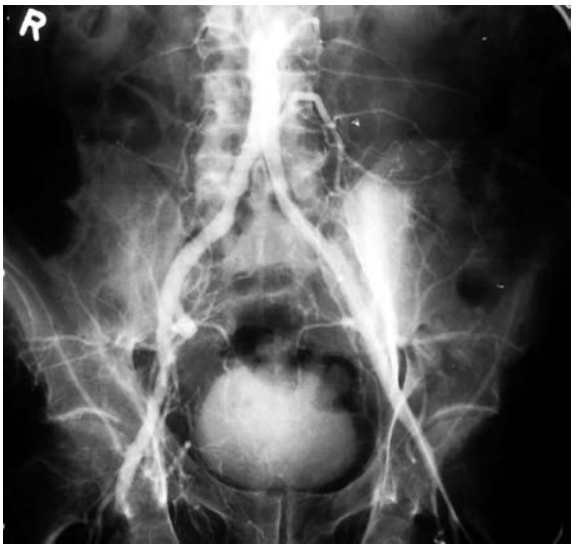

Figure 1.7 Large extravasation due to rupture of the left external iliac artery during balloon angioplasty.

always has to be considered and the outflow has to be checked routinely (Figure 1.8). Besides the risk of embolizing large particles, all interventions carry a risk for microembolic showers. The clinical sequelae of these microemboli can be clinically silent or fatal, depending on the affected vessel area. Much attention has been paid to avoid cerebral microembolization during carotid stenting,[2–8] and embolization during renal angioplasty leading to renal failure has also become an issue during recent years.[12] Most frequently, however, clinical signs of embolization can be observed at the foot (Figure 1.9). These emboli are usually extremely painful for the patient and it may take weeks to months until the pain completely resolves. Heparin, anti-inflammatory drugs, and corticosteroids are used to treat these patients. In this context, the entity of cholesterol emboli has to be mentioned, a rare clinical complication with signs of peripheral embolization, systemic inflammation, and progressive renal failure.

Systemic complications

Systemic complications include renal failure due to contrast nephropathy,[26] infection with septicemia, myocardial infarction, and stroke. Fortunately, the latter ones very infrequently are observed in territories other than coronary or carotid interventions. Renal failure remains a clinically relevant problem, particularly in diabetic patients, patients with pre-existent renal dysfunction, and patients with congestive heart failure.

Figure 1.8 Distal embolization after stenting of the proximal superficial femoral artery: the tibioperoneal trifurcation is occluded by embolic material.

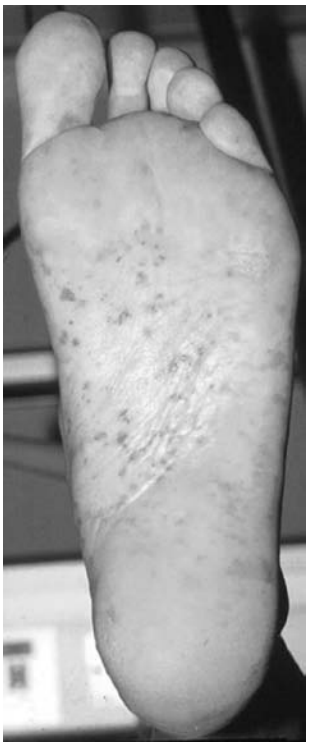

Figure 1.9 Microemboli to the foot after renal angioplasty with left retrograde arterial access.

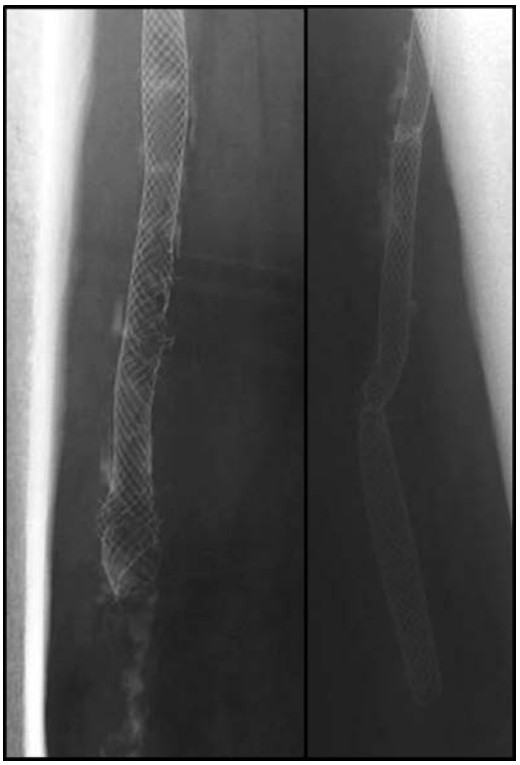

Figure 1.10 Stent fractures in the superficial femoral artery.

Device-related complications

Device-related complications during interventions are rather infrequent events, although broken wires, malfunctioning stents, and embolization of catheter shaft material has been reported in almost all vessel areas.

- Infection of implants also occurs very infrequently. Predominantly with historical covered stent grafts, larger numbers of infected implants were reported.
- In contrast to these anecdotal complications, chronic device failure due to stent fracture seems to occur in a considerable proportion of patients, particularly in the femoropopliteal vessel area, and has become a matter of concern (Figures 1.10 and 1.11).

Finally and most importantly, the *clinical impact and consequences of complications* of peripheral vascular interventions mainly depend on the skills of the interventionists. Almost all of the above mentioned complications can be prevented by careful patient selection, planning of the

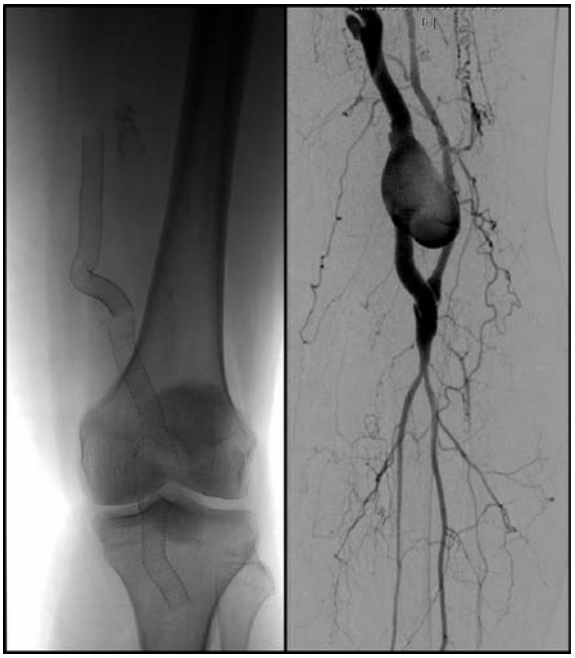

Figure 1.11 Stentgraft fracture and endoleak formation leading to recurrence of a popliteal aneurysm 14 months after initially successful stentgraft implantation.

procedure, and selection of adequate materials. If complications occur, it will be the skill and experience of the interventionist who has to resolve the problem in the cath lab that determine whether it will just be a challenging case with a good clinical outcome or a complicated case which results in a clinical catastrophe.

CLASSIFICATION OF COMPLICATIONS

According to the Society of Interventional Radiology guidelines, complications are classified as minor or major.
Minor complications:

- no therapy, no consequence, or
- nominal therapy, no consequence; includes overnight admission for observation only.

Major complications:

- require therapy, minor hospitalization (less than 48 hours)
- require major therapy, unplanned increase in level of care, prolonged hospitalization (greater than 48 hours)
- have permanent adverse sequelae, or
- result in death.

WORST SCENARIOS

The 'hit list' of worst scenarios is certainly a very individual ranking of personal nightmares. Nevertheless, statistics seem to hold true for most interventionists as some major complications occur sooner or later during an interventional career.

Vessel rupture and massive bleeding is one of the few acutely life-threatening complications which the interventionist always has to be prepared to deal with. Immediate recognition of the problem and rapid sealing of the site of rupture may save the patient's life. The premise for successful sealing of rupture sites is an adequate armentarium of the cath lab: this mainly includes large balloons for immediate balloon occlusion, covered stents with different diameters and lengths, and vascular coils in different sizes. Figure 1.12 shows an example of a ruptured renal artery during angioplasty of a left-sided ostial renal artery stenosis. The patient developed massive abdominal pain

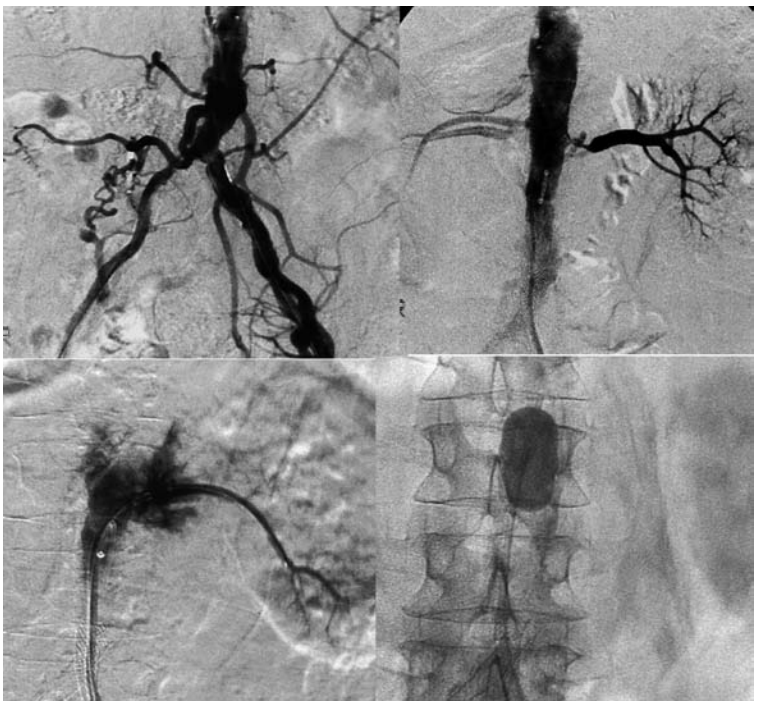

Figure 1.12 Rupture of the renal artery during balloon angioplasty of a left-sided ostial renal artery stenosis and successful sealing of the rupture site using a large compliant balloon. (Courtesy of Dr P Waldenberger, Innsbruck, Austria.)

during balloon inflation and became hemodynamically unstable immediately thereafter. The rupture site was acutely sealed by a large, compliant balloon in the abdominal aorta, covering the origin of the left renal artery. The patient was taken urgently to the operating theatre and underwent an emergency operation. The vascular surgeon found the renal artery completely ruptured from the aorta and was able to resolve the problem by bypass surgery. The patient survived with a prolonged stay in the intensive care unit.

Acute vessel occlusion where perfusion is crucial. Acute ischemia during endovascular treatment can be relatively benign or potentially life-threatening, mainly depending on the ischemia tolerance of the affected organ system. The human brain is without doubt the least tolerant to ischemia. Acute occlusion of the arteries of the brain therefore is a true nightmare of carotid interventionists. Figure 1.13 shows an example of an acute occlusion of the carotid artery during stent implantation. Fortunately, this was due to a severe spasm of the internal carotid artery which could be resolved by intra-arterial application of 0.1 mg nitroglycerin and removal of the filter wire without any clinical complications.

Perforation and compartment syndrome may complicate a procedure hours after the patient has left the cath lab, when subacute bleeding remains initially unrecognized or left untreated. Compartment syndromes more frequently occur in the popliteal fossa and below the knee, where smaller amounts of blood cause relevant compression and increase in compartment pressures. Figure 1.14 shows an angiogram with massive bleeding to the popliteal fossa after failed recanalization of a P1 occlusion. The complication could be managed by prolonged balloon inflation and external compression. Nevertheless, the patient had to undergo fasciotomy the day after the intervention and had a markedly prolonged hospital stay.

Finally, *contrast-induced renal failure* leading to permanent renal replacement therapy certainly belongs to the absolute worst scenarios after elective endovascular procedures.[26] Renal failure after endovascular procedures substantially increases patients' morbidity and mortality and reduces quality of life. Fortunately, this complication is rare, mostly predictable, and can be avoided by adequate patient selection, patient preparation, and careful use of contrast media.

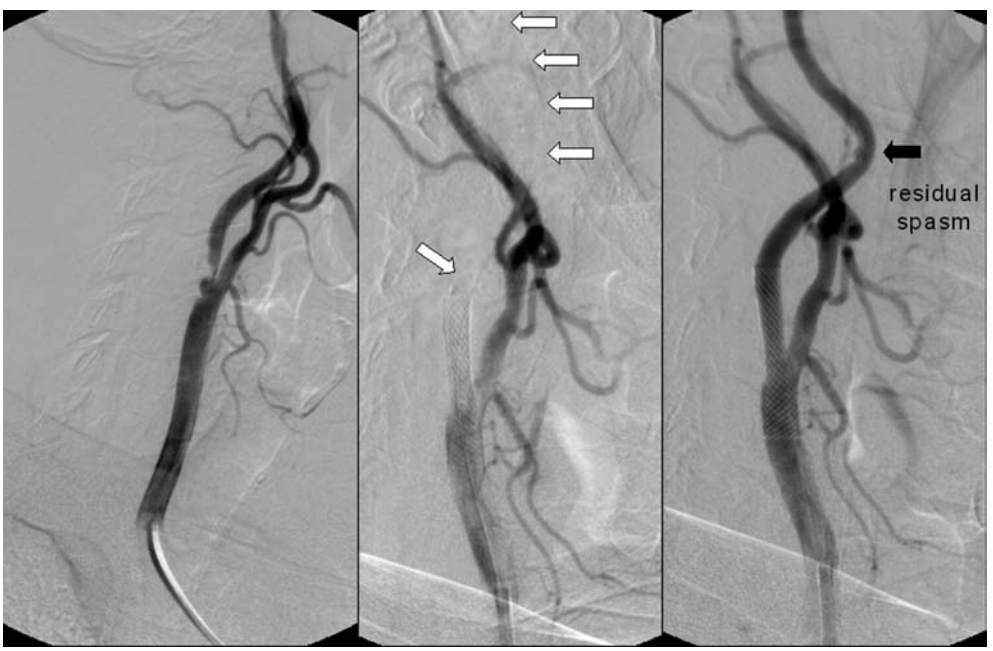

Figure 1.13 Acute occlusion of the carotid artery during filter-protected carotid stenting. Complete restoration of flow was achieved after application of 0.1 mg nitroglycerin, which resolved the severe spasm of the artery.

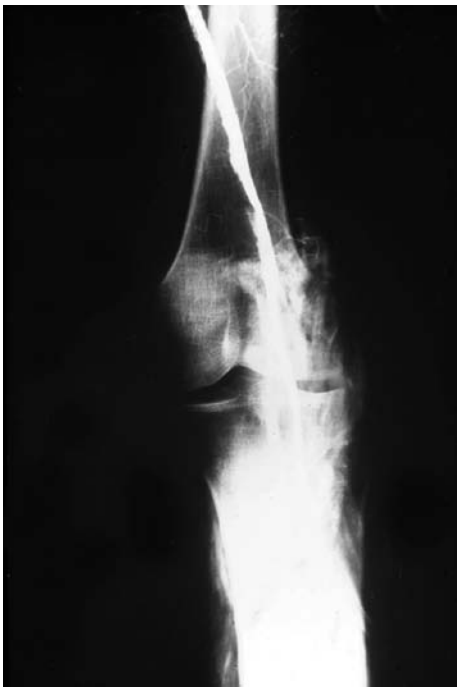

Figure 1.14 Perforation and bleeding to the popliteal fossa after failed recanalization of a P1 occlusion. The patient had to undergo fasciotomy the day after the procedure.

In conclusion, the hit list of worst complications will permanently change during the life of the interventionist. Certainly, we don't have to make all mistakes ourselves to learn how to avoid them. We hope that this book will help to clarify risk factors and mechanisms for complications and provide strategies to handle and avoid adverse outcomes.

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2

Identifying (high) risk patients for endovascular treatment – unfavorable medical comorbidities

Erich Minar

Importance of accurate identification of risk patients • Vascular comorbidity • Non-vascular comorbidity • Is risk reduction possible by drug application? • Summary

IMPORTANCE OF ACCURATE IDENTIFICATION OF HIGH RISK PATIENTS

Risk identification should allow the clinician to develop the optimal treatment strategy for the patient and to provide better informed consent. From a scientific point, evaluation of comorbidity is important in healthcare outcomes research because variation in baseline patient characteristics may significantly contribute to differences in outcome.[1,2] Clinical reports that evaluate revascularization procedures, particularly those that compare different treatment methods, may be difficult to interpret when differences in factors that can affect complication rate and outcome are not identified and characterized. The completeness and reliability of data concerning comorbidity and therefore the risk of any intervention affect the validity of risk adjustment models and the accuracy of comparisons between different patient cohorts. However, it should also be stressed that risk factors that affect perinterventional morbidity and mortality rates are not identical with those that relate to patency.

Concerning the group of patients undergoing endovascular procedures, the type of comorbidity can be classified as vascular or nonvascular. Due to lack of data in the literature, the recommendations given in this chapter with regard to pre-interventional evaluation to identify (high) risk patients for endovascular treatment are mainly based on personal experience and on data from surgical literature.

VASCULAR COMORBIDITY

Atherosclerosis as systemic disease

Most of the patients treated by endovascular procedures suffer from atherosclerotic disease. Other causes for occlusive or aneurysmatic disease – such as inflammatory diseases – are rare. Atherosclerosis is a systemic disease not limited to a single vessel region. This explains the often found coincidence of either symptomatic or asymptomatic vascular disease in the different areas.

Prevalence of cardiovascular comorbidity

The reported prevalence of coronary heart disease (CHD) in patients with peripheral arterial occlusive disease (PAOD) ranges from 14 to 90%, depending on the sensitivity of the diagnostic test.[3] In a landmark study by Hertzer et al,[4] coronary angiography was performed in 1000 patients (mean age 64 years) under consideration for elective peripheral vascular

reconstruction. The primary vascular diagnosis was abdominal aortic aneurysm (AAA) in 263 patients, cerebrovascular disease (CVD) in 295, and PAOD in 381. Severe correctable CHD was identified in 25% of the entire series (AAA, 31%; CVD, 26%; and PAOD, 21%). The prevalence of renal artery stenosis in patients with PAOD is reported up to 40%.

This high comorbidity is responsible for the poor long-term prognosis in many of these patient groups. The annual mortality rate derived from epidemiologic studies, e.g. of patients with lower extremity PAOD, is 4 to 6%, and is highest in those with the most severe disease. The 1-year mortality rate in patients with critical limb ischemia is approximately 25% and may be as high as 45% in those who have undergone amputation.

Data in the literature concerning cardiovascular risk evaluation

As a consequence of the coexistence of atherosclerosis in many vessel regions, there is an increased risk of myocardial infarction, stroke, and cardiovascular death in these patients. Independent of this long-term risk for cardiovascular events, patients undergoing an intervention for their vascular disease have an acutely increased peri-interventional risk. This is well established for patients undergoing vascular surgery. Although the overall perioperative event rate has declined over the past decades, the 30-day cardiovascular mortality still remains as high as 2–5%.[5] Myocardial infarction accounts for up to 40% of postoperative fatalities and can therefore be considered as the major determinant of perioperative mortality associated with vascular surgery.

A number of scoring systems have been developed over the years that aim to quantify the risk of perioperative morbidity and mortality. The majority of studies tried to validate an index for risk of cardiac complications. The identification of risk factors associated with increased risk of mortality should help in decision-making about the need for additional preoperative cardiac testing. It may also influence the decision about the type and timing of intervention. The ACC (American College of Cardiology)/AHA (American Heart Association) have published guidelines to provide a standardized method of evaluating the cardiac risk before non-cardiac surgery and selecting patients at risk for more extensive testing.[6] Otherwise, debate continues regarding the extent and type of cardiac evaluation necessary before major vascular surgery procedures. It has been reported that coronary revascularization before elective vascular surgery did not significantly alter the incidence of perioperative myocardial infarction among patients with stable CHD.[7] Furthermore, intensive non-invasive testing often triggers a clinical cascade, exposing the patient to progressively riskier testing and intervention, and results in increased costs and unnecessary delays. Therefore, screening of high-risk patients for cardiac ischemia seems not essential for revascularization, but rather to optimize the perioperative patient management concerning optimal medical therapy.

Compared to the surgical literature concerning perioperative risk evaluation, corresponding studies concerning the peri-interventional risk identification in patients undergoing endovascular procedures are rare.[8–10] This is probably due to the fact that until recently most endovascular interventions were low-risk procedures. This has only changed during the last years by rapidly increasing use of endovascular treatment of carotid stenosis and aortic aneurysms.

In a recently published study by Hofmann et al,[9] the authors did multivariable analysis to create a risk score identifying high-risk patients for carotid artery stenting. The primary endpoint reflecting periprocedural complications encompassed minor and major stroke, non-fatal myocardial infarction, and all-cause mortality within 30 days. Their analysis in 606 consecutive patients revealed diabetes mellitus with inadequate glycemic control (HbA1c > 7%), age ≥ 80 years, ulceration of the carotid artery stenosis, and a contralateral stenosis > 50% as independent risk factors. A risk score formed with these variables showed a superior predictive value compared with single risk factors. The presence of two or more of these risk factors identified patients with a risk of 11% for a periprocedural complication compared with 2% in patients with a score of 0 or 1.

There is uniform consent that cardiovascular complications are more often encountered in patients of older age. Furthermore, an increased

risk of hemorrhagic complications has been reported in women.[11]

There are only few data considering the major medical morbidity – not only cardiovascular events – after endovascular interventions, e.g. in patients with PAOD treated by angioplasty. Axisa et al[12] reported the outcome after peripheral angioplasty in 988 patients after 1377 interventions between 1995 and 1998. Major medical morbidity (including bronchopneumonia, renal failure, stroke, and myocardial infarction) complicated 33/1377 procedures (2.4%).

Recommendations concerning cardiovascular risk evaluation

It is generally assumed that endovascular treatment is associated with reduced risk of cardiovascular complications compared to open surgery. Furthermore, for most interventions there seems to be a significant mortality advantage for endovascular as compared with traditional surgery. Therefore proponents of endovascular treatment always stress these most important advantages – especially from the patient's point of view – of low procedural morbidity and mortality. This reduced peri-interventional cardiovascular morbidity and mortality is also the main reason for the dramatic shift in revascularization management over the last few years.

The extent of preinterventional risk evaluation is mostly guided by the severity of the intervention, e.g. patients with planned endovascular treatment of aortic aneurysm should be evaluated and managed with the same intensity as surgical candidates due to the potential necessity of conversion to open surgery. Otherwise, considering the potential risk – despite being (very) low for most endovascular procedures – of severe complications with the necessity of surgery, each patient with planned endovascular intervention should undergo some basic evaluation.

Identification of potentially serious cardiac disorders

History, physical examination, and electrocardiogram should focus on the identification of potentially serious cardiac disorders such as CHD (prior myocardial infarction and angina pectoris), heart failure, and severe arrhythmias. Diabetics should be evaluated with special care due to the increased prevalence of CHD and the possible presence of silent ischemia. Chest radiography and echocardiography are helpful procedures in patients with dyspnea on exertion and clinical suspicion of heart failure or valvular disease. Noninvasive stress testing, myocardial scintigraphy, and coronary (CT) angiography are only recommended in patients with clinically severe CHD.

Identification of potentially serious cerebrovascular disorders

History and duplex sonography are sufficient for diagnosis of (a)symptomatic carotid artery stenosis. This information is not necessary for most endovascular procedures except cerebrovascular treatment itself. However, in patients scheduled for aortic stent grafting, knowledge about the presence of high-degree carotid stenosis is helpful to avoid severe or prolonged hypotension during the intervention. Furthermore, such basic investigation of the carotid arteries is useful to help in the decision for carotid stenting in case of eventual further rapid progression in the degree of stenosis.

NON-VASCULAR COMORBIDITY

Identification of the patient with pulmonary disease

History and clinical examination are sufficient to identify potential problems concerning the patient's pulmonary status. History should include the following questions: smoking, asthma, dyspnea and severity of breathlessness, and cough. Especially chronic severe cough may cause problems during the intervention. Chest radiography and a lung function test are recommended before endovascular stent grafting of aortic aneurysm and in all patients with severe pulmonary disorders.

Identification of the patient with renal disease

Chronic kidney disease is in general a major and serious risk factor for cardiovascular disease, and endstage renal disease is the major contributor to the high morbidity and mortality observed in this population.

Determination of creatinine is sufficient for routine preinterventional evaluation. However, although creatinine is a specific marker for renal function, it may be insensitive to mild and moderate degrees of renal impairment. As a result, patients with subclinical renal disease may remain undiagnosed because of a normal serum creatinine value. Estimates of glomerular filtration rate (GFR) are the best overall indices of the level of renal function. The Cockroft–Gault equation is the most commonly used equation to estimate GFR. It is important to reduce the amount of contrast agent as much as possible in patients with impaired renal function. Furthermore, these patients may most benefit from the use of alternative contrast agents and periprocedural renal protection techniques.

Sufficient hydration – which is advised for all patients undergoing endovascular procedures – is absolutely necessary in patients with risk factors for chronic renal insufficiency to prevent contrast induced nephropathy.

Identification of further risk patients

Patients with diabetes

Correction of inadequate glycemic control in patients with diabetes mellitus before elective endovascular intervention is recommended.[9] Besides the well-known risk of diabetes for severe atherosclerotic disease and renal impairment, the patient with diabetes has to be carefully managed peri-interventionally with regard to the antidiabetic medication. Concomitant use of metformin may lead to lactic acidosis due to metformin accumulation. Thus, metformin should be discontinued prior to use of contrast media. Blood glucose should be controlled in short intervals in insulin-dependent diabetics to avoid hyper- and hypoglycemic episodes.

Patients with hypertension

The elevation of both systolic blood pressure (SBP) and diastolic blood pressure (DBP) is known to be contributory to cardiovascular mortality. Several population-based studies in hypertensive patients and also in the general population have also demonstrated pulse pressure (PP = SBP – DBP) as an independent risk predictor.[13] Central artery stiffness seems the main explanation for this relationship between a wide PP and cardiovascular events.

Patients with hypertension should be regularly monitored during and after the intervention to avoid hypertensive episodes with increased bleeding risk, especially at the puncture site. It is strongly recommended to continue antihypertensive treatment also on the day of intervention. (The special problems in patients with carotid stenting are discussed in the corresponding chapter.)

Patients with urologic disorders

Male patients with prostatic hypertrophy may develop urinary retention – favored by bed rest and compression bandage – with the necessity of urinary catheterization, and further urinary tract infection requiring antibiotics. Successful use of closure devices can reduce this risk.

Patients with thyroid disease

Application of conventional contrast media may rarely cause iodine-induced thyrotoxicosis. This risk is very low in euthyroid patients, however it is increased in patients with latent hyperthyroidism. In these patients, consultation with an endocrinologist is recommended to initiate the necessary premedication with perchlorate and a thyrostatic drug.

Patients with coagulation disorders

A history of spontaneous hemorrhagic complications and antithrombotic therapy as well as laboratory tests are necessary to identify patients with potential bleeding complications. Since antiplatelet agents are routinely used in all endovascular procedures, a platelet count is obligatory. Furthermore, global coagulation tests as prothrombin time and activated partial thromboplastin time should be done routinely. In patients with abnormal test results, consultation with a hematologist/hemostaseologist is recommended.

Since the common peri-interventional use of a combination of antiplatelet and anticoagulant (heparin) therapy significantly increases the bleeding risk, patients with potential bleeding

sources such as a gastric/duodenal ulcer should be identified at least by history.

Heparin-induced thrombocytopenia is a life-threatening disorder that rarely follows exposure to unfractionated or (less commonly) low-molecular-weight heparin. Patients classically present with a low platelet count or a relative decrease of 50% or more from baseline. Severe thrombotic complications may develop in the arterial and venous system. Patients with a history of heparin-induced thrombocytopenia should not be treated with low-molecular-weight heparins, since these have high cross-reactivity with circulating PF4–heparin antibodies. Three direct thrombin inhibitors are currently available for such patients: lepirudin, argatroban, and bivalirudin. Other therapies for heparin-induced thrombocytopenia are danaparoid and fondaparinux.

Patients with anemia

Anemia is a well-recognized factor that exacerbates myocardial ischemia in the presence of restricted coronary reserve. Data regarding the prognostic importance of anemia in patients who undergo peripheral interventions are lacking.[14] After percutaneous coronary interventions, patients with anemia had significantly higher mortality rates during hospitalization compared with those who did not.

Since anemia might be an indicator for a hitherto unrecognized bleeding source with the risk of aggravation by any antithrombotic treatment, this parameter is important for identification of high risk patients. The cause of anemia should be clarified and corrected before planned intervention.

Patients with allergy

History regarding a disposition to allergy, atopy, or drug hypersensitivity, and especially a known allergy to contrast agents, is very important. Iodinated contrast media can cause allergic reactions (itching, urticaria, angio-edema, and bronchospasm or arterial hypotension and shock) within minutes after administration. Life-threatening anaphylactic reactions due to iodinated contrast media are very rare. Despite the fact that the increased use of non-ionic iodinated contrast media has been associated with a decrease in the incidence of mild to moderate, and possibly severe, reactions, prophylactic drug regimens that aim to decrease the incidence of reactions (premedication) are still widely used in clinical practice despite a lack of data supporting the use of such premedication – steroids, antihistamines – in patients with a history of allergic reactions. Recently, Tramèr et al[15] published a systematic review of trials testing the efficacy of antihistamines and corticosteroids. The authors conclude that its usefulness is doubtful because of the large numbers of patients who would have to be treated to prevent one reaction.

IS RISK REDUCTION POSSIBLE BY DRUG APPLICATION?

The observation that manipulating and targeting certain parameters in selected patients can influence the general cardiovascular risk has been reported in numerous studies. Recently it was postulated that there is a need for a shift in emphasis from risk stratification by non-invasive testing to risk modification by the application of medical interventions which prevent perioperative ischemia.[16] Concerning the vascular patient, the use of *statins* and *β-blockers* in particular may reduce severe complications. β-Blockers can restore the supply/demand mismatch, by the reduction of myocardial oxygen use by decreasing sympathetic tone and myocardial contractility. There is some evidence suggesting that β-adrenergic receptor antagonists reduce cardiovascular morbidity and mortality in high-risk patients undergoing non-cardiac surgery.[17] The evidence to date is consistent and suggests that β-blockers reduce perioperative cardiac events in high-risk patients. There is no evidence that β-blockers are also helpful in low to moderate risk patients. As clinicians we need to be mindful of β-blocker withdrawal, and make every effort to prevent it.

The prehospital or preprocedural use of statins has been found to be associated with reductions in the incidence of in-hospital death in patients with acute coronary syndromes, of periprocedural myocardial infarction after percutaneous coronary intervention, and of perioperative mortality in patients undergoing major non-cardiac

vascular surgery.[18] However, there is a complete lack of studies and knowledge concerning peri-interventional application of such drugs in patients undergoing peripheral endovascular procedures. Statins may prevent plaque instability and thrombosis due to their pleiotropic effects, such as improvement of endothelial function, reduction of inflammation, and stabilization of atherosclerotic plaques. β-Blockers can restore the supply/demand mismatch by the reduction of myocardial oxygen use by decreasing sympathetic tone and myocardial contractility.

Peri-interventional *pain control* is helpful to avoid problems with restlessness of the patient. Furthermore, several studies suggest that effective pain management leads to a reduction in catecholamine increase and in hypercoagulability.

SUMMARY

Patients at increased risk for peri-interventional events mostly can be identified on the basis of simple clinical and laboratory markers. It has to be stressed that a good history and physical examination by an experienced physician are the basic measures to identify any risk patient. This enables effective risk evaluation despite keeping it simple and cheap.

Table 2.1 Minimal program for risk evaluation before any endovascular intervention

History and clinical examination:
- cardiac disorders: MI, angina, arrhythmia, heart failure
- cerebrovascular disorders: TIA, stroke
- pulmonary disorders: smoking, asthma, dyspnea, cough
- further history/(clinical examination) concerning
  - diabetes, hypertension, hemorrhagic and thrombotic complications, gastroduodenal ulcer, allergy
  - medication: antiplatelet, anticoagulant, antihypertensive, antidiabetic

Laboratory tests:
- blood glucose, hemoglobin, platelets, prothrombin time, creatinine, sodium, potassium, C-reactive protein, TSH (thyroide-stimulating hormone)

Electrocardiogram

Table 2.1 summarizes the recommended minimal program before any endovascular intervention. Further tests depend on the results of these examinations and on the risk of the intervention itself.

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3

Being prepared – standards for patient care and adequate bail-out equipment

Martin Schillinger

Introduction • Pre-, peri-, and postintervention care • Bail-out equipment

INTRODUCTION

The frequency and impact of complications depend on various factors including the patient's morbidity and risk profile, access site morphology, and characteristics of the access route and target vessel segment. These factors define low-risk, intermediate-risk, and high-risk patients/interventions, respectively, and define patients who are not suitable for an endovascular approach. The first step to safely perform an intervention therefore is to perform a thorough preintervention non-invasive work-up to classify the patient's risk and to develop an interventional strategy. Besides patient-associated factors, the performance of the interventionist is the second major determinant to influence the risk for complications. The third important factor is imaging during and after the intervention to recognize potential problems early. Finally, standardized postintervention care and surveillance help to improve patients' safety.

PRE-, PERI-, AND POSTINTERVENTION CARE

Before discussing bail-out material which should be available in the cath lab, some basic principles for planning of the intervention are listed; these are in accordance with recommendations international societies.[1–12]

Preprocedure

- A written *medical history* should be available including current symptoms, major comorbidities and risk factors, list of medication, history of allergic reactions, and details of previous vascular interventions and operations.
- Results of *physical examination* have to be available including heart and lung examinations and pulse status.
- *Laboratory results* including complete blood count, coagulation, serum creatinine, electrolytes, and thyroid hormone level have to be done before the intervention.
- Evaluation of the *access site* has to be done prior to bringing the patient to the cath lab. In patients with a regular pulse at the puncture site and without vascular bruits usually no further imaging is mandatory. Duplex sonography of the puncture site should be done in any patient with suspected pathology and is also helpful to precisely locate the artery in special indications (e.g. before puncturing the popliteal artery to avoid formation of an arterio-venous fistula (AV) fistula).
- *Complete imaging of the target vessel segment and the run-off* is required, although nowadays non-invasive methods like computed tomography (CT) angiography or magnetic resonance (MR) angiography seem adequate to

plan the procedure. Diagnostic conventional angiography can be omitted if these alternative imaging methods are available with excellent quality.
- Based on the findings of non-invasive imaging, the interventionist should define a *treatment strategy* before starting the intervention. This includes preparation of adequate material to access the target vessel segment and a selection of materials which likely will be necessary to treat the lesion. The preparation of these materials helps to keep the time of the intervention as short as possible.
- The interventionist has to *be aware of the potential complications* – knowing about what may happen helps to avoid it.

Periprocedure

- Interventions should be *completely documented*.
- All patients should have *continuous cardiac monitoring* and *intermittent blood pressure monitoring*; for some elective and all emergency interventions continuous invasive blood pressure measurements should be considered.
- All patients need an *intravenous access* for administration of fluids or medication. This access should be checked immediately before beginning the procedure.
- If the patient is *sedated, pulse oximetry* is required to monitor oxygen saturation.
- After completion of the intervention complete *final angiograms of the target vessel segment and run-off vessels* have to be done to identify potential complications early. Particularly in cases of new or increasing patients' complaints, interventionists have to search for problems.
- The interventionist has to know the *available bail-out equipment* and should be trained in using it.
- Finally, some complications cannot be resolved by endovascular solutions, therefore there is a definite need for cooperation with vascular surgery and availability for emergency operations.

Postprocedure

- All patients should be *observed at bed rest* in the initial postprocedure period. The time for bed rest depends on the size and location of the puncture hole. Before ambulation, the *puncture hole has to be checked* by a trained nurse or physician.
- The *first ambulation* should be done *under surveillance*.
- Surveillance at an *intensive or coronary care unit* is necessary only *after emergency interventions* in critical locations or in patients after *severe complications*.
- After the intervention trained professionals should regularly examine the patient for *signs of malperfusion of the treated organ system*. The intensity of this examination will depend on the treated vessel segment: e.g. pulse palpation should be done after intervention of arteries of the extremities, and neurologic evaluation has to be done after carotid stenting.
- *Renal function* should be checked at least once 24 hours after the procedure. In patients with risk factors for renal dysfunction, prolonged monitoring of serum creatinine is necessary to identify patients with late renal failure.
- Finally, the interventionist who has performed the procedure should be available in the early postintervention phase and should examine the patient before discharge.

BAIL-OUT EQUIPMENT

The following section gives an overview and comments on bail-out equipment used in the specific chapters of the book.

Emergency drugs

Interventionists and nurses have to be familiar with the following emergency medications. These drugs should be available in every cath lab, irrespective of which vascular interventions are performed at the facility.

Vasopressors like epinephrine, vasopressin, or dopamine are needed in hemodynamically unstable patients. This may be due to various causes like severe bleeding and hemorrhagic shock, allergic shock in response to contrast media, malign arrhythmias, or myocardial infarction, or in a worst case scenario during cardiopulmonary resuscitation. Epinephrine, of course, has to be available in the emergency crash cart.

The usual dosage of epinephrine is a bolus dosage of 1 mg during resuscitation or perfusion dosages of 0.1 to 1.0 μg/kg/min for treatment of hemodynamic shock. Vasopressin is given during cardiopulmonary resuscitation as a single dose by 40 IU in patients with asystole. Dopamine is usually administered in dosages of 3 to 12 μg/kg/min in patients with hemodyamic deterioration.

Anti-arrhythmic drugs which should be available mainly include atropine, particularly when carotid stenting is performed in the cath lab facility. Atropine increases heart rate, but per se does not increase blood pressure. The usual dosages of atropine are in steps of 0.5 mg; complete vagolysis is achieved by 3 mg, more than 3 mg atropine therefore should not be administered. Other anti-arrhythmic drugs such as amiodarone should be available in the emergency crash cart. Availability of *fluids* for intravenous volume expansion is mandatory. These include crystalloid fluids like physiologic sodium chloride, 5% glucose, and 20% or 33% glucose infusions, as well as colloid fluids for extra-volume expansion. Fluids are needed to handle most forms of hypotension and shock; glucose is needed to treat hypoglycemia. Specific *medications to treat allergic reactions* include cortisone and antihistaminic dugs, besides the above-mentioned epinephrine for treatment of allergic shock.

Anti-coagulant medication includes heparin, bivalirudin, glycoprotein (Gp) IIbIIIa antagonists, and lytics. Usual dosages of heparin are between 2000 and 10 000 IU; in complex interventions and high-risk patients heparin should be monitored by activated clotting time (ACT) measurements (keeping the ACT around 250 seconds). Bivalirudin is a relatively novel direct thrombin inhibitor which is administered in a fixed dose and infusion by kg body weight. Similarly, Gp IIbIIIa inhibitors are given adjusted to the patient's body weight. The dosage of lytics depends on the substance and indication. The usual dosage for acute lysis with recombined tissue plasminogen activator (rtPA) is a bolus of 6 mg and further steps of 2 mg until the clot has dissolved.

Procoagulant substances include protamine, which antagonizes heparin in a more or less 1:1 ratio, and prothrombin complex concentrate, which substitutes all factors of the prothombin complex in patients with acute bleeding complications and severe coagulation disorders (either due to medications like warfarin or due to bleeding diasthesis).

Vasodilators like nitroglycerin, papaverin, ilomedin, or calcium channel blockers are useful to handle or prevent vessel spasms. In particular, for radial or brachial access or during carotid stenting vasodilators can be essential. The usual dosage for nitroglycerin is in steps of 0.1 mg. *Anti-epileptic agents* should be available, particularly when cerebrovascular interventions are performed in the cath lab facility.

In summary, the list of medications includes:

- vasopressors: epinephrine, vasopressin, dopamine
- anti-arrhythmics: atropine
- fluids: crystalloid and colloid infusions, including glucose infusions
- anti-allergic drugs: cortisone and antihistaminic drugs
- anticoagulant medication: heparin, Gp IIbIIIa inhibitors (abciximab), lytics
- procoagulant substances: protamine, prothrombin complex concentrate
- vasodilators: nitroglycerin, calcium channel blockers, ilomedin
- anti-epileptic agents: lorazepam, phosphenytoin.

Various emergency tools

A *tracheostomy set* should be available for carotid stenting procedures. In rare cases with perforations of external carotid arteries, severe bleeding may cause compression of the larynx and can cause asphyxia.

A standard *emergency crash cart* including defibrillator, intubation set, and drugs for cardiopulmonary resuscitation has to be readily available.

Tourniquets are helpful to handle peripheral bleeding complications. Large blood pressure cuffs can be used for the extremities. These are particularly effective in combination with balloon blockage inside the vessel at the site of rupture. Many bleedings can be stopped by this combination of internal and external compression, particularly when the use of coils or (covered) stents needs to be avoided.

In summary, the list of various emergency tools includes:

- tracheostomy set
- emergency crash cart
- tourniquets, large blood pressure cuffs.

Wires and catheter material

The choice of *wires* will depend on operator preference. Wires in 0.014, 0.018, and 0.035 inch short (180 cm) and long length (260 to 300 cm) should be available. Extra stiff wires like Amplatz™ extra stiff, Lunderquist™ extra stiff, or Supra-core™ wires should be available for emergency purposes to guarantee sufficient back-up in critical situations. In particular, stent grafts are usually better deployed via an extra stiff wire.

Similarly, there is a wide variety of catheters and, for most situations, the skill of the interventionist will be more important than the curve of the catheter. Standard catheter forms include pigtail, multi-purpose, cobra, side-winder, straight, head-hunter, Sos-omni, IM, or Judkins right (JR) coronary. Some specific catheters suggested by the authors of this book are the Quick-Cross® Catheter (The Spectranetics Corp, Colorado Springs, CO), the Soft-Vu® Berenstein (AngioDynamics, Queensbury, NY), or the Impulse® IM Angiographic Catheter (Boston Scientific Corp, Natick, MA). Furthermore, for emergency intracranial interventions during carotid stenting 0.014- to 0.021-inch microcatheters and wires should be available when a skilled interventionist is adequately trained to perform intracranial bail-out interventions.

Summary of wires and catheters:

- 0.035-inch glide wire
- 0.035-inch extra back-up wire
- 0.018-inch wire (e.g. Boston Scientific V18 Control Wire)
- 0.014-inch wires including floppy intracranial wires
- standard diagnostic curves 4 to 6 French: pigtail, MP, side-winder, IM, JR, cobra, etc.
- 0.014- and 0.021-inch microcatheters.

Sheaths

The choice of *sheath* available will widely depend on the kind of procedures which are planned in the cath lab facility. As long as aortic interventions are not performed, sheath sizes of up to 12 French in short and long length will be sufficient. These include stable and long cross-over sheaths which are available from various distributors. Importantly, the size of the available sheaths has to be coordinated with the brand of covered stents which are on the shelf. Most of these stent grafts will need large sheath diameters. If aortic interventions are performed, even larger sheaths are needed to accommodate the devices. The authors of the book recommend 16–24 French Check-Flo introducers (Cook, Bloomington, IN).

Summary of sheaths:

- 4 to 12 French when aortic interventions are not performed; maximum size has to be coordinated with stent grafts for bail-out situations. Length of the sheath: 6, 7, and 8 French should be available in up to 90 cm for access to the supraaortic vessels or transbrachial access to the lower limbs; larger sheaths should be available in up to 45 cm to enable cross-over access.
- 16 to 24 French when aortic interventions are planned.

Thrombolysis catheters

A variety of *thrombolysis catheters* is available and none has been proved to be superior. In this book the Uni*fuse® Infusion Catheter (Angiodynamics), and EKOS LysUS® Infusion System (EKOS Corp, Bothell, WA) for *ultrasound-enhanced thrombolysis* are described. The authors also have good experience with Mewissen thrombolysis catheters and McNamara thrombolysis catheters. Importantly, the length of the thrombolysis catheter has to be sufficient to enable cross-over access. Various length in perfusion lumen can be helpful.

Summary of thrombolysis catheters:

- thrombolysis catheters in up to 8 French with a working length of 90 to 100 cm.

Rheolythic thrombectomy catheters

Rheolytic thrombectomy catheters are not a mandatory tool for the cath lab, but can be helpful in some situations. In this book the AngioJet® Thrombectomy System (Possis Medical, Inc, Minneapolis, MN) is described.

Summary of rheolythic thrombolysis catheters:

- none mandatory.

Aspiration thrombectomy catheters

In contrast to the above mentioned rheolythic thrombolysis catheters, *0.014 inch aspiration catheters* are mandatory. For small arteries the Diver CETM Clot Extraction Catheter (ev3, Inc, Plymouth, MN) or the Pronto aspiration catheter is useful. For peripheral applications, flexible guiding catheters with atraumatic tips like the Cordis bright-tip 6 to 9 French guide catheters with removable hemostatic valves are very effective.

Summary of aspiration catheters:

- 0.014 aspiration catheter for small vessel application
- 6 to 9 French guiding catheter with flexible tip and 90 to 100 cm working length with removable hemostatic valve for large vessel applications.

Embolization material

Embolization material can be crucial to handle perforations or pseudoaneurysms. There is a variety of *coils* available, either detachable coils or mechanistically more easily pushable coils. Besides coils, *liquid embolic agents* like NBCA or Onyx can be helpful in certain situations. In the author's opinion pushable coils will be sufficient for almost all peripheral applications, except for microcoil in supra-aortic indications.

Summary of embolization material:

- coils: detachable, pushable, microcoils
- liquid embolization material.

Retrieval devices

These devices are essential to retrieve particles, thrombi, or catheter material. Usually *snares* in different sizes should be on the shelf. Additionally, special *retrieval devices* like the Merci® retriever are described in this book.

Summary of retrieval devices:

- snares in different sizes like: EN Snare® Intravascular Retrieval Devices (InterV, Gainesville, FL), 15 mm and 25 mm Amplatz Goose Neck Snare® (ev3), 12–20 mm and 18–30 mm EN snare® (interv Medical Device Technologies, Inc)
- Expro® Elite (CoMed Medical Specialties, Littleton, CO)
- Merci® retriever.

Balloons

Besides the usual *angioplasty balloons*, which can also be used for vessel sealing, *large diameter angioplasty balloons* have to be available to block the aorta, such as the 12–26 mm Atlas™ PTA Dilation catheter (Bard Peripheral, Tempe, AZ). Furthermore, special *occlusion balloons* like the 20–40 mm Equalizer® (Boston Scientific) are available, which are less traumatic to the vascular wall and should not induce vessel injury and restenosis. Another useful tool is the *cutting balloon*. Although this device will hardly ever be used to resolve a complication, it can help to avoid complications by adequate plaque preparation and treatment of resistant lesions.

Summary of balloons:

- regular angioplasty balloons sized from 2 mm with low-profile OTW design to 10 mm
- large diameter balloon for blockage of the aorta: 10 to 26 mm
- optional cutting balloon and atraumatic occlusion balloons.

Stents

Stents became an important tool for the treatment of peripheral artery disease and the use of stents has resolved many frequent minor complications like vessel dissections or AV fistulas. Stents, however, also play an essential role in the handling of complications. *Covered stents* and *non-covered stents* can be used to seal rupture sites, pseudoaneurysms, and AV fistulas. *Balloon-expanding* and *self-expanding* formats in sizes of 2 to 12 mm are needed. Covered stents should be available from 6 to 14 mm. In the book the following covered stents are discussed: iCast™ Covered Stent (Atrium Medical Corp, Hudson, NH), VIABAHN® Endoprosthesis Stent-Graft (WL Gore & Associates, Inc, Flagstaff, AZ), Wallgraft® (Boston Scientific), and Fluency® (CR Bard, Inc, Murray Hill, NJ). *Stents* appropriately sized for the *intracranial circulation* like Neuroform or MiniVision should

be considered as bail-out material for supra-aortic interventions. Special stents exist for crossing the vertebral artery or left internal marmarian artery (LIMA) like the Bridge® Assurant Stent (Medtronic, Inc, Minneapolis, MN), a modular design less likely to jail these vessels. Finally, *aortic stent graft extension*s are needed when aortic disease is treated, like the 23, 26, 28.5 mm aortic extender (Excluder, WL Gore & Associates, Inc) or the 22–32 mm main body extension (Zenith, Cook, Bloomington, IN).

Summary of stents:

- self-expanding bare stents 4 to 12 mm
- balloon-expanding bare stents 2 to 12 mm
- self-expanding or balloon-expanding covered stents 6 to 14 mm
- intracranial stents, stents to cover the vertebral artery or LIMA
- aortic stent graft extensions.

Protection devices

Protection devices are most frequently used in carotid stenting, mainly to avoid complications rather than for actual treatment of complications. Besides a wide variety of *filter devices* and distal balloon occlusion systems, *proximal balloon occlusion* systems like the PAES® Parodi Anti-Embolic System (WL Gore & Associates, Inc) or the MoMa® anti-embolic device (Invatec, Italy) should be available in the cath lab to manage rare situations of thrombotic or embolic occlusion of the carotid arteries. Besides their role in carotid stenting, filter systems are also used during renal stenting or high-risk peripheral interventions. Current devices, however, are not ideally designed for these applications. Furthermore, retrievable *filters for protection during thrombolysis* in venous applications exist like the Recovery G2™ (Bard Peripheral, Tempe, AZ), the Gunther Tulip™ (Cook), or Optease® (Cordis, Miami Lakes, FL).

Summary of protection devices:

- filter systems
- proximal balloon occlusion systems
- venous filters.

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4a

Contrast media associated complications

Rainer Oberbauer

This chapter focuses on radiocontrast media induced acute renal failure (CM-ARF) and only briefly discusses other complications such as allergies and hyperthyroidism at the end.

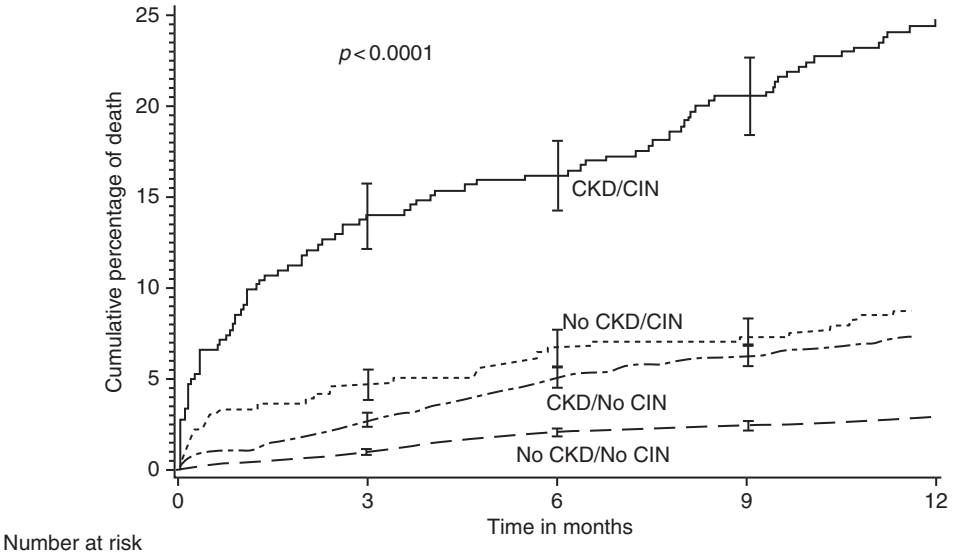
DEFINITION OF CONTRAST MEDIA INDUCED ARF

Comparability of epidemiologic data as well as preventive and therapeutic strategies among studies depends on the uniform definition of the outcome parameter. In the case of CM-ARF however, this basal requirement is not met. The definition of CM-ARF is not uniform and at least four different classifications exist that are commonly used. Some authors refer to ARF as doubling of baseline creatinine, others as increase of baseline value by more than 25% or 50%, or as absolute increase of creatinine by more than 0.5 mg/dl or more than 1 mg/dl (25%,[1] 50%,[2] >0.5[3]). Definition of ARF as the clinically important hard outcome of dialysis dependency is very rare.

CLINICAL IMPORTANCE OF CONTRAST MEDIA INDUCED ARF

The clinical impact of CM-ARF again depends on its definition and the indication for the contrast media application (comorbidities). It is intuitive that mild reversible elevations of an initial normal serum creatinine are of no major concern. However, more severe impairments of renal function are associated with profound changes in the risk of developing other complications and death.[3] Marenzi and colleagues found that an increase in serum creatinine within the first 3 days after percutaneous intervention by 0.5 mg/dl or more in patients with acute myocardial infarction was associated with prolonged hospitalization and a significantly higher mortality. Mortality is even exaggerated if patients with underlying chronic kidney disease develop CM-ARF after percutaneous coronary intervention.[4] Dangas and coworkers used a similar study setting and definition of CM-ARF as Marenzi and showed that the effect of CM-ARF on overall mortality in patients without chronic renal failure (CRF) is roughly the same as the mortality of patients with CRF who did not develop CM-ARF. In both groups, CRF without CM-ARF and CM-ARF without prior CRF, between 5 and 10% of patients died within one year. The development of CM-ARF in patients with CRF, however, was associated with a 1-year mortality of almost 25% (Figure 4a.1).

Now this high mortality is clearly explainable by the underlying comorbidity of CRF and tightly associated problems such as cardiovascular disease and frequent infection. To address the issues of the impact of comorbidities on the high mortality in patients with CM-ARF, Levy and coworkers performed a retrospective cohort study of 16 248 patients.[1] One hundred



Number at risk					
CKD/CIN	384	313	305	289	251
CKD/No CIN	1641	1599	1560	1539	1378
No CKD/CIN	637	608	595	591	542
No CKD/No CIN	4906	4858	4805	4788	4375

Figure 4a.1 One-year survival after percutaneous coronary intervention in patients with or without chronic kidney disease (CKD) and with or without contrast induced nephropathy (CIN). Reprinted with permission from Dangas et al 2005.[4]

and eighty-three subjects developed CM-ARF defined as an increase in baseline serum creatinine of at least 25% and above 2 mg/dl. Even after adjustment for the more comorbidities in the CM-ARF group, the OR of dying was 5 times higher in these subjects (Figure 4a.2). As in other similar studies investigating the association of postoperative ARF and mortality, death from renal causes was rare.[5] The conclusion of these studies is that renal failure appears to modify the propensity for other non-renal complications which cannot be treated by hemofilatration or dialysis. Examples of these conditions are systemic inflammation, catabolism, hemorrhagic diathesis, gastrointestinal ulcerations, hypercirculation, cardiomyopathy, and pulmonary edema.

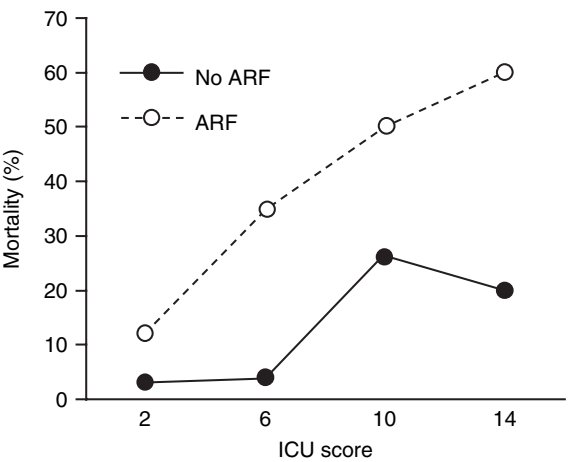


Figure 4a.2 Acute renal failure is an independent predictor of mortality. Figure modified with permission from Levy et al 1996.[1]

FREQUENCY OF CONTRAST MEDIA INDUCED ARF

The true rate of CM-ARF in clinical routine is probably underestimated given the fact that many contrast media utilizing procedures are performed on an outpatient basis without sequential creatinine measurement. Furthermore, elderly patients in particular may exhibit normal serum creatinine values despite having reduced glomerular filtration rates. On the other hand, misclassification of CM-ARF may occur in cases where other factors such as cholesterol emboli, infections,

altered hemodynamics, or nephrotoxic comedication are actually responsible for ARF.

In clinical studies the incidence rate varies considerably depending on patient selection, the contrast medium used, and the definition of CM-ARF. Patients without major comorbidities develop CM-ARF defined as a rise in baseline creatinine of more than 50% in the low single digit percentage range.[2] Even patients with pre-existing CRF and diabetes mellitus exhibit CM-ARF in only 9% of cases.

If less stringent criteria of CM-ARF are applied in high-risk patients, the incidence of CM-ARF ranges from less than 5% in iodixanol trials to 50% and above in trials of iopentol and ioxilan (Figure 4a.3).[6] Even trials where the same contrast medium was used show considerable heterogeneity of incidence. Five trials using iohexol, for example, reported CM-ARF rates between 10 and 40%. These wide ranges show impressively that, as mentioned above, the frequency of CM-ARF is highly dependent on the definition of variables.

RISK FACTORS OF CONTRAST MEDIA NEPHROPATHY – IDENTIFYING HIGH-RISK PATIENTS

Similiar to the ARF developing in ICU patients, CM-ARF is rarely caused by the single insult of contrast media use alone. In the majority of patients experiencing CM-ARF, chronic conditions of the cardiovascular system as well as other risk factors such as diabetes mellitus, multiple myeloma, CRF, infections, or nephrotoxic comedications are present.

The main single risk factor for CM-ARF is probably dehydration, although this statement is only indirectly supported by published data. Several studies have shown that intravenous volume expansion prior to the application of contrast medium reduces the rate of CM-ARF. This has

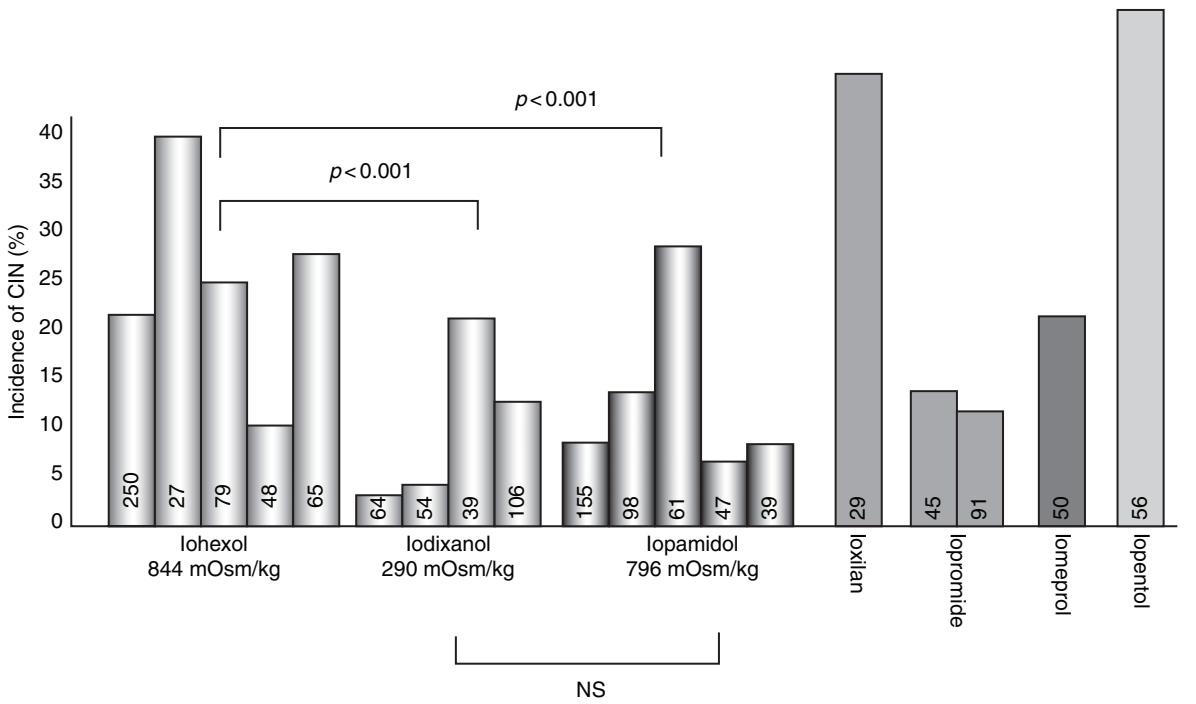


Figure 4a.3 Incidence of contrast media induced nephropathy (CIN) in patients with chronic renal insufficiency receiving non-ionic contrast agents in various prospective studies. Numbers in bars refer to the references in the paper by Solomon.[6] Reprinted with permission.

been shown for normal vs half normal saline, and sodium bicarbonate vs normal saline.[7–9] However, these studies are limited due to a huge type two error.

Besides dehydration the amount rather than the type of contrast medium is predictive for the development of CM-ARF, because nowadays only low- or iso-osmolar non-ionic contrast media are used. A recent systematic review by Solomon concluded that factors other than contrast medium osmolarity such as patient's age and the applied volume are more important risk factors for CM-ARF.[6] This study as well as others showed, however, that iopamidol and iodixanol are probably associated with less risk for CM-ARF than iohexol.[10] Alternatively, if patients exhibit a contraindication to iodinated contrast media, gadolinium chelates may be used instead to perform angiography.[11]

It is generally well accepted that patients with diabetes mellitus have a higher risk for the development of CM-ARF. However, as with many other risk factors, diabetes is not a dichotomous state but rather represents a continuum of a disease ranging from asymptomatic abnormal regulation of blood glucose to the most severe end organ damage including macro- and microangiopathy. This may explain why some authors identified diabetes mellitus as a major risk factor for the development of CM-ARF whereas others did not find a significant association with CM-ARF in multivariate analyses.[6,12] In the multivariate logistic regression model designed by Mehran et al to predict the development of CM-ARF after percutaneous coronary intervention, congestive heart failure, arterial hypotension, CRF, diabetes, and anemia were significantly associated with CM-ARF (Table 4a.1). The same group of authors showed more recently that there is no linear relationship between hematocrit and CM-ARF. The odds of developing CM-ARF were only increased if the hematocrit dropped below 36%, which was the lowest quintile in their analysis.[13] This cohort study, however, does not address whether correction of anemia before intervention will result in decreased rates of CM-ARF.

Further potential risk factors for CM-ARF are nephrotoxic comedications such as the frequently used NSAIDs, but also aminoglycosides, amphotericin B, cisplatin, or calcineurin inhibitors. Although there is no hard evidence that these drugs may further increase the rate or duration of CM-ARF, it can be assumed based on their pharmacodynamics.

PREVENTION OF CONTRAST MEDIA INDUCED ARF

The best preventive measure for CM-ARF is to think about it in advance. As is true for so many other situations in life, prevention is much more efficient than dealing with the adverse consequences of a situation. This consideration should include an estimation of the risk to benefit ratio of the planned diagnostic or therapeutic intervention and potential alternative strategies without contrast medium in patients at high risk for CM-ARF.

The single best preventive measure of CM-ARF is intravenous hydration, if possible up to

Table 4a.1 Multivariate predictors of CM-ARF after percutaneous coronary intervention. Modified and reprinted with permission from Mehran et al 2004[12]

Variable	*OR*	*95% CI*	*p value*
Hypotension	2.537	1.973–3.262	<0.0001
Intra-aortic balloon pump use	2.438	1.677–3.544	<0.0001
Congestive heart failure	2.250	1.682–3.011	<0.0001
Serum creatinine >1.5 mg/dl	2.053	1.586–2.658	<0.0001
Age >75 years	1.847	1.509–2.260	<0.0001
Anemia	1.601	1.328–1.930	<0.0001
Diabetes mellitus	1.508	1.260–1.806	<0.0001
Contrast volume (per 100 ml)	1.290	1.210–1.375	<0.0001

8 hours prior to CM application. The type and volume of choice is not entirely clear but 20 ml/kg of a full electrolyte solution or 154 mEq/l at a rate of 3 ml/kg bolus followed by a continuous infusion of 1 ml/kg of a sodium bicarbonate solution has been shown to be efficient.[8,9] Addition of mannitol and furosemide to half normal saline in patients with underlying CRF or to normal saline in patients without CRF does not seem to be additionally effective.[14,15]

In addition to volume expansion, several drugs have been investigated for the prevention of CM-ARF. Among the most recently and widely studied medications is acetylcysteine (ACC). Among the first randomized controlled trials in patients with CRF and thus at higher risk, Tepel and coworkers showed that two doses of 600 mg ACC given on the day before and after the application of a non-ionic low-osmolar contrast agent for a CT scan could reduce the incidence of CM-ARF.[16] All patients were also hydrated with saline in this trial. In this paper 10 subjects experienced a rise in serum creatinine by more than 0.5 mg/dl at 2 days after radiocontrast application, one in the ACC and nine in the control group. Furthermore, mean serum creatinine even decreased in the ACC group after CM application but rose in the control group. To account for potential interference of ACC with creatinine measurement, the authors spiked the control group samples with ACC at 2.5 mM but did not derive different values for serum creatinine with and without the ACC supplementation.

In a more recent study, however, Hoffmann and coworkers showed that ACC reduced serum creatinine in 50 healthy volunteers in the absence of contrast media but did not affect cystatine c serum concentrations, which is another indicator of the glomerular filtration rate.[17] Based on these data it may be speculated that tubular secretion but not glomerular filtration of creatinine is enhanced by ACC. It is well appreciated that tubular secretion of serum creatinine increases with decreasing GFR. Patients in the Tepel study exhibited a mean serum creatinine of about 2.5 mg/dl. An alternative explanation may be the fact that ACC alters creatinine metabolism in vivo by activation (suppression of inhibitors) of the creatinine kinase as described by Genet et al.[18]

From the many studies published after the Tepel paper in 2000, no clear conclusion can be drawn in terms of ACC efficiency to prevent CM-ARF. Some of the earlier and small studies showed benefits, others did not find any advantage over placebo control[19–23] (Figure 4a.4). This is also reflected by the inhomogeneous findings of the 10 meta-analyses covering ACC and CM-ARF to date.[24–33] This heterogeneity is even more astonishing since there are only a few randomized controlled trials of ACC on CM-ARF of better quality and these systematic reviews included the same original studies.

In conclusion, since ACC may be beneficial and is rather cheap and well tolerated it may be used for prophylaxis of CM-ARF, at least in patients who cannot tolerate vigorous hydration. However, adequately hydrated patients with a low risk of CM-ARF will probably derive no measurable benefit from an ACC pretreatment.

Adenosine antagonists have long been evaluated for their diuretic and natriuretic properties in several circumstances of renal impairment.[34] Among the most widely studied adenosine antagonists is theophylline, which has been shown in clinical trials of low statistical power to maintain GFR after contrast medium application.[35–38] Few published studies, however, do not support these findings, which may also be seen as publication bias towards positive outcomes.[39] The situation is rather similar to the ACC trials, where, depending on the covariables, different results were found.

Other medical interventions that have been evaluated for their protective efficacy against contrast induced ARF are ascorbic acid, prostaglandin E1, dopamine, fenoldopam (a selective dopamine receptor agonist), and statins.[40–45] Most of these published studies showed a beneficial effect of the respective intervention with the exception of fenoldopam, which has been proven ineffective in the largest randomized trial in patients undergoing percutaneous coronary interventions.[46,47] However, the relative paucity of reproduced data and the likely publication bias of these small trials preclude a firm conclusion.

In the clinical routine a frequently asked question of the thoughtful interventionist is whether CM-ARF can be prevented by a postinterventional hemodialysis or hemofiltration. Since contrast medium is eliminated mainly by glomerular

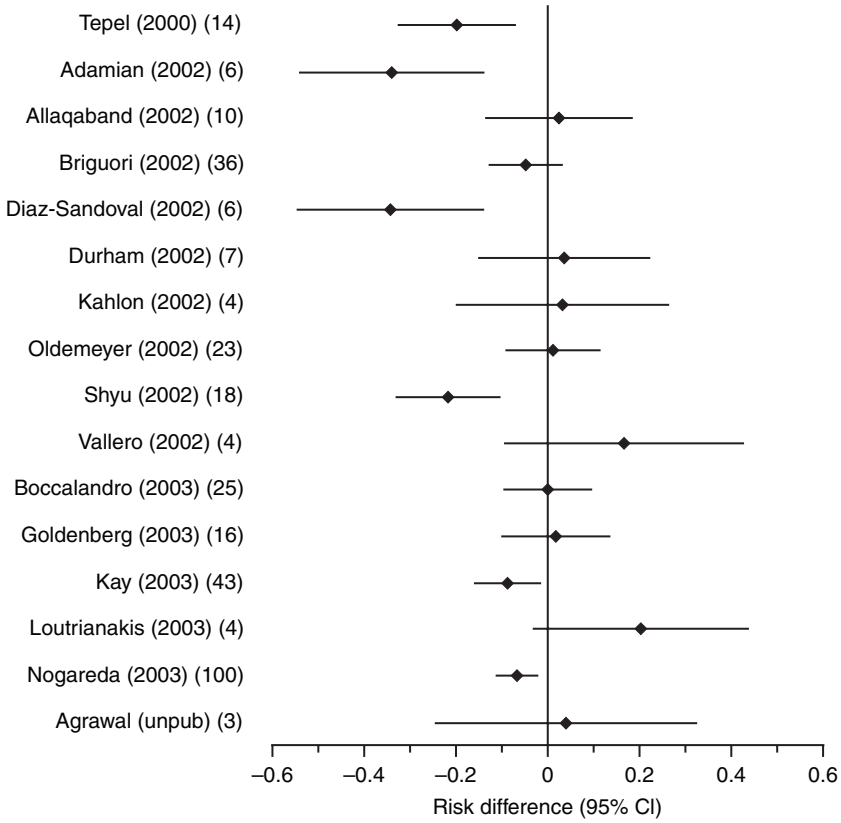


Figure 4a.4 Forest plot of weighted risk difference of all 16 controlled clinical trials. Relative weight is reported in parentheses after year of publication. Reprinted with permission from Kshirsagar et al 2004.[30]

filtration, 70% of the injected dose is cleared within a few minutes from the circulation. Thus in patients without major renal impairment the renal plasma flow of more than 1000 ml/min guarantees rapid contrast elimination. Now should prophylactic hemodialysis or hemofiltration be performed in patients with severely impaired renal function? Sterner and colleagues showed that immediate hemodialysis after contrast exposition could lower the contrast plasma levels by 80%, but the authors did not observe a difference in the postinterventional GFR between the control and the dialysis group.[48] It is of note that both groups received adequate preinterventional hydration. Berger and colleagues came to a similar conclusion although their sample size was small.[49] These authors noticed, however, that in some patients hemodialysis even seemed to have a negative effect on CM-ARF. This was also concluded by a much larger study published in the same year by Vogt and colleagues from Bern.[50] The authors randomized 113 patients with mild to moderate renal impairment to postinterventional hemodialysis or no extracorporeal therapy. Patients with hemodialysis showed a significantly higher rise in serum creatinine after intervention compared to the non-dialyzed subjects (Figure 4a.5). Unexpectedly, in a more recent study, Marenzi and colleagues used a similar study setting although with larger contrast volumes and identical sample size but derived the opposite results using hemofiltration rather than hemodialysis to remove the contrast dye from the patients' circulation.[51] The hemofiltration sessions were started before the intervention and continued in an ICU setting for 18 to 24 hours. The reported effect of this intervention was a reduction in the risk for CM-ARF by 90% which is larger than that observed for all

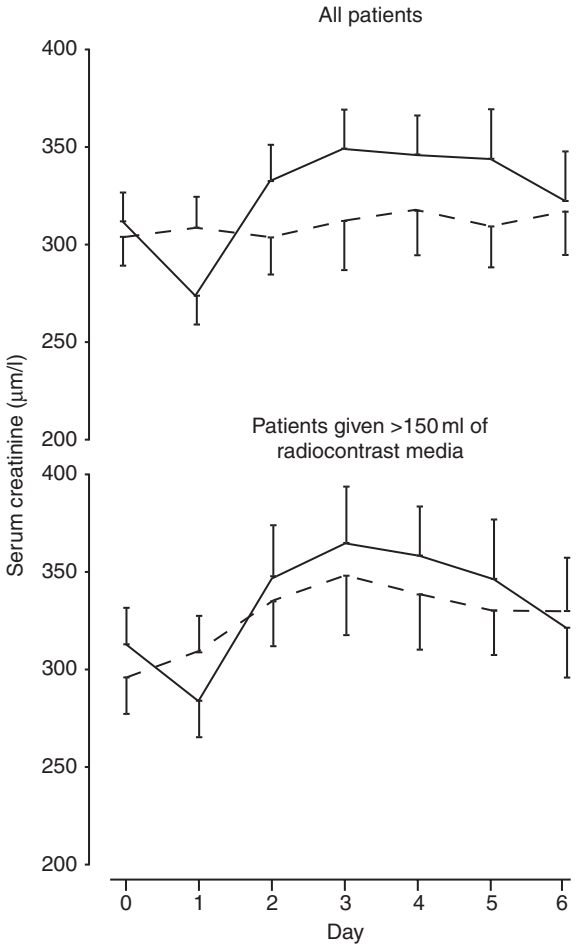


Figure 4a.5 Mean (± SE) serum creatinine concentrations before and after the administration of radiocontrast media in patients with chronic renal insufficiency. Only data from patients who did not require subsequent hemodialysis are included. Reprinted with permission from Vogt et al 2001.[50]

other therapeutic interventions so far. It is of note that 25% of all control subjects in this trial required at least one hemodialysis treatment for clinical indications.

Based on the findings from these different trials it is generally accepted nowadays that postinterventional hemodialysis is not to be performed even in patients with moderately impaired baseline renal function. Whether longer term prophylactic hemofiltration should be considered in patients with moderately impaired baseline renal function who are expected to receive a large amount (>250 ml) of contrast agent remains to be determined. In the study by Marenzi and colleagues, the benefits of randomization could have been attenuated by confounding by indication.[51] Patients in the hemofiltration group also received anticoagulant therapy and intensive care observation/treatment. Therefore the effectiveness of pre- and postinterventional hemofiltration after percutaneous coronary intervention needs to be validated by other investigators and a modified study design before prophylactic hemofiltration can be unequivocally recommended. Until then the attending physician may decide on the basis of the patient's background characteristics and availability of resources.

OTHER CAUSES OF ARF AFTER CONTRAST APPLICATION

Not every ARF occurring after percutaneous interventions is causally related to the contrast media application. As mentioned above, CM-ARF occurs predominately in patients with many other risk factors for ARF such as cardiovascular disease, infections, diabetes, pre-existing CRF, etc. In clinical praxis an increase in serum creatinine is almost always classified as contrast nephropathy, whereas other factors such as cholesterol crystal embolism after percutaneous interventions may occur. A popular rule of thumb is that a rising serum creatinine in the first day(s) after intervention occurs predominately as a consequence of contrast application, whereas a later rise of creatinine and LDH is more predictive of cholesterol emboli. The validity of this rule however remains to be investigated.

The reported incidence of cholesterol emboli in the kidneys is below 1%.[52] This low number reported in clinical studies is derived by using the incidence of peripheral signs of cholesterol emboli such as black toes as proxy for the incidence of cholesterol emboli in the kidneys. However, the renal plasma flow is usually considerably higher than the perfusion of the atherosclerotic legs of resting patients. Since renal biopsies and serial sectioning of the biopsy core are virtually never performed in patients experiencing ARF after intervention the true incidence will remain unknown. Nevertheless, autopsy studies reported an incidence of cholesterol microembolization of between 0.8 and 12%.[53]

TREATMENT OF CONTRAST MEDIA INDUCED ARF

As in most cases of multifactorial ARF developing in the ICU, no established causal therapy of CM-ARF exists. Among the key issues in the treatment of CM-ARF is the avoidance of additional renal insults after CM-ARF has occurred. This includes averting or discontinuation of medications that alter renal hemodynamics such as NSAIDs, calcineurin inhibitors, maybe angiotensin converting enzyme inhibitors, or angiotensin II receptor blockers. Furthermore, tubulotoxic medication such as amphotericin B or aminoglycoside antibiotics should not be used, nor re-exposure to radiocontrast medium if not vitally necessary.

In general, we are aiming for improvement in the systemic hemodynamic situation by providing sufficient hydration and by fighting systemic inflammation if possible. If all efforts are ineffective and the patient needs renal replacement therapy, hemodialysis or hemofiltration is started. Which of the two extracorporeal therapies is better suited depends on the clinical situation; however, in hemodynamically instable patients continuous hemofiltration will be the clear treatment of choice. The recovery of native renal function is generally good unless other severe risk factors for ARF such as congestive heart failure or pre-existing chronic renal failure exist.

COMPLICATIONS OF CONTRAST MEDIA OTHER THAN ARF

Hypersensitivity/anaphylaxis

Hypersensitivity reactions have been reported for all groups of contrast media including high-osmolar and low-osmolar ionic dimmers, as well as non-ionic monomers and iso-osmolar contrast media. However, the non-ionic media such as iohexol, iopamidol or iopromide (low-osmolar monomers) and iodixanol or iotrolan (iso-osmolar dimers) tend to induce less allergic reaction compared to high-osmolar ionic contrast media. The incidence of delayed type reactions (>1 hour after contrast application) was reported to be in the low single digit percent range.[54] The clinical presentation of the hypersensitivity ranges from urticaria and skin rash to more severe phenotypes such as laryngeal edema, bronchospasm, true anaphylactic shock, and, exceptionally rarely, sudden death. Since the exact pathophysiology behind these events remains unclear, many different terminologies such as anaphylaxis, anaphylactoid, allergic, pseudo-allergic, or idiosyncratic are in use to describe the reactions following contrast media applications.

Unfortunately there is no pre-exposure test that may be used to predict the individual's risk for such adverse effects. The cutaneous iodine path test is not predictive at all and the intra/subcutaneous iodine injection carries the same risk of true hypersensitivity as the intravenous contrast media investigation itself. Interestingly, the intra-arterial administration of contrast media is associated with less hypersensitivity. About every other subject known to be allergic against contrast media exhibits a hypersensitivity reaction again after rechallenge. The non-ionic media have a much lower rate of complications, and for all groups, intravenous injection carries a much higher risk than intra-arterial injection. The only disadvantage of non-ionic media is their cost.

Thyrotoxicosis

All contrast media contain about 30% iodine. Assuming an average volume of 100 ml per angiography, roughly 30 g of iodine are applied. This is about 200 000 times more than the 150 μg daily amount required for thyroid hormone synthesis. Although the thyroid maintains normal function in the vast majority of subjects investigated with contrast media, a few people (especially those with euthyroid goiter) may develop hyperthyroidism. There is, however, no valid prediction rule for the individual patient at risk. Furthermore, there seems to be no cross-reactivity between contrast hypersensitivity, development of hyperthyroidism, and other types of true IgE mediated allergy (Gell and Coombs's type I reaction) such as asthma (for review see reference 55). Thus an effective preventive measure for this scenario is not known.

SUMMARY

It is critical to consider potential adverse effects of contrast media before application. Patients with

Table 4a.2 Prophylactic strategy for the prevention of contrast media induced acute renal failure

1	Evaluate hydration status and cardiac function of the patient; avoid concomitant nephrotoxic substances such as NSAIR, aminoglycosides, or vasopressors
2	Intravenous hydration of the patient with full electrolyte solutions (isotonic saline) at roughly 100 ml/h for 6 to 12 h. Alternatively isotonic sodium bicarbonate solution may be used at the same rates
3	Acetylcysteine at 600 mg bid before and on the day of the intervention
4	Use low volume of low- or iso-osmolal contrast medium in patients at higher risk for CM-ARF
5	No prophylactic use of hemodialysis or hemofiltration

documented allergies against contrast media who need to have re-exposure may benefit from pre-treatment with corticosteroids and antihistamines.

The most effective preventive measure for ARF is adequate hydration; full electrolyte solutions are probably ideal for that purpose. Acetylcysteine may be used since it is really cheap and has almost no side-effects; its efficacy, however, is unclear to date and there is good evidence that only tubular handling of creatinine is altered by acetylcysteine (Table 4a.2).

ACKNOWLEDGMENTS

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4b

General complications of angiography and peripheral interventions – radiotoxicity

Eberhard Kuon and Michael Wucherer

Frequency and identification of radiotoxicity due to interventional angiography • Risk factors for radiotoxicity • Prevention of radiotoxic effects • Diagnosis and therapy of radiotoxic effects • Conclusion

The one waits for times to change, another tackles challenging times
Dante Alighieri

The first angiography was performed in 1896 (Figure 4b.1). In the course of time, however, it became evident that even low doses cannot be considered safe or harmless with respect to carcinogenesis.[1] Currently mean patient radiation exposure due to percutaneous interventions is relatively high and varies greatly between different centers and interventionists[2] (Figure 4b.2): for percutaneous cardiac interventions (PCIs), typical mean published dose area product values (DAPs), range from 7[3] up to 190 Gy × cm^2.[4] For special interventional procedures deterministic radiation effects like chronic radiodermatitis or even deep musculocutaneous injury may result,[1,5] and represent a matter of serious concern (Figure 4b.3). For this reason, directives of the International Commission on Radiologic Protection (ICRP) and the EURATOM Council [6,7] stipulate that 'All medical exposure for radiodiagnostic purposes . . . shall be kept as low as reasonably achievable' (ALARA), even below accepted reference values recently proposed[8] in consideration of both state of the art and individual circumstances. The ICRP indeed points out that, unfortunately, 'many interventionists are not aware of the potential for injury from procedures, their occurrence, or simple methods for decreasing their incidence utilising dose control strategies'[1] and recommends credentialing radiation protection training programs for interventionists over and above that required by general radiologists.[9,10] Up to today, however, there exists worldwide no validated educational course in radiation reducing techniques which has proven of significant benefit in reducing patient radiation exposure in daily routine.

FREQUENCY AND IDENTIFICATION OF RADIOTOXICITY DUE TO INTERVENTIONAL ANGIOGRAPHY

Definitions

The former radiation units Roentgen (R), rad, and rem have been replaced by the SI units Gray (Gy; 1 Gy = 100 rad) for air kerma (kinetic energy released in matter) and absorbed dose, as well as by the Sievert (Sv; 1 Sv = 100 rem), now applied for dose equivalent. For X-rays the radiation weighting factor is 1 for conversion from absorbed dose to dose equivalent (1 Sv = 1 Gy). Entrance skin air kerma (ESAK) prescribes the dose in the

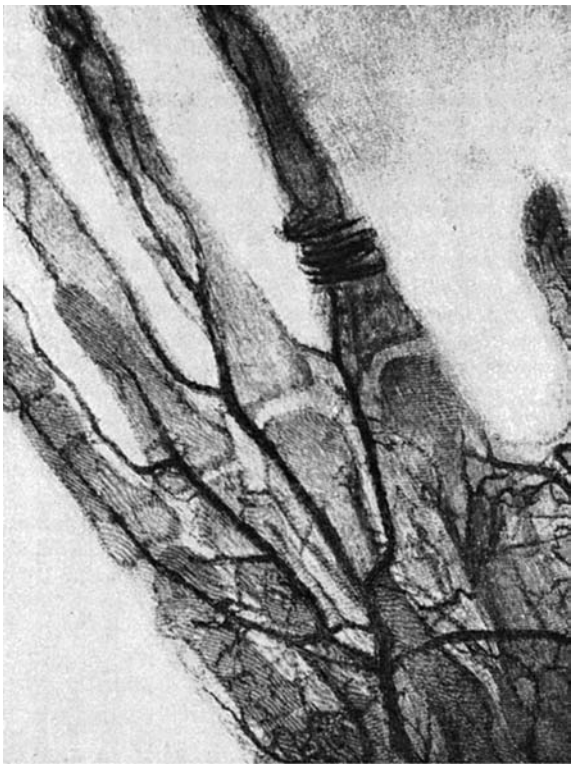

Figure 4b.1 The first angiography: postmortem depiction of a hand (von Haschek and Lindenthal, Vienna, January 1896; German museum of X-ray technology); contrast medium was a mixture of lime, mercury, and paraffin oil.

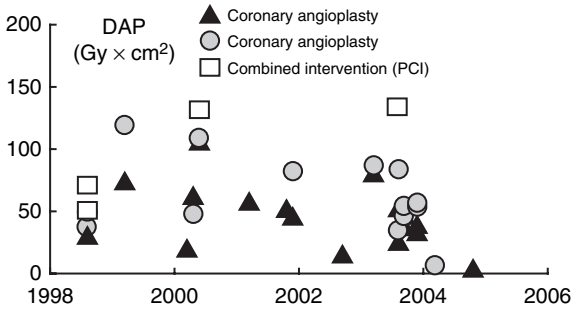

Figure 4b.2 Patient dose area products (DAPs) from coronary angiography (filled triangles), percutaneous transluminal coronary angioplasty (gray circles), and combined coronary interventions (open squares), published from 1998 to 2004, vary greatly in extent.

entrance plane of the patient without backscatter radiation. Entrance skin dose includes backscatter and represents the most appropriate quantity for characterization of *deterministic risks*, especially radiation induced skin lesions.

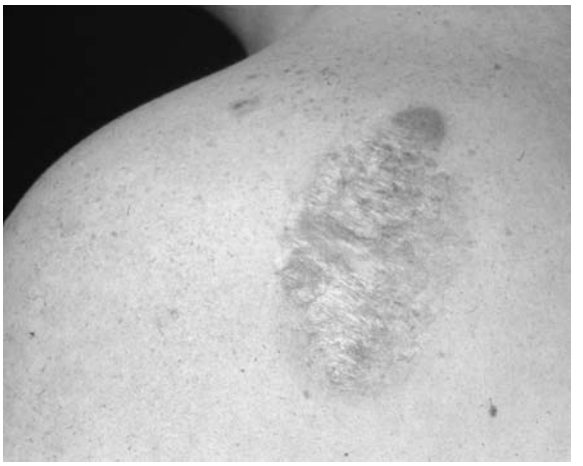

Figure 4b.3 Chronic radiodermatitis of the left shoulder.

DAP is the product of the air kerma in the entrance plane of the patient and the area of the irradiating beam, and can be easily measured near the X-ray tube. It is independent of the distance from the X-ray source; it is best suited to estimate radiation exposures of fluoroscopy guided interventions with varying angulations.

The effective dose (ED) is the sum of all risk weighted organ dose equivalents and was primarily defined by the ICRP to stipulate limits for occupational radiation exposures. The *stochastic risk* is proportional to the effective dose. DAP to ED conversion factors for special conditions (undercouch tube position, 80 to 110 kV and 2 to 5 mm aluminium filtration, adult standard patient) have been calculated to range between 0.13 and 0.26 mSv/Gy × cm^2 for thoracic, 0.18 and 0.33 mSv/Gy × cm^2 for abdominal, and 0.15 and 0.33 mSv/Gy × cm^2 for hip examinations.[11]

Therefore two types of radiotoxic effects – deterministic as well as stochastic – are of major relevance and both should be taken into account in clinical routine.

Deterministic effects

Table 4b.1 summarizes skin reactions and their threshold doses. There exist no reliable data about the incidence of various types of deterministic skin lesions. These effects are likely to occur after prolonged exposure to the same skin area. In clinical routine faint erythema due to local exposure

Table 4b.1 Threshold doses, calculated fluoroscopy time and DAPs, respectively, for various skin effects as well as onset time toward skin reaction (chest region)

Threshold values for	*Single dose (Gy)*	*Fluoroscopy time*[1] *(min)*	*DAP*[2] *(Gy × cm²)*	*DAP*[3] *(Gy × cm²)*	*Onset (weeks)*
Early transient erythema	2	50	120	80	hours
Temporary epilation	3	75	180	120	3
Main erythema	6	150	360	240	1.5
Permanent epilation	7	175	420	280	3
Dry desquamation	10	250	600	400	4
Invasive fibrosis	10	250	600	400	
Dermal atrophy	11	275	660	440	14
Teleangiectasis	12	300	720	480	52
Moist desquamation	15	375	900	600	4
Late erythema	15	375	900	600	6–10
Dermal necrosis	18	450	1080	720	10
Secondary ulceration	20	500	1200	800	6

[1]Mean fluoroscopic DAP rate 40 ± 16 mGy × cm²/s for the 17 cm image intensifier field (110 interventionists – performing 10 coronary angiographies each – at 20 cardiac centers): equivalent to a skin dose (irradiated skin area approx 60 cm²) of 0.04 Gy/min.
[2]For one angulation and an irradiated skin area of 60 cm².
[3]For one angulation and an irradiated skin area of 40 cm².

of 2 to 3 Gy, eliciting an activation of histamine like substances, typically goes unnoticed because of its brief presence. Main erythema following threshold values of 2 to 8 Gy is caused by an inflammation subsequent to the destruction of basal cells in the epidermis. With a prevalence of 50% at about 21 Gy necrosis as a result of vascular damage in the dermis will develop 10–16 weeks after exposure.[12,13]

For the 17 cm and the 13 cm image intensifier field (and a focus image intensifier/focus skin magnification ratio of approximately 2) patient entrance skin areas of approximately 60 cm² and 40 cm² will result.[14] According mean fluoroscopic DAP rates at levels of approximately 40 ± 12 mGy × cm²/s generated in clinical routine (Table 4b.1)[12,15] reported threshold doses for the chest region will be achieved by the fluoroscopy times and DAP values under conditions of different image intensifier sizes respective entrance skin areas.

Stochastic effects

Although there are clear benefits from the use of diagnostic X-rays and in especially for interventional procedures, it is generally acknowledged that their use involves some risk of cancer. In 14 developed countries, estimates of the risk attributable to diagnostic X-rays ranged from 0.6 in the United Kingdom up to 4.4% in Japan, corresponding to an estimated annual X-ray exposure frequency of 0.49 up to 1.57 per individual, respectively.[16] Indeed a survey of UK practice[17] has suggested that the comparatively low frequency of diagnostic X-ray use is due in part to the detailed guidance for doctors on the indicators for X-ray examinations issued by the Royal College of Radiologists.[18] The additional individual stochastic lifetime cancer mortality risk of an effective dose of 1 Sv over the course of 40 years has been calculated as 7–11% for high-level and 5–10% for low-level (<0.1 Sv/h) radiation intensity,[19,20] and the stochastic lifetime cancer mortality risk of a cardiac intervention generating an effective dose of 10 mSv is calculated to amount to approximately 0.4‰.[14,21–23] For patients with a mean age of around 60 years undergoing cardiac interventions, approximately 0.2‰ of them will die from stochastic hazards of the related radiation exposure. In the UK the prospective incidence of cancer due to cerebral and coronary angiography has been calculated to amount to 0.18‰ and 0.28‰, respectively, and therefore again to be

lower than in other developed countries.[16] Indeed, a recently performed European benchmarking project revealed slightly lower DAPs for coronary interventions in Ireland and the UK.[8]

Statistical models indicate a fatal cancer risk increment range of 0.4 to 1.2‰, the latter figure characterizing the upper 90% confidence limit. Conclusively the risk of mortality from a malignancy induced during a typical cardiologic intervention with a DAP of 200 Gy × cm^2 was considered in the actual ACC/AHA Clinical Competence Statement to be less than 1%.[10] Optimized interventional techniques in clinical routine, however, have facilitated mean DAPs of 4.2 ± 1.6 Gy × cm^2 for elective coronary angiography and 7.8 ± 6.1 Gy × cm^2 for coronary angioplasty.[3,24]

RISK FACTORS FOR RADIOTOXICITY

The deterministic as well as stochastic risk of patients undergoing interventional procedures increases with obesity, procedure complexity, high-resolution magnification or image intensifier entrance dose level, and operator fatigue. Furthermore, that risk will depend on equipment performance and the interventionist's experience in radiation reducing techniques – as reported below – for example, correct beam collimation. Keeping the image intensifier as close to the patient as possible minimizes the source to image distance (SID), which results in less blurring of the image, and also allows the image intensifier to serve as a barrier between the patient and the operator.[24]

PREVENTION OF RADIOTOXIC EFFECTS

Efficient interventional techniques towards reduction of patient exposure include measures as follows:

- *Restriction to essential radiographic frames and runs* essential for diagnostic purposes. Interventionists should be aware of (compared with fluoroscopy) the typically 12- to 25-fold higher intensity of radiography, which creates 60–70% of total DAP. A new rotary switch, triggering each coronary run towards one to two heart cycle lengths, has enabled a reduction of patients' effective dose from coronary angiography to 0.8 mSv.[25]
- *Collimation to the region of interest ('buttonhole' technique)* The senior cardiologist should show the interventional cardiologic beginners how to collimate during fluoroscopy by short taps on the foot switch, with advantage taken of the 'last image hold' function. Beginning from partly closed lateral tube attached lead blinds, fluoroscopy guided collimation to the region of interest will occasion far less DAP than collimation from a wide open image intensifer entrance field.[14,26] Collimation to the region of interest moreover improves image quality and will efficiently reduce backscatter and in consequence the operator dose while, for example, aspirating an occluding thrombus (Figure 4b.4).
- *Adequate instead of best possible image quality.* The widely accepted ALARA principle obliges interventionists to achieve adequate instead of best possible image quality for both radiography and fluoroscopy, which occasions slightly higher contrast and produces

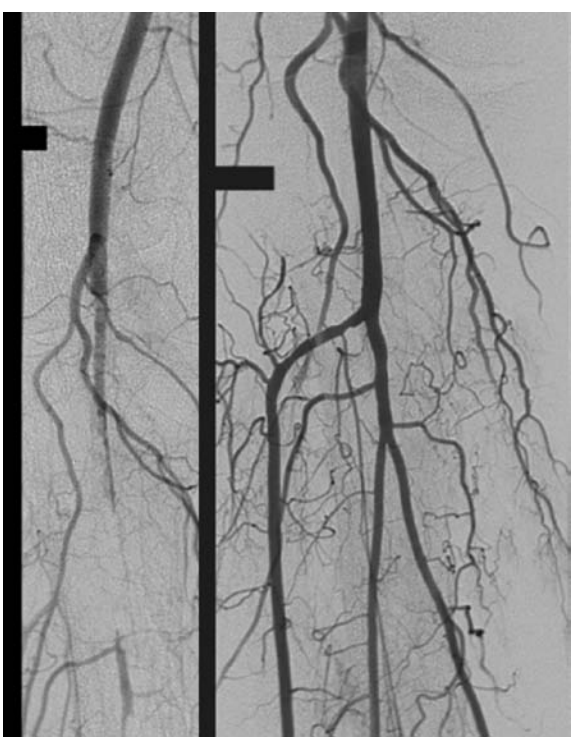

Figure 4b.4 Collimate even during emergency interventions such as absorption of occluding thombus (left panel) and for documentation of the final result.

insignificantly more background mottling.[27] In addition, a low-level fluoroscopy mode should be used as often as possible. If the interventional communities accept a radiographic frame rate of 12.5/s for an adequate documentation of the coronary arteries in motion, an identical fluoroscopic pulse rate of 12.5/s, supported by the commonly available technical advancement of 'gap filling', should consequently be judged sufficient to guarantee diagnostic and interventional safety and accuracy.[14,15] The coronary mode instead of the digital subtraction technique facilitates DAPs below 15 Gy × cm^2, even for complex interventions such as excimer laser angioplasty (ELCA) of renal in-stent restenoses (Figure 4b.5).

- *Lowest justifiable magnification.* Use of the lowest degree of image magnification required for accurate interpretation substantially reduces skin dose. Dose increments due to magnification are generally higher for conventional image intensifier systems than for flat panel detector systems.[10,27]
- *Full inspiration during radiography* for chest regions of interest reduces superimposition of the diaphragm and in consequence radiation intensity.
- *Preference for tube angulations that rotate out skeletal structures out of the radiation beam.*
- *Geometric considerations – heed the inverse-square law.* The distance between the X-ray tube and the patient should be practicably maximized. Keeping the image intensifier as close to the patient as possible minimizes the source to image distance, which decreases blurring of the image and allows the image intensifier to serve as a barrier between the patient and operator.[10] The operator's occupational dose, moreover, depends on his or her case load, adequate use and acceptance of lead protection devices, and distance from the isocenter.[28–30] Interventionists, however, should remember to step back from the patient's isocenter diagonal to the couch, and not simply backwards, in order not to leave the ceiling-attached lead glass protection.[29]
- *Well-experienced and well-rested operators.* Radiation exposure to patients resulting from PCIs is influenced by fatigue and significantly rose by 28%, due to more and longer radiographic runs, after the cardiologists' workload amounted to more than 6 h.[31]
- *Keep DAP in sight and mind* in order to promote self-surveillance of the personnel.[32]
- *Radiation-reducing planning of diagnostic catheterization* requires profound knowledge about less irradiating angulations.[24] In invasive cardiology six standard runs are used – one for the left ventricle, three for the left coronary artery (LCA), and two for the right coronary artery (RCA) – depending on anatomy and diagnostic details supplemented by 1 to 4 well-collimated variable projections.[2] At an anthropomorphic Rando–Alderson phantom, for the chest region and during fluoroscopy, the mean patient DAP rate and the respective operator dose were lowest in the postero-anterior (PA) angulation and rose significantly by 3.7 and 10.6 times the PA 0°

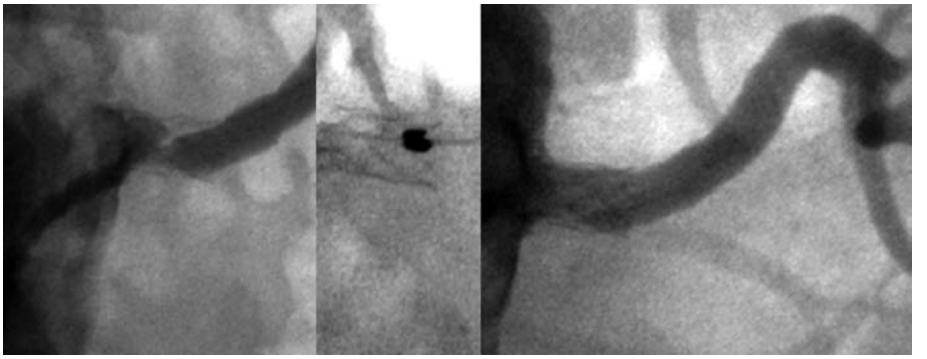

Figure 4b.5 Adequate instead of best possible image quality: test angiographic mode instead of digital subtraction technique in the abdominal and pelvis region. Excimer laser angioplasty (ELCA) of a recurrent renal in-stent restenosis.

baseline values toward left anterior oblique (LAO) 100°, and 3.7 and 2.4 times toward right anterior oblique (RAO) 100°, respectively. Patient and operator values for all PA projections, angulated to the right and left, increased approximately 2.5 times toward 30° craniocaudal angulations[24,33] (Figures 4b.6 and 4b.7).

- *Rotational angiography*, rotating the gantry at 40°/s throughout an angle of 120° around the region of interest, facilitates a three-dimensional impression under conditions

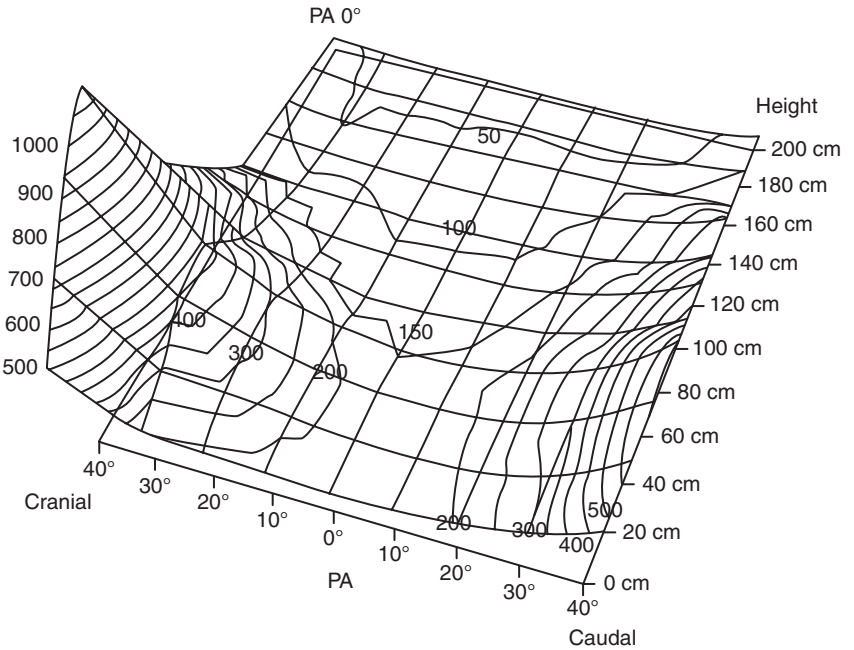

Figure 4b.6 Isodose lines in a three-dimensional graph of the operator's personal dose per time (μSv/h), as a function of tube angulation and height above ground for craniocaudal postero-anterior (PA) angulations.[33] Reproduced from Kuon et al. Fortschr Röntgenstr 2004; 176: 739–45 with permission from Georg Thieme Publishers.

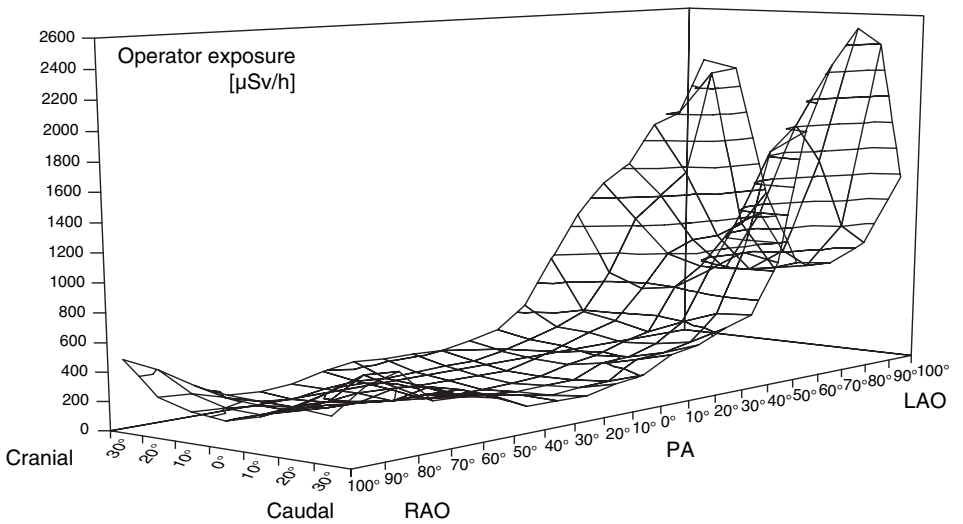

Figure 4b.7 Calculated isodose lines in a three-dimensional graph of the operator's mean personal dose per time (μSv/h), as a function of tube angulation. LAO = left anterior oblique, PA = postero-anterior, RAO = right anterior oblique.[24]

of adequate image quality and represents, even in invasive cardiology, a new, safe, and useful method for the special indication of advanced renal insufficiency: the volume of contrast medium, the overall DAP, and the number of radiographic frames are significantly below typical published values in the standard mode.[34]

Conclusively a patient's anatomic state, e.g. weight, as well as the complexity of intervention is a relevant, influencing factors of patient dose. For routine clinical cardiac procedures, consistent collimation could be proved to be the most efficient influencing factor. For diagnostic purposes, again collimation and restrictions to the essential number of radiographic frames and to adequate instead of best possible image quality were more efficient than optimization of fluoroscopy time.[26]

Operator's radiation exposure

In addition to the above mentioned recommendations, the operator's occupational exposure also depends on an adequate use and acceptance of lead protection devices, case load, and distance from the isocenter. Halving the source to operator distance will quadruple the original occupational scatter radiation.

Use of 1.0-mm overcouch and undercouch shielding facilitated a reduction of stray radiation in the operator's position during fluoroscopy towards an anthropomorphic Rando–Alderson phantom from a mean of 4.7 $\mu Sv/Gy \times cm^2$ to 6% of baseline. The closure of radiation leakage between the table-attached over- and undercouch protection devices by a 1.0-mm lead equivalent undercouch top and overcouch flap adjacent to the table reduced mean stray radiation in the operator's position to approximately 1%. The additional use of a 0.5 mm lead apron, collar, glasses, foot-switch shield, and 1.0 mm lead cover around the patient's thighs was efficient down to mean levels below 10 $nSv/Gy \times cm^2$ and in consequence to mean levels of 0.2% of baseline[29] (Figure 4b.8).

DIAGNOSIS AND THERAPY OF RADIOTOXIC EFFECTS

Deterministic radiotoxic effects typically will and should be treated by dermatologic specialists familiar with and experienced in therapeutic challenges of radiogenic skin injuries. If an interventional procedure carries a significant risk of such injury, in addition to risks of embolism, stroke, and contrast medium allergy patients

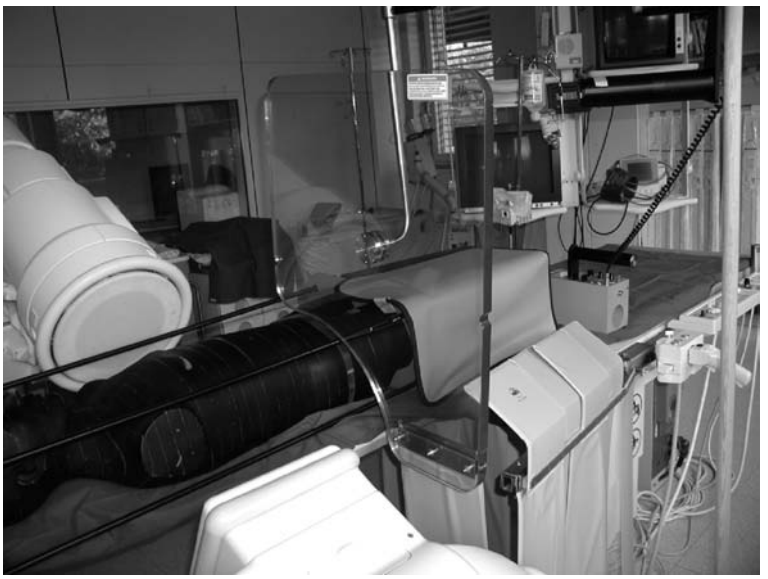

Figure 4b.8 Optimized table-attached radiation protection with closure of radiation leakage between overcouch and undercouch lead protection devices and a lead cover around the patient's thighs.

should be counselled on the future possibility of erythema or more serious skin injury. Moreover, all patients with estimated skin doses of ≥ 2 Gy should be counselled after the procedure and followed for up to 2 weeks after exposure.[1]

CONCLUSION

Adequate radiation reducing techniques and consistent use of table-attached and individual protection devices in clinical routine will indeed prevent observable deterministic injuries and will avoid a significant increase in cancer risk. A new practical 90 minute minicourse in radiation reducing techniques enabled cardiologic interventionists to optimize mean patient DAP values of coronary angiography by 47%.[15] Conclusively, this validated pilot initiative of the Encourage to Less Irradiating Cardiologic Interventional Techniques (ELICIT) study group is promising and resolves discussions about adequate training and supervision in those techniques.[1,9,10,35] In efforts to validate efficient training programs in invasive cardiology and angiology, regular documentation of fluoroscopic and radiographic DAP fractions, and number of radiographic frames – i.e. time-adjusted dose parameters DAP^R/frame and DAP^F/time – in addition to fluoroscopy time and total DAP, has been proved to be a reliable instrument for self-surveillance and supervisory control of each operator's individual long-term efforts towards less radiation exposure.[15,28]

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Part II

Specific complications by vessel area or specific scenarios

5

Arterial and venous access site complications

Martin Schillinger

Introduction to the frequency and kind of access site complications • Factors identifying high-risk patients for complications • Complications of specific interventional steps and tools • Methods to detect potential complications – which diagnostic steps are needed routinely to rule out or identify complications? • Endovascular, surgical, and medical techniques to resolve complications • Methods to avoid complications • Summary • Check list for emergency equipment

INTRODUCTION TO THE FREQUENCY AND KIND OF ACCESS SITE COMPLICATIONS

Percutaneous transluminal procedures are associated with a considerable risk of access site complications.[1,2] Although life-threatening complications rarely occur after routine percutaneous vascular approaches, a 1 to 6% incidence of hematoma, pseudoaneurysms, or arteriovenous (AV) fistulas is reported after coronary and peripheral procedures,[2–4] and 20 to 40% of these patients require surgical repair.[5,6] In particular, the widespread use of aggressive platelet inhibition tends to increase the frequency of complications at the vascular access site,[7–9] and lead to considerable morbidity and costs due to prolongation of the hospital stay.[10] Optimization of access site management after percutaneous transluminal procedures is thus recognized as a matter of immediate clinical importance.[11]

Access sites

Technically feasible arterial access routes include routinely transfemoral, transradial, and transbrachial punctures. Transpopliteal, transaxillar, pedal, or carotid approaches are less frequently performed due to an increased risk of complications. For venous access, transfemoral and transjugular approaches are most frequently used. Arterial and venous access site complications include hematoma, bleeding, pseudoaneurysm formation, AV fistula, infection, nerve injury, vessel dissection, and vessel occlusion.

Incidence of complications

Reported frequencies of access site complications depend on whether diagnostic or therapeutic procedures are considered. After purely diagnostic procedures severe hematoma (requiring transfusion or surgery, or causing delayed discharge) are reported in 0 to 0.68%, dissection or occlusion are reported in 0 to 0.76%, and formation of pseudoaneurysms or AV fistulas in 0.04 to 0.2% of cases.[12] In interventional procedures, these frequencies rise due to larger sheath sizes, more aggressive anticoagulation, and longer duration of the procedures. Bleeding is reported in 3.4%, pseudoaneurysms or AV fistulas in 0.6%, and dissections or occlusions in up to 1%.[13] Retroperitoneal hematoma is an infrequent (0.15%) but morbid complication.

Blood loss

Bleeding and hematoma (Figure 5.1) may occur either acutely during the intervention due to failed puncture of the artery or vein, during removal of the sheath, or subacutely hours after the intervention. Risk factors for bleeding include female gender, advanced age, low body weight, obesity, hypertension, renal insufficiency, coagulation disorders, aggressive anticoagulation, and diseased access sites. Furthermore, aortic insufficiency was reported to associate with poor vascular closure. Puncture technique and sheath size are procedural factors which influence the likelihood for bleeding. Bleeding most frequently occurs after popliteal and antegrade femoral access. Axillary puncture also is associated with a higher risk for bleeding. Radial puncture is safest with respect to bleeding; retrograde femoral access also is considered quite safe in this context.

Persistent bleeding can lead to hemorrhagic shock, and development of large hematomas. Secondary problems of hematomas are infection, hemorrhagic shock, and compression/compartment syndromes. Persistent bleeding is a particular problem at access sites where external compression cannot be performed adequately, e.g. after transaxillary access (Figure 5.2), and at access sites where compartment syndromes easily occur, e.g. after brachial or popliteal access. Treatment of bleeding consists of compression, either manually or by external compression devices such as Femostop™ (RADI Medical Systems, Uppsala, Sweden). Patients with persistent bleeding have to be monitored with respect to heart rate, blood pressure, and blood count. Alternative treatments include prolonged balloon inflation, coiling of the leakage, implantation of covered stents, and vascular surgery.

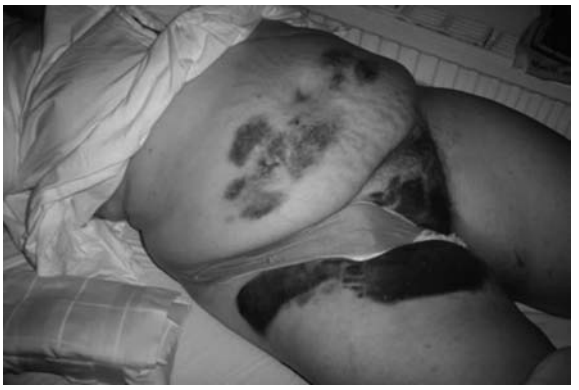

Figure 5.1 Large hematoma after 8 French transfemoral access. The complication could be managed by prolonged manual compression.

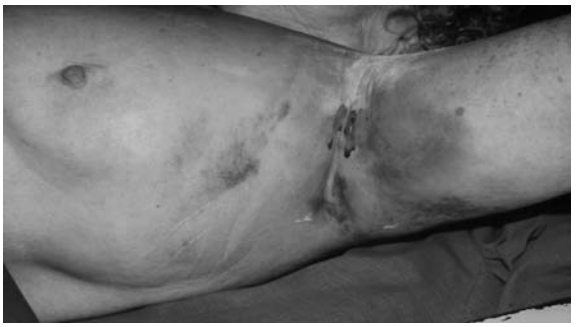

Figure 5.2 Hematoma after transaxillary access. This approach has been abandoned at our institution.

Bleeding to deep subcutaneous tissue or *retroperitoneal bleeding* may initially not cause any apparent clinical signs and thus can be easily overlooked with catastrophic clinical consequences. There are two potential manifestations of retroperitoneal bleeding: first, an ilipsoas hematoma when blood enters and is confined within the fascia of the iliopsoas muscle. This complication is associated with the risk of compression neuropathy as the lumbar plexus may be affected due to compartment syndrome by the hematoma. Second, retroperitoneal bleeding can occur to the space between the peritoneum and retroperitoneal structures, which is vast, can contain huge quantities of blood and can be difficult to detect clinically until hemodynamic deterioration occurs. Infection usually is a problem of large hematomas, or in patients after repair of pseudoaneurysms. Other complications like permanent nerve injury very rarely occur.

Hematoma can be a rather harmless complication leading to ecchymosis. In contrast, large hematomas can cause *compression* or *compartment syndromes*, and may be complicated by *infection*.

Compression of adjacent structures by hematomas can occur. For example, compression of a femoral or iliac vein can lead to lower extremity deep venous thrombosis with its complications.

This is an especially worrisome complication as deep vein thrombosis should be treated by anticoagulation; recent bleeding and large hematomas usually prohibit an immediate start with full-dose anticoagulation and these patients therefore are at a considerable risk for pulmonary infarction. Compression of nerves may lead to irreversible injury, and neurologic deficit due to nerve compression is a clear indication for surgical decompression. Finally, large hematomas with massive swelling may also cause considerable tension on the skin and can induce skin necrosis.

Depending on the size of the compartment, relatively large amounts of blood are required to cause *compartment syndromes* at the thigh, whereas smaller amounts of blood can cause popliteal or brachial compartment syndrome. Swelling, massive pain, paresthesia, and later on motor dysfunction are signs of compartment syndrome which must be urgently treated by fasciotomy, otherwise the extremity and the life of the patient are endangered. Various techniques exist to measure compartment pressures, in most cases clinical judgment will prompt the decision for surgery.

Infection

The rate of infection at the access site is very small (below 0.1%) in the absence of hematoma and secondary procedures to resolve access site complications. This incidence increases when large hematomas, surgical procedures, or thrombin injection complicate vascular access. Therefore, antibiotic prophylaxis seems indicated in patients with very large hematomas, particularly when ultrasound indicates a large volume for the hematoma, and also in patients with secondary surgical interventions at the access site.

Pseudoaneurysms

These are the most frequent arterial access site complications (Figure 5.3) and mostly are due to primarily insufficient access site management, e.g. inadequate manual compression or failed closure devices. Pseudoaneurysms bear the risk of late rupture, and therefore have to be treated even when the diameter of the pseudoaneurysm is small. Besides the risk of rupture, infection of the pseudoaneurysm can complicate the further course of the patient. Embolization from a pseudoaneurysm is a very rare event.

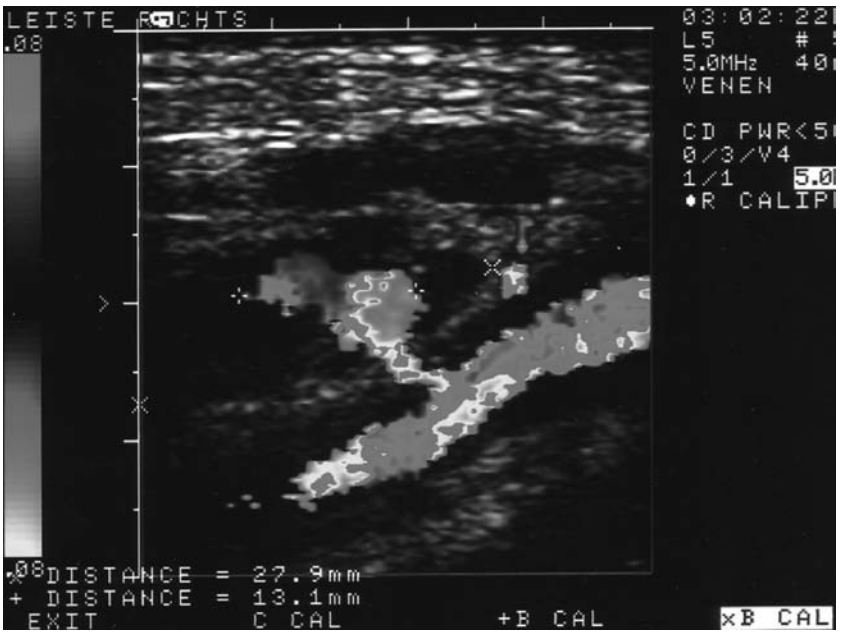

Figure 5.3 Ultrasound image of a partially thrombosed inguinal pseudoaneurysm after transfemoral access with a 6 French sheath.

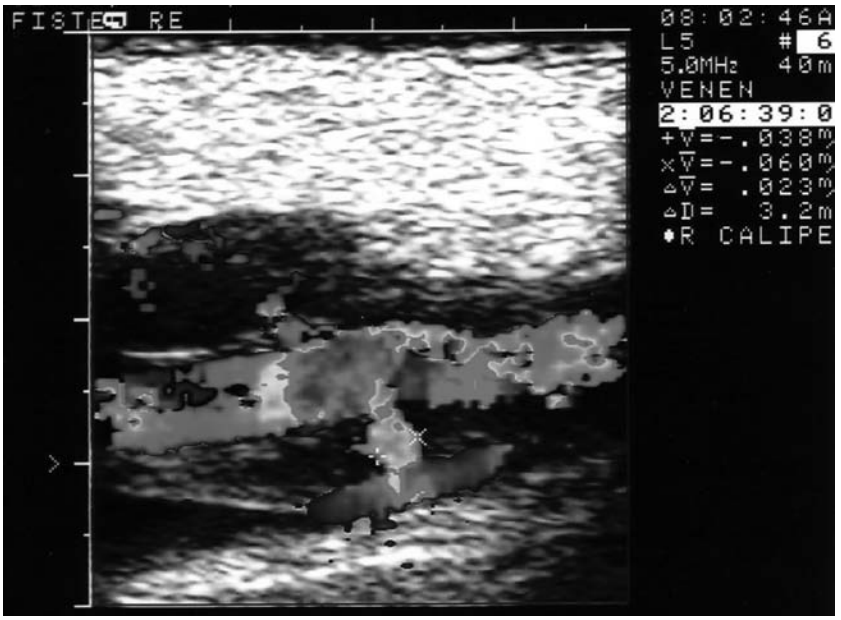

Figure 5.4 Ultrasound image of an inguinal arteriovenous fistula and a partially thrombosed pseudoaneurysm after transfemoral access with a 6 French sheath.

Arteriovenous fistulas

These are the result of a failed puncture when the artery and the vein are punctured (Figure 5.4). Depending on the shunt volume, an AV fistula may remain asymptomatic and can be treated conservatively when the shunt is small, but may also cause signs of leg ischemia or heart failure in cases with large shunt volumes. There are also cases with a combination of an AV fistula and a pseudoaneurysm (Figure 5.5). The highest risk for development of AV fistulas is reported after popliteal puncture, and prepuncture ultrasound is definitively recommended to localize the artery and vein before accessing the vessel.

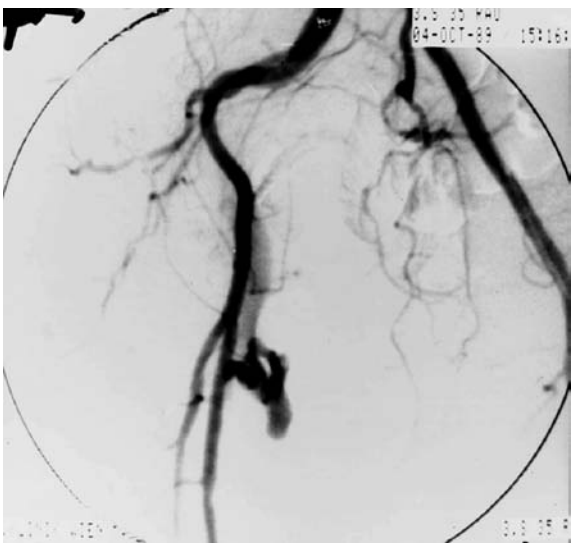

Figure 5.5 Angiographic image of an arteriovenous fistula and a pseudoaneurysm after transfemoral arterial access.

Access vessel dissection, occlusion

Dissection or occlusion of the access vessel rarely occurs in healthy vascular segments. In patients with heavy disease at the access site – e.g. common femoral artery stenosis – puncturing the plaque and advancing the wire may cause plaque disruption, vessel dissection, and occlusion. Hydrophilic guidewires usually have a higher risk for dissection. The risk for dissection is also increased when the vessel segment proximal to the access site is severely stenosed or occluded – in these patients pulsatile flow can be absent even in the true lumen and differentiating between true and false lumen can be difficult.

FACTORS IDENTIFYING HIGH-RISK PATIENTS FOR COMPLICATIONS

Several risk factors identifying high-risk patients for access site complications have been described, unfortunately some of these risk factors like obesity or severe aortic insufficiency cannot be modified. Nevertheless, adequate puncture technique and puncture site management allow safe access even in these high-risk patients.

Morphology of the access site

Mechanical constriction of the arterial wall at the puncture hole after removal of the sheath in combination with platelet aggregation is the key feature of local hemostasis at the arterial access site. The morphology of the access site therefore plays a major role. Increased *patient's age*, *female sex*, *obesity*, uncontrolled *arterial hypertension*, and *previous procedures* via the same access route are well known risk factors in this context. Plaques, severe calcification, or even pre-existent stenosis at the site of puncture increase the risk for bleeding, dissection, and acute or subacute occlusion. Furthermore, the puncture at atypical sites and the *puncture of prosthetic or vein grafts* are associated with higher rates of adverse events. For the most frequent arterial access, the transfemoral approach, puncture of the common femoral artery is recommended and puncture of the superficial femoral artery (distal puncture) as well as puncture of the external iliac artery (proximal puncture) are associated with higher frequencies of pseudoaneurysms (for the superficial femoral artery puncture) and bleeding (for the iliac puncture).

Systemic coagulation disorders

Low platelet counts are known to predict bleeding complications after vascular surgery. In this context, a strong association between low preintervention platelet counts and occurrence of pseudoaneurysms after arterial puncture recently has also been acknowledged as a risk factor for pseudoaneurysm formation after percutaneous interventions in patients with a platelet count below 200.000/L.[14]

Considering the importance of platelet aggregation for local hemostasis, an association between *antiplatelet medications* and subacute puncture site complications is not unexpected.[14] Combined platelet inhibition by acetylsalicylic acid and clopidogrel has been recognized previously as a risk factor for local hemorrhagic complications.[15,16] The additional administration of abciximab synergistically attenuates platelet aggregation[17] and thus increases the risk for bleeding and pseudoaneurysms. Patients with combined and aggressive antiplatelet medications thus have to be considered as high risk for access site complications.

Artificial coagulation disorders, like oral anticoagulation or therapy with low molecular weight heparin, have to be considered important risk factors for access site complications. In these patients, optimization of coagulation prior to puncture should be anticipated whenever possible. Low molecular heparin should be stopped on the day of the procedure whenever possible.

Sheath size

The size of the arterial or venous sheath is a major determinant for complications. The larger and the stiffer the sheath, the higher the risk for local injury. Routine sheath sizes for transfemoral arterial access range from 4 to 8 French and have a relatively low risk for arterial injury. Particularly when larger sheaths are used for implantation of stent grafts, access vessel anatomy has to be assessed in advance to ensure that these large sheaths will pass through the pelvic arteries without troubles.

Location of the puncture site

Retrograde transfemoral access is considered the safest approach to endovascular therapies. The antegrade femoral approach has a higher risk for bleeding and pseudoaneurysm formation. Transradial access is considered the safest approach with respect to bleeding, however it bears a higher risk for vessel thrombosis. Brachial or axillary puncture has a higher risk of neuropraxia involving the median nerve or other branches of the brachial plexus. With decreasing diameter of the punctured vessel, the risk for dissection and thrombosis increases and has

been reported to be as high as 15% for transradial access with sheath sizes above 6 French.

Puncture technique

Finally, another most important determinant for access site complications is puncture technique. This will be described later in this chapter.

COMPLICATIONS OF SPECIFIC INTERVENTIONAL STEPS AND TOOLS

The most common technique and probably still the gold standard for achieving local hemostasis at the arterial puncture site is conventional manual compression. Thereafter, prolonged bed rest is recommended. Recommendations range from 4 hours after removal of a 4 French sheath, to 6 hours after 5 French sheaths, to overnight bed rest after removal of 6 French or larger sheaths after interventional procedures. Although safe,[18,19] this technique is time consuming, sometimes painful for the patient, potentially induces *vasovagal reflexes* with a drop in blood pressure and heart rate, requires prolonged immobilization and an overnight hospital stay, and thus may have cost implications. Nevertheless, if adequate compression times are ensured,[20] the rate of complications can be reduced to below 2%. In this context, compression times of at least 15 to 20 and 5 minutes after bleeding has stopped have been recommended. During manual compression a vasovagal reflex may cause bradycardia and hypotension. Blood pressure and heart rate monitoring is therefore recommended during removal of the sheath; fluids and atropine (in steps of 0.5 mg iv) are useful to handle these adverse events and can be used as a prophylactic measure in patients with low blood pressure and/or low heart rate. It has to be acknowledged that atropine *per se* increases only the heart rate but not the blood pressure, therefore hypotension without bradycardia is not adequately treated by atropine.

The development of specific *closure devices* promised faster time to ambulation, and an increase in safety and patients' comfort. Several studies addressed the efficacy and safety of suture-mediated closure devices compared with conventional compression;[21–27] however, a clinical benefit has not as yet been demonstrated unequivocally,[22,28,29] as no large randomized trial reported a reduction of complications. Most closure devices have been approved only for retrograde femoral access. Furthermore, closure devices may introduce complications rather than avoiding them. Complications associated with closure devices are acute vessel occlusion, dissection, and bleeding.

The following case illustrates a complication induced by the closure device Angioseal™ (St Jude Medical), which was used to close a 10 French transfemoral access site after carotid angioplasty with a MoMa™ (Invatec) proximal balloon occlusion system. After the intervention, the patient developed progressive rest pain in the right foot and lower limb. Duplex™ sonography of the access site in the right groin revealed an acute occlusion of the superficial femoral artery where the Angioseal™ device was implanted and the patient was therefore returned to the cath lab. An angiogram from cross-over revealed a flush occlusion of the superficial femoral artery (Figure 5.6). The occlusion was recanalized and repeatedly dilated, but the intravascular anchor of the closure device reoccluded the artery immediately. Therefore, a 7/20 self-expanding nitinol stent (Smart Control™, Cordis™) was implanted at the origin of the SFA (Figure 5.6) and patency was restored.

METHODS TO DETECT POTENTIAL COMPLICATIONS – WHICH DIAGNOSTIC STEPS ARE NEEDED ROUTINELY TO RULE OUT OR IDENTIFY COMPLICATIONS?

Clinical examination of the vascular access site after percutaneous procedures before patient discharge and identification of subacute complications is becoming increasingly recognized as a matter of the utmost importance.[30] For clinical routine, *duplex sonography* is suggested to be the gold standard in the assessment of the vascular access site after arterial puncture.[30–33] In this context, *color coded duplex ultrasound* is very helpful in visualizing complications like pseudoaneurysms (Figure 5.3) or arteriovenous fistulas (Figure 5.4). Ultrasound can further precisely document the success of complication

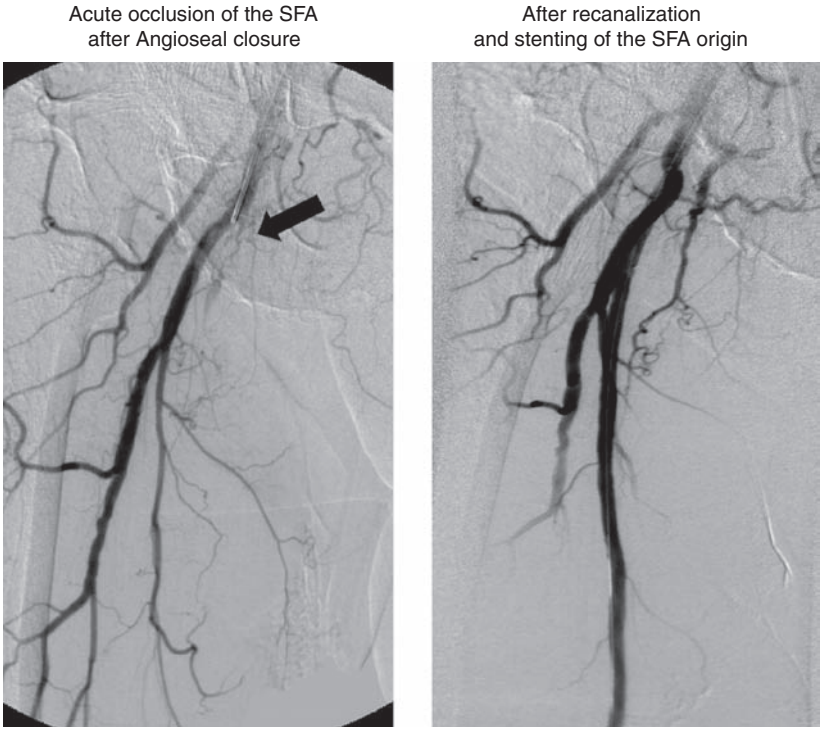

Figure 5.6 Acute occlusion of the superficial femoral artery (SFA) after access site closure using the Angioseal™ (St Jude Medical) closure device (left image). The occlusion was recanalized by cross-over balloon angioplasty and implantation of a 7.0/20 self-expanding nitinol stent (SMART Control™, Cordis™) at the origin of the SFA (right image).

management, e.g. by manual or ultrasound guided compression (Figure 5.7).

The question whether all patients have to undergo duplex sonography, or whether *physical examination* is reliable to exclude access site complications remains a debated issue. However, recent research[14] has indicated that physical examination indeed is very reliable in excluding iatrogenic pseudoaneurysms. The presence of pulsatile groin masses was 100% predictive of pseudoaneurysms in duplex sonography without false positive findings.[14] Vascular bruits are sensitive indicators for arteriovenous fistulas. For routine purposes it seems acceptable to rely on physical examination for the postintervention evaluation of the puncture site and to perform confirmatory ultrasound evaluation only in patients with pulsatile groin masses, rather than mandatory duplex ultrasound after all percutaneous transluminal interventions.

In patients with unexplained back or abdominal pain, or hemodynamic deterioration postintervention, acute bleeding has to be considered as a most important differential diagnosis. As long as these patients can be initially stabilized, *computed tomography* will be the diagnostic method of choice to assess the site of bleeding and, in particular, to assess whether occult retroperitoneal bleeding is ongoing. In intractable unstable patients, exploratory surgery has to be considered as a primary measure.

Angiography will be the diagnostic method of choice when a repeat intervention is planned to resolve an access site complication, e.g. coiling or stent graft implantation. Otherwise, angiography can be replaced by non-invasive evaluation in almost all cases.

ENDOVASCULAR, SURGICAL, AND MEDICAL TECHNIQUES TO RESOLVE COMPLICATIONS

The choice of technique to resolve an access site complication mainly depends on the kind and acuity of the complication. The following section

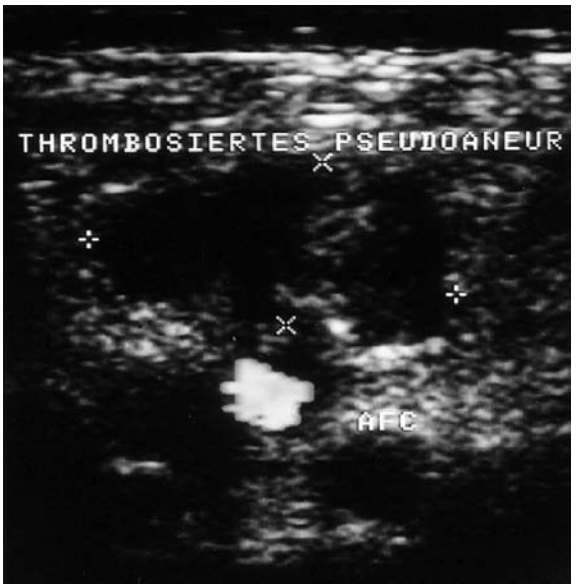

Figure 5.7 Thrombosed pseudoaneurysm after successful ultrasound guided compression for 20 minutes.

will outline various treatment options for access site complications.

Compression

The method of first choice in stable patients with access site complications, particularly pseudoaneurysms, is *prolonged manual or ultrasound compression*. Manual compression over a time period of 25 to 30 minutes followed by a pressure bandage and overnight bed rest has a success rate of approximately 60%. This can be improved to 80–90% by ultrasound guidance.[34–38] In this case, the neck pseudoaneurysm is compressed directly with the ultrasound transducer over a time period of 25 to 30 minutes, leading to stasis in the sack of the aneurysms and subsequent thrombosis. The procedure is followed by an overnight pressure bandage. Alternatively, a compression device like the Femostop™ device (RADI Medical Systems, Uppsala, Sweden) can be placed under ultrasound guidance on the pseudoaneurysm; the expected success rate also ranges around 80%. Although quite effective, ultrasound guided compression is frequently extremely painful for the patient, and very time consuming for the physician; alternatives are therefore needed. Complications of ultrasound guided compression are extremely rare. Case reports describe the rupture of pseudoaneurysms during ultrasound guided compression which had to be resolved by surgery. Compression therapy can also be effective in patients with arteriovenous fistulas, although the success rate is usually below 50%, mainly depending on concomitant antiplatelet and anticoagulant therapy.

Compression therapy is also the treatment of choice for persistent bleeding at the access site. Additionally, these patients have to be monitored with respect to heart rate and blood pressure.

Vascular surgery

Vascular surgery is traditionally the treatment of choice when compression has failed, as well as in all patients with ruptured pseudoaneurysms or acute bleeding from the access site which cannot be handled by endovascular procedures.[39–42] Furthermore, patients with hemodynamically relevant arteriovenous fistulas which do not respond to compression therapy frequently have to undergo surgery. The success rate of surgical procedures approaches 100%, and frequently the operation can be done under local anesthesia. In patients with a large hematoma, these clots can be removed, although this approach usually requires general anesthesia. Unfortunately, infection, nerve injury, lymph fistulas, and formation of seromas frequently complicate the postoperative course and prolong hospitalization in 15 to 25% of the patients. Surgery is also the treatment of choice for patients with compartment syndromes, large hematomas, and ongoing (retroperitoneal) bleeding.

Thrombin injection

During the late 1990s, reports described the successful closure of iatrogenic pseudoaneurysms by instillation of fibrin and fibrin derivates, and later on bovine, recombinant, and human thrombin.[43–49] Today, thrombin injection has replaced most other substances. Technically, the injection is performed under ultrasound guidance. Ideally, the neck of the pseudoaneurysm is compressed by the ultrasound transducer during injection of the procoagulant substance. The success rate of

thrombin injection is 95 to 98%. The most serious complication is peripheral embolization of the procoagulant material in up to 2%. Fortunately, most peripheral emboli are resolved spontaneously and critical limb ischemia necessitating thrombolysis or surgery hardly ever develops.[43] Both human and bovine thrombin can be used for injection in the pseudoaneurysm. The potential disadvantages of bovine thrombin are allergic reactions and cross-reactions with factor V of the coagulation cascade.[50–54] Direct comparison of human vs bovine thrombin, however, showed no significantly lower complication rate with human thrombin, but a significantly higher success rate with bovine thrombin, suggesting that this substance may be preferred.[45]

We routinely use bovine thrombin in increments of 5000 IU under ultrasound guidance. The following case report demonstrates the utility of thrombin infection in a 42-year-old female patient. The patient was submitted 12 weeks after a neuroradiologic intervention due to increasing swelling of the right groin. Duplex sonography revealed a 50 × 30 × 30 mm pseudoaneurysm with a short and large caliber neck (3 mm diameter). Systolic peak velocity in the neck was above 4 m/s, suggesting a very high flow within the aneurysm – not an ideal candidate for thrombin injection (Figure 5.8). The patient refused surgical therapy and opted for thrombin injection, despite the higher risk for peripheral emblization in patients with wide necks of the pseudoaneurysm. After disinfection of the skin, an 18 G needle was advanced under sonographic control and manual compression of the common femoral artery until the tip of the needle was visualized centrally within the pseudoaneurysm. Thereafter, 5000 IU thrombin (D-Stat flowable haemostat™, Vascular Solutions, Mn, MI) was slowly injected under sonographic control; complete occlusion was achieved after injection of another 5000 IU of the substance (Figure 5.9). Immediately after thrombin injection, the right lower leg was pale and cold, and the pulse of the arteria dorsalis pedis was not palpable, suggesting peripheral embolization. Since the patient remained asymptomatic, a pressure bandage was applied on the right groin and the patient was observed overnight. Two hours after thrombin injection, clinical signs of ischemia had disappeared and 24 hours after the injection ultrasound revealed a regular perfusion of the ipsilateral arteria dorsalis pedis (Figure 5.9), suggesting spontaneous lysis of the embolic material. Ten days after the intervention the pseudoaneurysm remained completely occluded and the patient was free of symptoms (Figure 5.10).

Alternatively, in patients with wide necks, a combined procedure can help to resolve the problem: by an endovascular cross-over approach the access site can be sealed by an occlusion balloon (Figure 5.11), under balloon protection thrombin usually can be safely injected.

Stent implantation

In case of dissection or vessel occlusion at the access site, balloon dilation and stent implantation with self-expanding stents can usually resolve the problem, as shown in Figure 5.6. For inguinal complications, either a cross-over access or a transbrachial access is technically possible; long sheaths are mandatory in these cases. Entering the true lumen sometimes can be challenging, the choice of an adequate wire is most helpful in these cases. We prefer a Boston Scientific™ 0.018 control wire with flexible tip for these cases.

Stent graft implantation

This is a relatively novel and still debated option to treat access site complications. Most access sites are located in vessel areas with high mechanical stress, like the groin for arterial access or the neck for venous interventions. The formerly available stent grafts were very rigid, and frequently balloon expandable, which seems not an adequate option for these vessel areas. Today more flexible and self-expanding stent grafts are available, which can be used in certain indications to manage access site complications. The initial success rate approaches 100%. However, some permanent limitations of the use of stent grafts have to be considered: most importantly, the access site cannot be used for later interventions after implantation of a stent graft. Secondly, stent graft fractures have

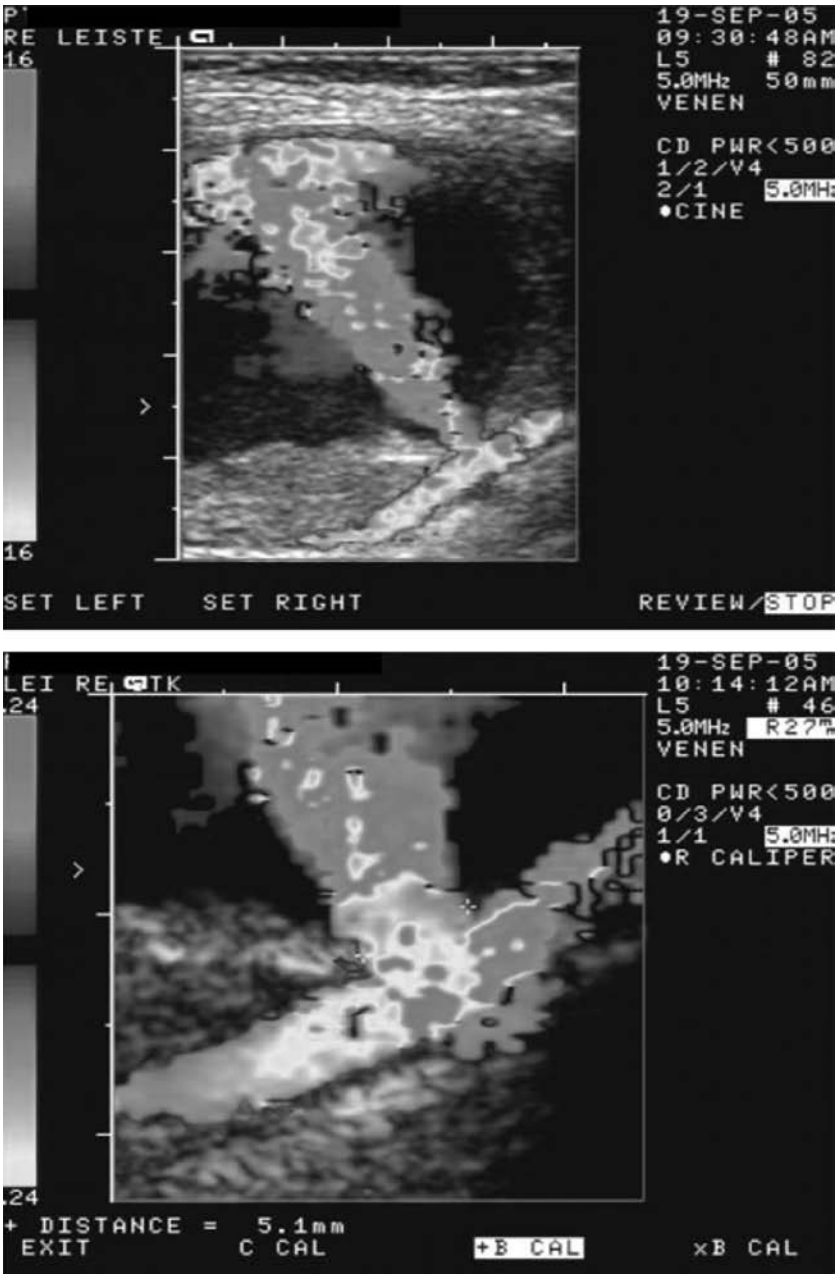

Figure 5.8 Duplex sonography of an iatrogenic pseudoaneurysm in the common femoral artery with a central jet (upper image) and a wide neck (lower image).

been reported and may cause late problems. Thirdly, stent graft restenosis occurs in up to 50% of the patients, depending on the vessel area. Therefore, stent grafts should not be considered the treatment of first choice for access site complications. The following two cases briefly describe stent graft implantations for management of arterial and venous access site complications.

A 59-year-old male patient was submitted to our cardiology department suffering an acute coronary syndrome. The patient received aspirin,

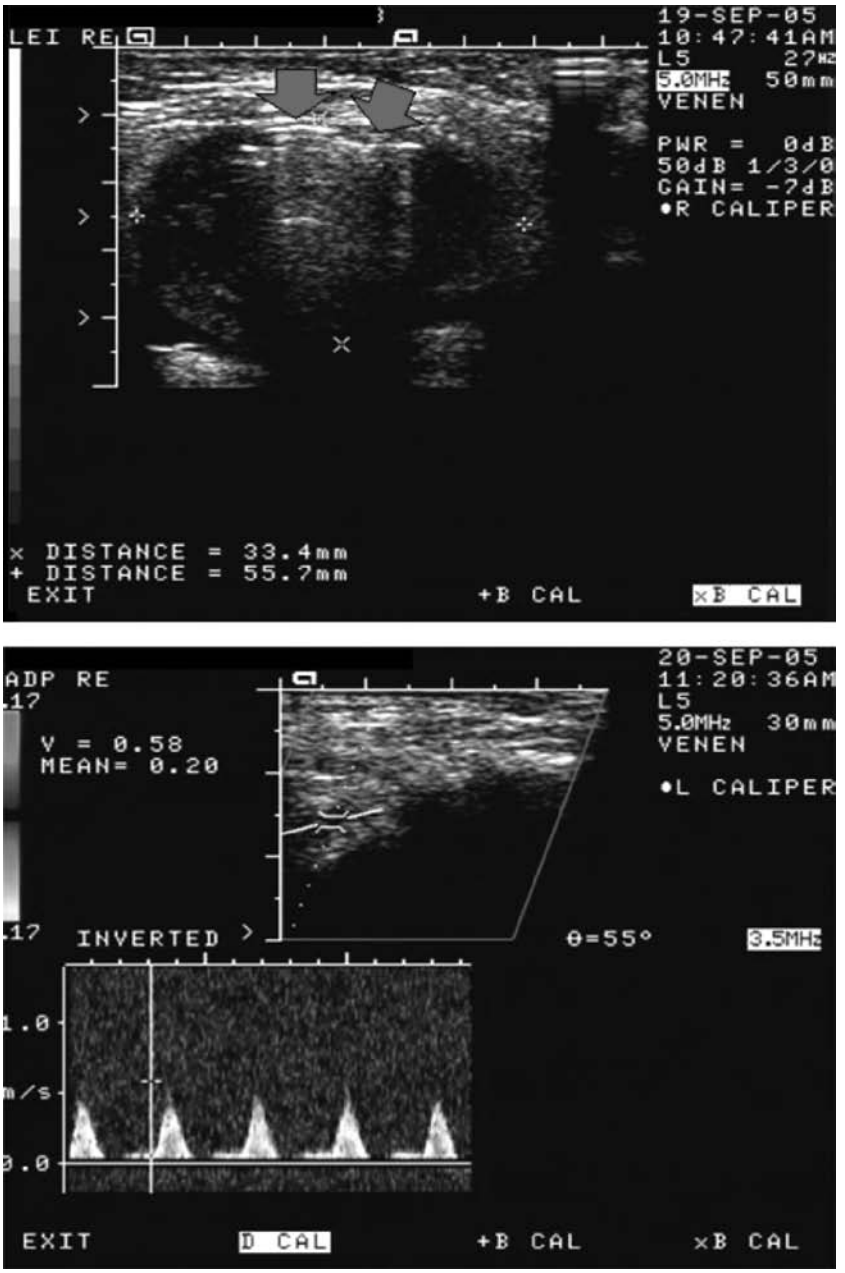

Figure 5.9 Ultrasound B-image immediately after thrombin injection and complete thrombosis of the pseudoaneurysms; the hyperechogenic reflex indicates the site of the thrombin depot (red arrows, upper image). The lower image shows the ultrasound Doppler signal of the ipsilateral arteria dorsalis pedis.

clopidogrel 300 mg loading dose, full dose low molecular heparin and abciximab, and underwent urgent coronary angiography. Due to diffuse coronary three-vessel disease, endovascular revascularization was not attempted; the patient could be stabilized and was scheduled for elective bypass surgery. Two days postintervention, an increasing swelling and enlarging hematoma

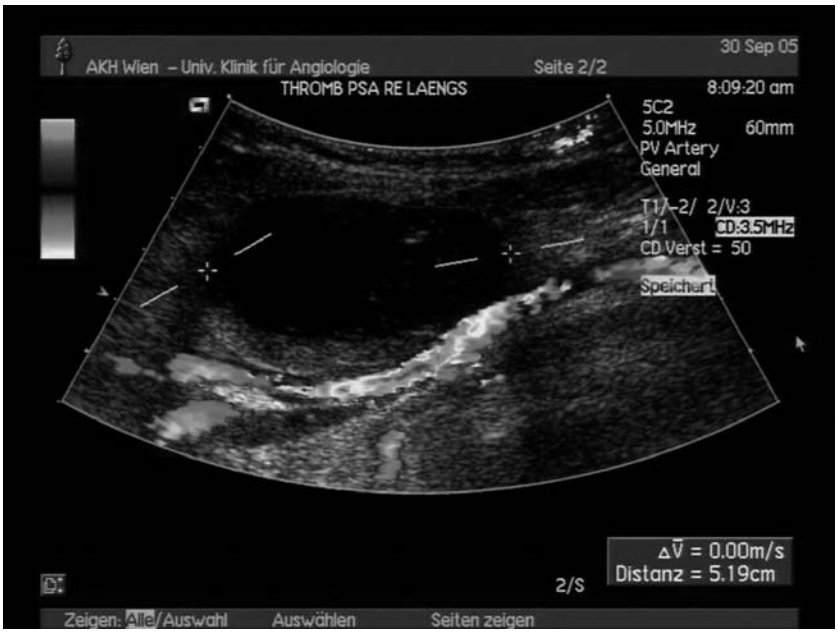

Figure 5.10 Duplex sonography 10 days after thrombin injection demonstrates complete occlusion of the pseudoaneurysm and regular patency of the common femoral artery.

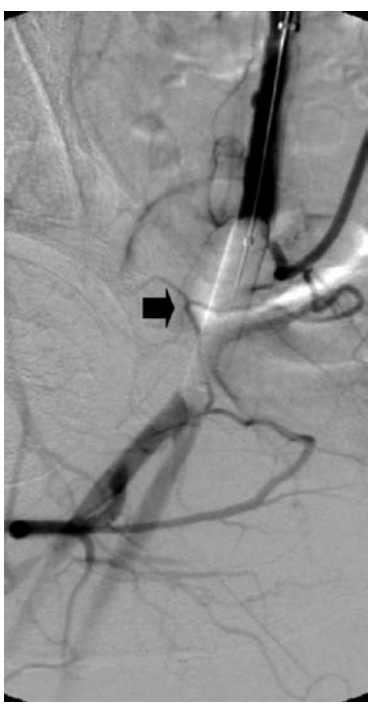

Figure 5.11 Balloon occlusion for a femoral iatrogenic pseudoaneurysm – under balloon protection, thrombin injection can be performed even in cases with very wide aneurysm necks to minimize the risk of embolization.

in the right groin was detected and ultrasound confirmed a large hematoma and diffuse pseudoaneurysm without a detectable neck. The patient was therefore not considered a candidate for thrombin injection and the vascular surgeon refused to operate on the bleeding due to the aggressive anticoagulation regimen. The patient was therefore brought back to the cath lab and an angiogram was obtained via the contralateral approach (Figure 5.12). Thereafter, a 45 cm 9 French sheath was placed over the bifurcation via a stiff 0.035-inch Amplatz™ wire. The same wire was used to guide a self-expanding 6.0/60 Fluency Stentgraft™ (CR Bard, Inc) to the bleeding site and seal the bleeding site (Figure 5.13). The postintervention course was uneventful and the patient later underwent aortocoronary bypass surgery.

The second case describes the course of a 38-year-old patient who suffered an arteriovenous fistula and subacute bleeding following a venous access to the right jugular vein (Figure 5.14). The patient was not suitable for surgery due to severe comorbidities, therefore stent graft repair was considered. After diagnostic angiography and confirmation of the bleeding, a long 9 French

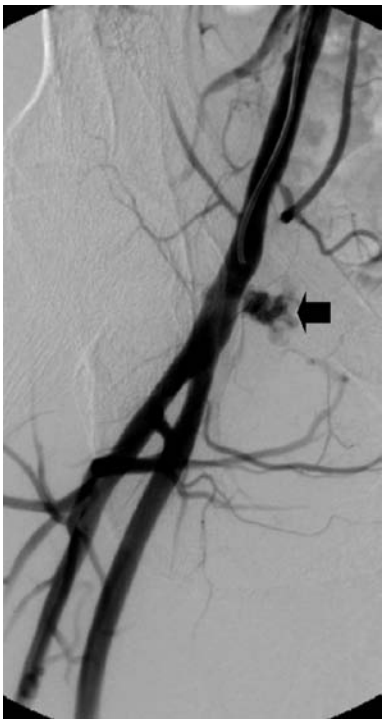

Figure 5.12 Angiography of a bleeding and diffuse pseudoaneurysm of the right groin.

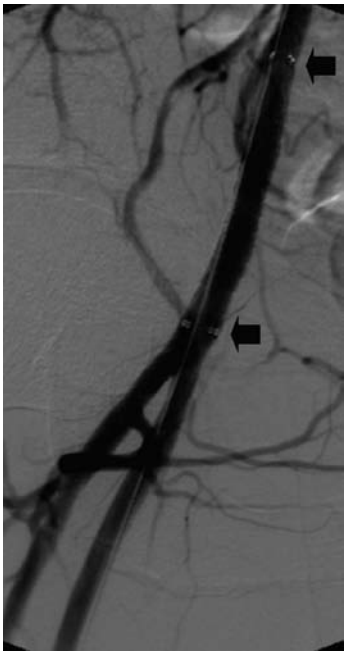

Figure 5.13 Implantation of a 6.0/60 Fluency Stentgraft™ (CR Bard, Inc) to seal an inguinal bleeding site and pseudoaneurysm.

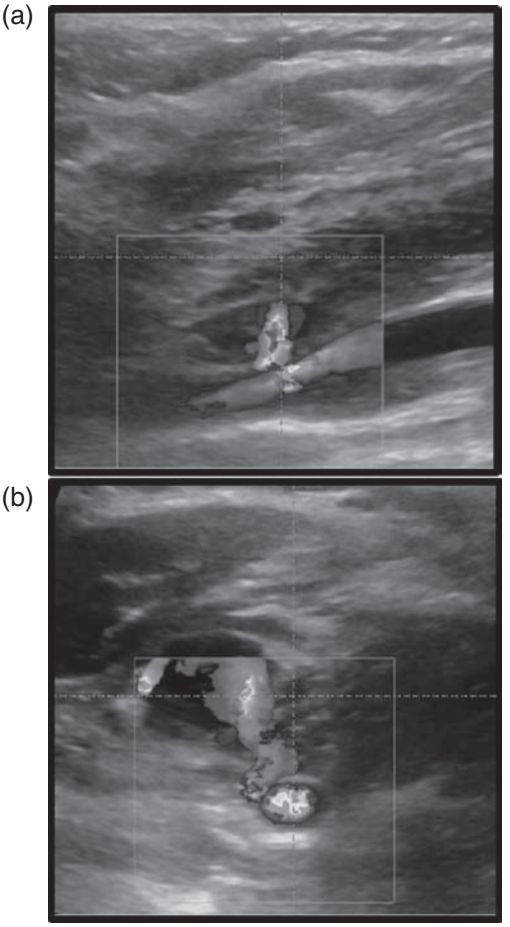

Figure 5.14 Duplex ultrasound revealing an arteriovenous fistula between the internal jugular vein and the common carotid artery after venous access. a) Sagittal view b) Transverse view.

sheath was placed in the common carotid artery via a stiff wire (Figure 5.15). Then a Fluency Stengraft™ 8.0/30 (CR Bard, Inc) was implanted and the bleeding site and arteriovenous fistula was sealed successfully (Figure 5.16).

Coil embolization

The reported experience with coil embolization of access site complications is very limited. This option may be considered, when the neck of the pseudoaneurysm is long enough to safely position a catheter and place the coils. Nevertheless, there is a substantial risk for dislocation of the coils, if the neck of the bleeding site is too short

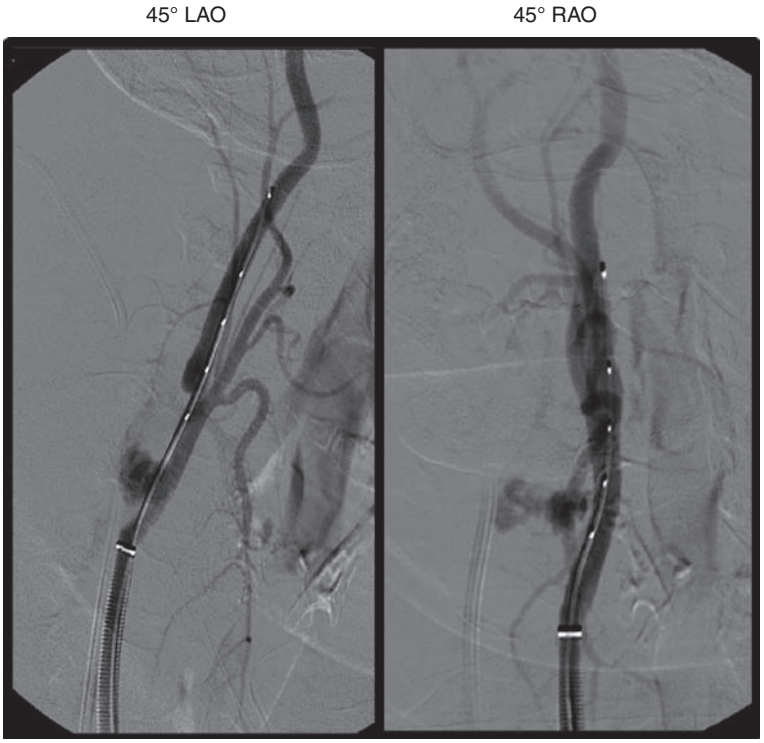

Figure 5.15 Angiographic images of the arteriovenous fistula and bleeding of the common carotid artery – a large sheath and guidewire for subsequent stent graft implantation are already in place.

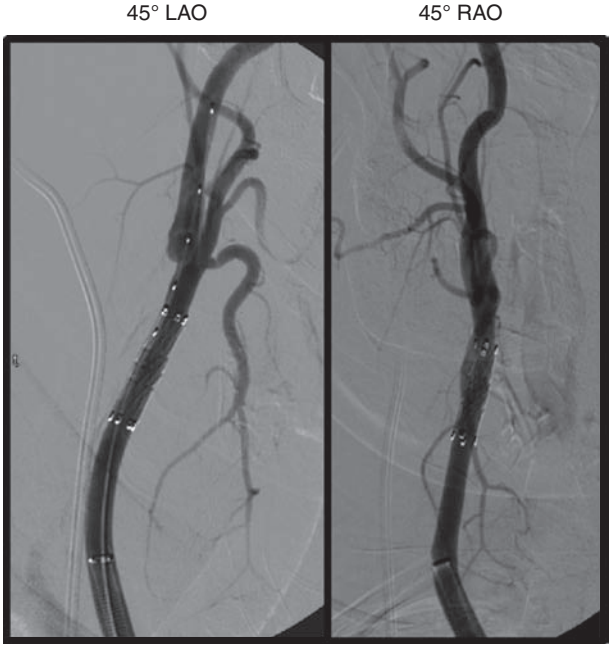

Figure 5.16 Implantation of a covered stent graft (Fluency™ 8.0/40, CR Bard, Inc) to cover the bleeding site in the common carotid artery.

and, usually, percutaneous liquid embolization by thrombin is the method of choice.

METHODS TO AVOID COMPLICATIONS

Preprocedure assessment

In patients without a history of peripheral artery disease, without previous punctures at the planned access site, and with a regularly palpable pulse no additional preprocedure imaging seems necessary. If there is any doubt on disease at the access site, preprocedure ultrasound examination helps to estimate the feasibility and risk for a puncture. Particularly, when the puncture site is heavily diseased, the interventionist who will perform the puncture should perform the ultrasound examination to get an idea of potential problems. If ultrasound is not available – e.g. the patient is already in the cath lab – plain fluoroscopy of the puncture site may visualize heavy calcifications and identify pre-existent stents nearby the puncture site. Fluoroscopy of the puncture site should always be done if previous stent implantation in this area is suspected or documented. Ultrasound guided punctures can be used when access is extremely difficult.

Choice of access site

Using the *transfemoral puncture*, the femoral head should be located by fluoroscopy before puncture, as the common femoral artery is usually located exactly at the level of the femoral head. External anatomic structures are relatively unreliable with respect to locating the common femoral artery.

For access sites other than transfemoral certain premises always have to be considered. As stated above, the *popliteal access* is associated with a higher rate of arteriovenous fistulas; ultrasound guided puncture is extremely helpful in these cases. In patients with planned access through the arteries of the upper extremities two options can be considered: transbrachial or transradial access. *Transbrachial access* has a lower rate of vessel thrombosis (1 to 2%), but in cases when thrombosis occurs, the clinical consequences can be deleterious and frequently necessitate surgery. Transbrachial puncture should be done 2 cm proximally to the elbow joint to avoid the radial bifurcation. *Transradial access* is associated with a higher rate of vessel thrombosis (5 to 10%), but in patients with patent palmar arc, clinical consequences of radial artery thrombosis usually remain negligible. If long segment radial artery thrombosis occurs without adequate collateral flow, severe consequences may arise (Figures 5.17 and 5.18). Before the radial approach, testing for collateral flow – e.g. by the Allen test – is recommended.

Patient selection and preparation

Bleeding disorders should be corrected before the intervention in all patients undergoing elective treatment. This includes stopping low molecular weight heparin on the day of the intervention whenever possible, monitoring the amount of heparin administered during the procedure by ACT measurements, and checking the ACT or activated partial thromboplastin time (aPTT) before removing the sheath.

Puncture technique and choice of needle

Whenever possible 'anterior wall puncture' should be performed to avoid bleeding and minimize the extent of vessel injury. One-part needles (open needles) support anterior wall puncture, whereas the classical two-part Seldinger needle frequently causes puncture through the artery and entry to the lumen during backward movement of the puncture device. The Seldinger technique is considered outdated by

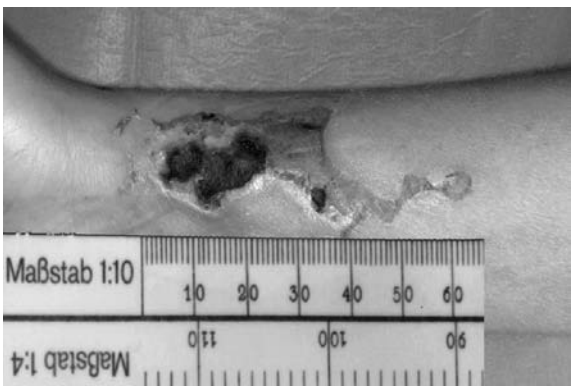

Figure 5.17 Severe skin necrosis after radial access and radial artery thrombosis.

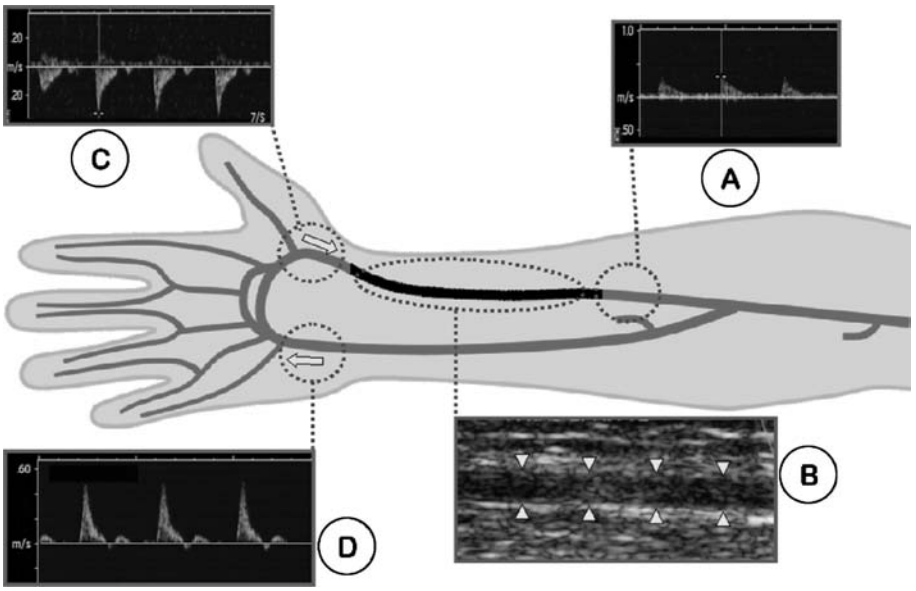

Figure 5.18 Doppler flow profiles in a patient with occluded radial artery after radial access.

many interventionists and should be avoided in all patients under aggressive anticoagulation or in patients undergoing thrombolysis. Introduction of the wire has to be done cautiously, and has to be avoided when pulsatile flow is absent or attenuated (particularly if no proximal lesion is suspected). Hydrophilic (glide) wires bear the potential danger of easily dissecting the vessel rather than entering in the true lumen. We still frequently use hydrophilic wires for arterial punctures, but the interventionist has to be aware of this risk. In case the appropriateness of the puncture is in doubt, a small amount of contrast should be administered to perform a 'needle angiography' and assess the puncture site by angiography. The wire then can be advanced under fluoroscopic view. Special attention should be brought to the tip of the wire – the tip should be freely moving, otherwise vessel dissection has to be considered. A useful test to reassure true lumen entry with the wire is to advance the wire to the first bifurcation: if the wire follows the expected course of the bifurcating vessel true lumen access is almost guaranteed; in cases with subintimal entry, the wire will get stuck at the first bifurcation. It seems essential to reassure true lumen entry with the wire before the sheath is inserted.

During the intervention

Regularly aspirating and flushing the sheath and adequate anticoagulation help to reduce the risk for thrombosis. For aspiration maneuvers only sheaths with removable hemostatic valves should be used as clots frequently get stuck in the sheath at the level of the hemostatic valve. If in doubt, when aspiration through the sheath is not possible, the sheath should be exchanged rather than flushed to avoid embolization.

Removing the sheath and access site closure

If closure devices with anchor (Angioseal™, St Jude Medical™), clip (Starclose™, Abbott Vascular™), or needle (Perclose) systems are planned, a final angiogram of the access site should be obtained to assess whether collaterals (e.g. deep femoral artery) are involved in the access route and to assess the diameter of the punctured artery. Most currently available closure devices are approved only for retrograde femoral access and are not recommended for a vessel diameter below 4.5 mm. Personally, we avoid the use of closure devices in locations other than the common femoral artery, as we experienced serious adverse events with different closure devices in the superficial femoral

artery and the brachial artery. Furthermore, if the access site shows heavy calcification, closure devices frequently do not work properly. In these cases manual compression or compression with external devices like the Femostop compression device is recommended. Timing for removing the sheath for manual compression depends on the size of the sheath and the amount and kind of anticoagulation. With sheath sizes up to 6 French, immediate removal seems safe with any kind of anticoagulation. If larger sheaths are in place, the effect of anticoagulation (heparin, bivalirudin) should be minimized until the sheath is removed – for heparin this can be checked by the ACT or aPTT.

Control of blood pressure

Before removing the sheath, blood pressure should be checked – and lowered if elevated. Personally, we prefer systolic blood pressures at maximum 140 mm when the sheath is removed.

Pressure bandage and bed rest

There are no uniform recommendations for bed rest and pressure bandages and no scientific evidence for their use. We routinely apply prolonged pressure bandages in all patients after manual compression of the access site, and even in patients who received a closure device, a short-term pressure bandage (4 hours) seems useful. After manual compression we recommend 4 hours of bed rest for a 4 French sheath, 6 hours for 5 French, and overnight bed rest for 6 French or larger. All patients with closure devices have a bed rest of 4 hours at our institution.

Postintervention care

The access site should be checked regularly during the first few hours postintervention by a trained nurse or physician, particularly before first ambulation. First ambulation should be done under surveillance. Before discharge the access site again has to be checked by a trained physician – we recommend that the interventionist personally checks the access site before ambulation.

SUMMARY

Access site complications are the most frequent complications encountered after percutaneous procedures. Occurrence of these complications can be a severe burden for the patient and the healthcare system and can extinguish the advantage of a minimally invasive endovascular approach. Several risk factors for access site complications are known and high-risk patients can be identified preprocedure. Adequate puncture technique and thorough postprocedure access site management can minimize the frequency of these complications. Several methods to handle access site complications are available and the interventionist has to be familiar with these techniques.

CHECK LIST FOR EMERGENCY EQUIPMENT

- thrombin, e.g. (D-Stat flowable haemostat™, Vascular Solutions, Mn, MI)
- occlusion balloons 4 to 10 mm depending on the size of the access vessel
- self-expanding bare metal nitinol stents for treatment of dissections and occlusions
- self-expanding stent graft, e.g. Fluency stent graft (CR Bard), Wallgraft (Boston Scientific), or Viabahn (Gore) in adequate sizes to fit the access vessel
- pushable coils
- ultrasound machine with duplex mode
- CT facility for emergency imaging of retroperitoneal bleeding.

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6a

Complications of pharmacologic interventions: antiplatelet, antithrombotic, and anticoagulant agents

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Introduction to frequency and type of complication with antiplatelet, antithrombotic, and anticoagulant agents • Factors identifying patients at risk for bleeding complications • Bleeding complications of specific interventional steps and tools • Methods to detect potential complications – which diagnostic steps are needed routinely to rule out or identify complications • Endovascular, surgical, or medical techniques to resolve complications • Methods to avoid complications • Summary • Check list for emergency equipment

INTRODUCTION TO FREQUENCY AND TYPE OF COMPLICATION WITH ANTIPLATELET, ANTITHROMBOTIC, AND ANTICOAGULANT AGENTS

In recent years a dramatic increase in the number of percutaneous transluminal interventions has occurred. As a result of technologic advances and the increasing number of training centers, catheter-based interventions are performed in more extensively diseased arterial segments than has been carried out in the past. As vessel wall injury is the unavoidable consequence of endovascular treatment, more complex interventions go along with an increased thrombotic risk.[1] Today, it is the supplementary aggressive medical therapy (Table 6a.1) that provides good clinical patency even in complex peripheral interventions, but at the cost of bleeding events. The following review gives the reader an overview on current guidelines, opinions, and possible complications due to antiplatelet, antithrombotic, and anticoagulant agents and their management.

Antiplatelet and antithrombotic agents

Acetylsalicylic acid (aspirin) exerts its major antithrombotic effect by irreversibly acetylating platelet cyclo-oxygenase-1, thereby inhibiting prostanoid biosynthesis.[2] Peak plasma levels occur 30 to 40 minutes after aspirin ingestion and the virtually complete inhibition of platelet function is evident by 1 hour. As 10% of the circulating platelets are replaced each day, 5 to 6 days following aspirin ingestion will be needed for approximately 50% normal platelet function.

The role of aspirin to prevent cardiovascular events has been shown in numerous large-scale trials.[3,4] In addition, aspirin reduces the risk of vascular graft or arterial occlusion by about 40%.[5,6] The dose of aspirin has been the subject of some debate, with 75–325 mg once a day shown to be efficient.[3,7] Larger doses have no apparent additional benefit, but increase the relative risk of upper gastrointestinal bleeding by 5.6% for plain aspirin, and 7% for buffered aspirin.[8] Other adverse effects such as gastrointestinal discomfort (1.22%), rash (0.10%), diarrhea (0.11%), or

Table 6a.1 Antiplatelet, antithrombotic, and anticoagulant agents commonly used

Generic name	*Trade name™*			
	Switzerland	*USA*	*Germany*	*Austria*
Acetylsalicylic acid	Aspirin Tiatral Thrombace Aspegic	Aspirin	Aspirin ASS-ISIS	Aspirin Thrombo AS Herz ASS
Clopidogrel	Plavix	Plavix	Plavix Iscover	Plavix Iscover
Abxicimab	Reopro	Reopro	Reopro	Reopro
Tirofiban	Aggrastat	Aggrastat	Aggrastat	Aggrastat
Eptifibatid	Integrilin	Integrelin	Integrilin	Integrilin
Unfractionated heparin	Liquemin	Heparin	Liquemin	Heparin
Warfarin		Coumadin	Coumadin	
Phenprocoumon	Marcoumar		Marcoumar	Marcoumar
Acenocoumarol	Sintrom			Sintrom
Lepirudin	Refludan	Refludan	Refludan	Refludan
Bivalirudin	Not available	Angiomax	Angiox	Angiox
Argatroban	Not available	Acova	Not available	Argatra

intracranial hemorrhage (0.47%) are rather rare.[4] Aspirin resistance has been reported to vary from 5 to 57% based on a large variety of measurement techniques.[9,10] Until further data are forthcoming, we do not recommend laboratory testing for patients with aspirin resistance nor do we recommend the use of alternative agents. Similar conclusions have been reached by the Working Group on Aspirin Resistance.[11]

A minority of patients are unable to tolerate aspirin because of allergic reactions and hypersensitivity, which can be clinically manifest as respiratory tract disease (rhinitis and asthma, 10%) or urticaria/angioedema (0.07 to 0.2%).[12] We do recommend the use of alternative agents such as clopidogrel if appropriate.

Clopidogrel is an effective antithrombotic agent that blocks the activation of platelets by irreversible binding to the adenosine diphosphate (ADP) receptors. This, in turn, prevents ADP-dependent activation of the glycoprotein IIb/IIIa (GP IIb/IIIa) complex, the primary platelet receptor for fibrinogen, and von Willebrand factor, the final common pathway in platelet aggregation.[13] Clopidogrel given 75 mg daily inhibits platelet aggregation by 25 to 30% on the second day of ingestion, and reaches steady state (50 to 60% inhibition) after 4 to 7 days. A loading dose of 300 to 600 mg accelerates its activity and is recommended if an urgent endovascular intervention is planned and the patient was not on aspirin or clopidogrel before. In the CAPRIE trial,[13] the efficacy of 75 mg of clopidogrel daily was compared to aspirin 325 mg for secondary prevention of atherothrombotic events. Clopidogrel was marginally more effective than aspirin and resulted in a moderately lower rate of gastrointestinal bleeding (0.5% vs 0.7%). Due to high costs its prescription is still limited to patients intolerant to aspirin, or after coronary stenting, acute coronary syndrome, and cerebrovascular insult with additional risk factors.[4,14,15] To date, no data exist to support the routine use of clopidogrel or aspirin plus clopidogrel in patients with peripheral arterial disease (PAD) undergoing peripheral endovascular interventions, although the majority of interventionalists advocate clopidogrel on top of aspirin for at least for 28 days.[14,16]

Life-threatening bleeding was shown to be increased when comparing single (aspirin or clopidogrel) antiplatelet with dual (aspirin plus clopidogrel) antiplatelet therapy given for longer terms (CURE[14] 1.8% vs 2.2%, MATCH[15] 1.3% vs 2.6%); whether this is clinically relevant for short-term therapy after peripheral endovascular interventions is uncertain (it probably is not).

A history of gastrointestinal bleeding is associated with the highest risk of recurrent bleeding. In a recent study 320 patients with a history of gastrointestinal bleeding were randomized to receive 75 mg clopidogrel daily or 80 mg of aspirin plus esomeprazole at a dose of 20 mg daily. The bleeding rate was 8.6% (96% CI, 4.1 to 13.1%) versus 0.7% (95% CI, 0 to 2.0%, $p = 0.001$), underlining the need to combine aspirin as well as clopidogrel therapy with proton pump inhibitors to avoid serious bleeding complications.[17] Clopidogrel non-responders have been reported to vary between 25 and 30%, of which the clinical relevance has not been adequately established.

Intravenous *platelet GP IIb/IIIa receptor inhibitors* have shown convincing clinical efficacy in percutaneous coronary interventions (PCIs), unstable angina/non-Q-wave myocardial infarction, and in combination with thrombolytics in myocardial infarction. Indication for 'off-label' use in peripheral interventions is more restricted, because its application has to be balanced against bleeding complications and high costs. At present, its adjunctive use during peripheral endovascular interventions is justified in patients being at risk of early re-occlusion, i.e. subacute or long-segment arterial occlusions, poor run-off, residual intraluminal thrombus, or profound distal embolization.[18]

Abciximab, a monoclonal antibody that inhibits the binding of fibrinogen to platelet GP IIb/IIIa receptors, is the most widely studied of the GP IIb/IIIa inhibitors. A bolus of 0.25 mg/kg was found to result in approximately 80% receptor blockade, needed to be clinically efficient. Gradual recovery of platelet function occurs over time, with bleeding times returning to near-normal values by 12 hours. A large-sized randomized clinical trial (RIO trial) to test the safety and efficacy of the adjunctive use of abciximab (0.25 mg/kg bolus, followed by infusion of 0.125 μg/kg/min for 12 hours) during endovascular revascularization of long-segment femoro-popliteal occlusions is underway. Bleeding and thrombocytopenia represent the most frequent serious adverse effects of abciximab treatment. In a randomized study performed at our center, all bleeding complications associated with abciximab were limited to the access site (abciximab vs placebo; OR 2.9, 95% CI 1.04 to 8.2, $p = 0.04$). None of the patients had to be treated by red blood cell substitution or surgery, nor needed intensive care. There was a non-significant trend for more local bleedings in patients with additional heparin infusion after the procedure (OR 1.51, 95% CI 0.44 to 5.24), and more bleeding with higher age, female sex, increased creatinine, and larger size of sheath.[18]

A significant increase in major bleeding in patients treated with abciximab and concomitant heparin was also described in the EPIC trial.[19] A reduction in concomitant heparin dosage (70 U/kg with the introduction of an arterial sheath; followed by infusion up to a maximum of 7 U/kg/hour), and more rapid sheath removal greatly reduces bleeding owing to abciximab. Thrombocytopenia with a platelet count <50 000 cells/μL is reported to vary between 1 and 2% of cases treated.[20] In almost all cases, thrombocytopenia can be resolved by withdrawing the offending drug and, if necessary, by platelet transfusion. Spontaneous recovery occurs within 5 to 7 days.[19,21]

Results of a randomized clinical pilot trial (PROMPT) on intra-arterial pulse-spray infusion thrombolysis using urokinase in combination with abciximab or placebo were presented by Duda, Tepe, and colleagues.[22,23] There were 70 patients with acute or sub-acute non-limb–threatening ischemia enrolled in the study. Results showed a 9% amputation rate in patients treated in combination with abciximab vs 22% in patients treated with placebo, whereas non-invasive arterial measurements (i.e. ankle–brachial index) were comparable in both groups. The dose of urokinase and time required for vessel reopening were lower in patients treated in combination with abciximab. However, the non-fatal major bleeding rate was 8% in the urokinase plus abciximab arm.[22]

Anticoagulant agents

Unfractionated heparin (UFH) is traditionally administered during endovascular interventions to prevent expansion of thrombi, embolization, and new thrombus formation. Heparin complexes with endogenous antithrombin III and inactivates coagulation factors IIa, IXa, Xa, XIa,

and XIIa, but it does not resolve already existing thrombus, thus limiting its efficiency. The half-life of heparin is approximately 60 minutes depending on the dose administered, and is prolonged in patients with renal or hepatic dysfunction. Despite widespread use, there are no solid recommendations regarding dosing of heparin, as no randomized study has established the beneficial role of any antithrombotic agent during peripheral endovascular interventions. With this uncertainty in mind, heparin is commonly administered as a bolus of 50 to 100 IU/kg following vascular access, supplemented by 25 to 50 IU/kg every 60 to 90 minutes or adjusted based on ACT measurements until the procedure is finished.[24] Heparin in combination with GP IIb/IIIa inhibitors increases the risk of major bleeding up to 14% and minor bleeding up to 7.4%, respectively.[19,25]

In addition to its well-known bleeding complications, heparin may induce immune-mediated platelet activation leading to heparin-induced thrombocytopenia with more than 5 days of treatment, a condition that is rare but potentially fatal if not recognized in the early state.

Low molecular weight heparins (LMWH) are derived from UFH by chemical and enzymatic depolymerization and, like heparin, exert their major anticoagulant effects by activating antithrombin. LMWH has reduced antifactor IIa activity relative to antifactor Xa activity. It has a more favorable benefit/risk ratio and superior pharmacokinetic properties compared to UFH. There are no firm clinical data reporting a significant effect on overall mortality or cardiovascular events for LMWH in patients with intermittent claudication and no convincing data exist for their routine use in peripheral endovascular interventions. We prefer the use of UFH during peripheral interventions. Advantages of UFH over LMWH are two-fold: firstly the possibility to adapt the dose in severe renal insufficiency, and secondly the possibility to neutralize the antithrombin activity by protamine in case of severe bleeding complications.

Oral anticoagulation: there are no firm clinical data reporting a significant effect on overall mortality or cardiovascular events of vitamin K antagonists in patients with intermittent claudication. Therefore, there is no firm indication for oral anticoagulation in PAD as the complexity of management and bleeding risks seem to far outweigh the benefits, unless the patient has other concomitant diseases needing anticoagulation such as atrial fibrillation.

Direct thrombin inhibitors: in contrast to heparin, which blocks thrombin generation indirectly, thrombin inhibitors directly bind to thrombin and block the interaction with its substrate fibrinogen. Direct thrombin inhibitors are increasingly used with encouraging success rates.

- *Hirudin* inhibits thrombin by irreversible binding to two sites of the thrombin molecule; no specific antidote exists. Hirudin is cleared by the kidney and should not be used in patients with renal failure. The TIMI 9B trial[26] in the coronary settings compared hirudin (0.1 mg/kg bolus, followed by infusion of 0.1 mg/kg per hour) to heparin as an adjunct to thrombolytic therapy and reported hirudin to be at least as effective as heparin. Major hemorrhage was similar in the heparin (5.3%) and hirudin (4.6%) groups; intracranial hemorrhage occurred in 0.9% of heparin and 0.4% of hirudin treated patients, respectively.
- *Lepirudin*, a recombinant derivative of hirudin, is the prototype of a direct thrombin inhibitor. The dose for patients with normal renal function is a bolus of 0.4 mg/kg followed by infusion at 0.15 mg/kg per hour. The effect is monitored by measurement of the activated partial thromboplastin time (aPTT). Lepirudin is safe and effective for patients with heparin-associated antiplatelet antibodies.[27]
- *Bivalirudin* is a synthetic polypeptide, an analog of hirudin, which binds to the active site of thrombin. Its plasma half-life is 25 minutes after intravenous injection and only a fraction is excreted via the kidneys. Potential benefits of bivalirudin over heparin include reduced periprocedural thrombosis, more reliable anticoagulation with a reduced need for activated clotting time measurements, and fewer bleeding complications.[28] It was demonstrated to be superior to heparin in reducing ischemic events in the REPLACE-2 trial.[29] Except for observational results reported by single centers, no evidence exists for the use of bivalirudin in peripheral endovascular interventions.

Table 6a.2 Contraindication for thrombolysis and GP IIb/IIIa inhibitors

Absolute contraindications
Active clinically significant bleeding
Intracranial hemorrhage
Presence or development of compartment syndrome
Relative contraindications
Cardiopulmonary resuscitation within the past 10 days
Major non-vascular surgery or trauma within the past 10 days
Uncontrolled hypertension (systolic >180 mmHg or diastolic >100 mmHg)
Puncture of non-compressible vessel
Intracranial tumor
Recent eye surgery
Neurosurgery (intracranial, spinal) within the past 3 months
Intracranial trauma within 3 months
Recent gastrointestinal bleeding within the past 10 days
Established cerebrovascular event (including transient ischemic attacks) within the past 2 months
Recent internal or non-compressible hemorrhage
Hepatic failure
Bacterial endocarditis
Pregnancy and immediate postpartum status
Diabetic hemorrhagic retinopathy
Life expectancy <1 year

- *Argatroban* is a synthetic direct thrombin inhibitor with activity against free and clot-bound thrombin. Standard dosing for heparin-induced thrombocytopenia is 2 μg/kg per minute intravenously titrated to achieve an aPTT 1.5 to 3 times control.[30] In the settings of heparin-induced thrombocytopenia patients undergoing PCI, argatroban has been used at a dose of 25 mg/kg per minute following a 350 mg/kg bolus. The maintenance dose is titrated to achieve an activated clotting time of 250–300 seconds, with results comparable to historic heparin controls.[31] Despite multiple studies reporting the usefulness of direct thrombin inhibitors in the coronary circulation, its use in peripheral vascular interventions has not been well established. Extrapolation of data from PCI to the peripheral interventional field is difficult. More trials specifically looking at interventions in the periphery are clearly warranted.

FACTORS IDENTIFYING PATIENTS AT RISK FOR BLEEDING COMPLICATIONS

Contraindication for pharmacologic therapy is based on medical conditions thought to increase the risk of local and systemic bleeding. General attention must be paid to patient-related risk factors, which identify them for increased bleeding complications, such as higher age, female sex, increased creatinine, larger size of sheaths, and a higher dose or a combination of antiplatelets and anticoagulants. A history of gastrointestinal bleeding is associated with the highest risk of recurrent bleeding. Absolute and relative contraindications of intravenous thrombolysis as defined by the National Institute of Health[32] were also adopted for off-label use of *platelet GP IIb/IIIa receptor inhibitors* (Table 6a.2).[33] According to clinical experience and recommended caveats, the list of relative contraindications should be completed by severe renal failure (serum creatinine > 2.5 mg/dl), genitourinary bleeding of clinical significance within the previous 6 weeks, a history of bleeding diathesis a platelet count < 100 000/mm^3, arteriovenous malformations or aneurysms, vasculitis, and contraindications or known allergic reactions to GP IIb/IIIa inhibitors.

BLEEDING COMPLICATIONS OF SPECIFIC INTERVENTIONAL STEPS AND TOOLS

Major differences in pharmacotherapy-associated complications in different vessel areas have been observed. Pharmacotherapy-associated bleeding

in abdomino-pelvic arteries may be life-threatening and warrants urgent diagnostic work-up with angiography or computer tomography. Bleeding in peripheral arteries of the limb can be diagnosed by ultrasound, or by angiography for confirming the diagnosis and concomitant therapeutic intervention.

METHODS TO DETECT POTENTIAL COMPLICATIONS – WHICH DIAGNOSTIC STEPS ARE NEEDED ROUTINELY TO RULE OUT OR IDENTIFY COMPLICATIONS

Crucial in reducing the risk of bleeding is to recognize risk factors and to reconsider indications before administration of antiplatelets, anticoagulants, or their combination. Most risk factors can be noted from the patient history. Baseline laboratory assessment emphasizing the plasma coagulation system, hematologic parameters, and renal function is clearly needed prior to each intra-arterial intervention. In cases with a suspicion of hepatic dysfunction, liver enzymes should be assessed. Ultrasound and Doppler analysis may provide additional information about the target lesion and the access site. In cases where ultrasound cannot be performed (e.g. adipositas, multilevel arterial disease) diagnostic angiography or MR angiography should be performed first in order to plan the definitive intervention, thus minimizing periprocedural complications.

When abciximab is administered, platelets need to be followed at 4 and 12 to 24 hours after the intervention in order to recognize thrombocytopenia during maintenance infusion of the drug.

To minimize bleeding complications with therapeutic doses of heparin the aPTT is monitored. The aPTT should be measured approximately 6 hours after the bolus dose of heparin, and the start of maintenance infusion, which should be adjusted according to the result.

ENDOVASCULAR, SURGICAL, OR MEDICAL TECHNIQUES TO RESOLVE COMPLICATIONS

When clinically relevant bleeding of the vessel area is suspected, diagnostic work-up should be performed, according to the urgency of the situation, to identify the bleeding site and potential appropriate ways to treat the underlying cause. Contrast-enhanced computer tomography or angiography is the diagnostic tool of choice. Discontinuation of antiplatelet agents and anticoagulation drugs has to be assessed according to the condition of the patient and the severity of bleeding.

Duplex ultrasound has a high sensitivity and specificity in detecting a false aneurysm (pseudoaneurysm) at the access site,[34] and specific treatment,

Figure 6a.1 Clinical finding of a huge pseudoaneurysm in a patient after left-sided access for endovascular intervention (oral anticoagulation, INR 3).

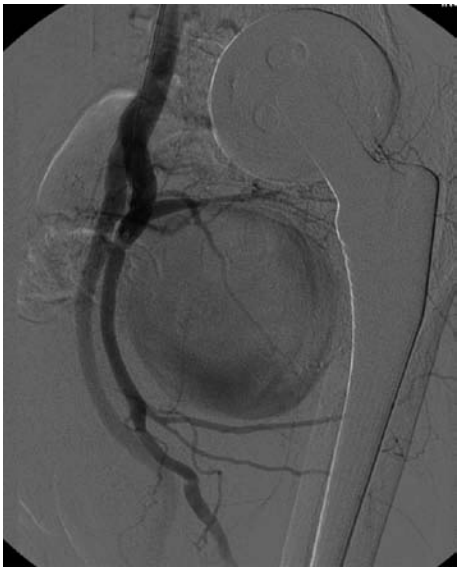

Figure 6a.2 Angiographic documentation of the pseudoaneurysm emerging from the deep femoral artery.

i.e. ultrasound-guided compression or, in carefully selected patients, ultrasound guided thrombin injection, can be initiated.[35] Ultrasound-guided thrombin injection is particularly useful in patients on anticoagulants or on GP IIb/IIIa inhibitor therapy and with a low probability of successful closure by ultrasound-guided compression alone. Endovascular coil embolization or covered stent deployment are options to seal frank bleeding related to vessel laceration or rupture, but can also be used to seal the neck of a large pseudoaneurysm in cases where surgery bears a substantial risk and the other options have failed (Figures 6a.1–6a.3). Surgery always remains an option if other less invasive measures fail.

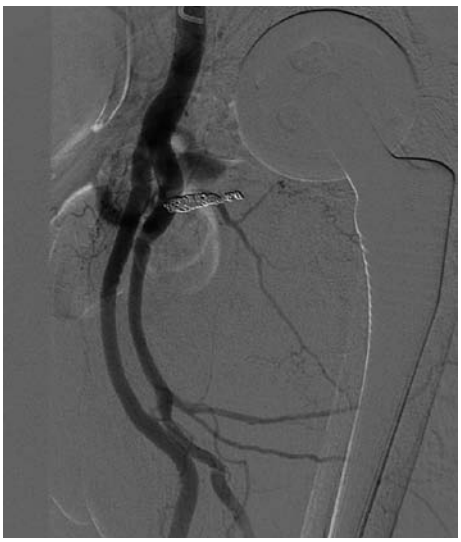

Figure 6a.3 Exclusion of the pseudoaneurysm after coil embolization.

In cases of bleeding complications due to aggressive anticoagulation with heparin, 1 mg of protamine as a bolus rapidly neutralizes approximately 100 U of heparin. The effect of GP IIb/IIIa inhibitors can be reversed by transfusion of platelets. No direct antidotes exist to counteract the effect of aspirin, clopidogrel, LMWH, and direct thrombin inhibitors. Serious, acute bleeding complications need replacement of fluid (saline 0.9%, colloidal fluids), transfusion of erythrocytes, and rarely administration of platelets, fresh frozen plasma, or prothrombin complex concentrate.

METHODS TO AVOID COMPLICATIONS

The best approach to avoid local bleeding complications at the access site is to use the smallest introducer sheaths possible, and to remove them rapidly at the end of the procedure. The indication for an aggressive dual antiplatelet therapy or anticoagulation should always be balanced against the risk/benefit ratio for the patient treated. A reduction in the dosage of concomitant heparin and rapid sheath removal reduce bleeding complications due to abciximab.[36] Comorbidities and laboratory parameters should be available before each intervention, and additional diagnostic work-up should be performed if necessary.

Table 6a.3 Recommended dose of commonly used antiplatelet, antithrombotic, and anticoagulant agents

Generic name	*Dosage*	*Plasma half-life*
Acetylsalicylic acid	75 to 325 mg daily; we recommend 100 mg daily for PAD – higher doses do not provide more benefit, but are associated with higher bleeding complications[14]	2 to 3 hours
Clopidogrel	Loading dose 300 mg; maintenance dose 75 mg daily	8 hours
Abciximab	0.25 mg/kg bolus, followed by maintenance infusion of 0.125 μg/kg/min for 12 hours	10 to 30 min
Unfractionated heparin	50 to 100 IU/kg bolus with vascular access, followed by 25 to 50 IU/kg every 60 to 90 min or adjusted according to ACT until the procedure is finished	Dose-dependent 1 hour (100 IU/kg) 2.5 hours (400 IU/kg)

Table 6a.4 Reversing the effects of antiplatelet, antithrombotic, and anticoagulant agents

Generic name	*Antidote*
Acetylsalicylic acid	No direct antidote available; reverse the effect by transfusion of platelets if appropriate
Clopidogrel	No direct antidote available; reverse the effect by transfusion of platelets if appropriate
Glycoprotein IIb/IIIa	No direct antidote available; reverse the effect by transfusion of platelets if appropriate
Unfractionated heparin	1 mg of protamine rapidly neutralizes approximately 100 U of unfractionated heparin, fresh frozen plasma
Low molecular weight heparin	No direct antidote available; reverse the effect by transfusion of fresh frozen plasma if appropriate
Vitamin K antagonist	Vitamin K (2 to 10 mg) orally or intravenously depending on the urgency of the situation, fresh frozen plasma, prothrombin complex concentrate, or recombinant factor VIIa if appropriate
Thrombin inhibitors	No direct antidote available; reverse the effect by transfusion of platelets if appropriate

SUMMARY

Endovascular therapy for PAD is rapidly expanding. Therefore, there is clearly a need for more evidence on periprocedural antiplatelet and anticoagulant treatment during and after these interventions. To date, an intra-arterial UFH bolus during, and dual antiplatelet therapy using aspirin and clopidogrel for 28 days after endovascular therapy represent the most commonly used standard. Access site and gastrointestinal bleeding are the most commonly seen complications, usually managed by local repair, proton-pump inhibitors, and, if needed, fluid replacement and rarely blood transfusion, protamine, or fresh frozen plasma.

CHECK LIST FOR EMERGENCY EQUIPMENT

Be familiar with commonly used drugs, their indication, dosage, and application (Table 6a.3). Be aware of the possibility of reversing the effects of antiplatelet, antithrombotic, and anticoagulant agents (Table 6a.4). Be aware of contraindications for thrombolysis and treatment with GP IIb/IIIa inhibitors. The decision to use abciximab must clearly outweigh the risk of bleeding. Be aware of peri- and postprocedural bleeding complications and recommend close monitoring (vital signs, local puncture site) and proton-pump inhibitors in patients at high-risk for bleeding.

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6b

Complications of thrombolytic therapy in peripheral vascular interventions

Jose A Silva and Christopher J White

Introduction to the frequency and type of complications with thrombolysis • Factors identifying high-risk patients for complications • Methods to detect potential complications • Summary

INTRODUCTION TO THE FREQUENCY AND TYPE OF COMPLICATIONS WITH THROMBOLYSIS

The vascular system is vulnerable to thrombus formation, which may lead to partial or complete interruption of blood flow and may cause tissue hypoxia and result in tissue loss. Therapies aimed at thrombus dissolution are of paramount importance in vascular and endovascular medicine. Fibrinolytic agents have historically been considered the archetype of the thrombus dissolving agents, and have been shown to be of great clinical utility in almost every vascular territory.

The most frequent complications of fibrinolytic therapy are bleeding complications, which vary in severity depending upon the agent use, whether therapy is given systemically or locally, the dose and length of infusion, the clinical circumstances, and the vessel(s) treated. In general terms, the reported incidence of major bleeding complications (defined as intracranial bleeding, or any bleeding requiring transfusion or discontinuation of therapy) ranges from 7 to 45% (see below). Other complications include mild allergic reactions, which are not uncommon and are usually associated with the use of streptokinase; however, serious allergic/anaphylactic reactions are rare and occur in less than 1% of the cases (see below).

FACTORS IDENTIFYING HIGH-RISK PATIENTS FOR COMPLICATIONS

There are well-recognized patient and clinical characteristics which increase the likelihood of complications associated with fibrinolytic therapy and therefore may preclude its use in an absolute or relative degree (Table 6b.1). As a general rule, intravenous thrombolysis is precluded in patients with absolute contraindications, and must be avoided in patients with relative contraindications. The use of intra-arterial thrombolysis in those circumstances requires individual judgment. The choice to proceed with this form of therapy may be considered if the anticipated benefits significantly outweigh potential complications.

Other factors that affect the incidence of complications are related to the specific agent used or those related to the clinical condition for which the thrombolytic agent was used.

Fibrinolytic agent-related complications

It is beyond of the scope of the present discussion to review the pathophysiology of the fibrinolytic system or to address the specific mechanisms of action of each of the current fibrinolytic agents. However, the reader should remember that under physiologic as well as non-physiologic conditions, plasmin is ultimately responsible for

Table 6b.1 Contraindications for intra-arterial fibrinolytic therapy

Absolute contraindications
Profound, intolerable limb ischemia
Active internal bleeding
Cerebrovascular accident within 3 months
Intracranial pathologic condition

Relative contraindications
Recent major surgery or trauma
Minor gastrointestinal bleeding
Severe hypertension
Valvular heart disease
Atrial fibrillation
Endocarditis
Coagulation disorder
Pregnancy
Minor surgery
Severe liver disease
Extra-anatomic axillofemoral bypass graft or knitted Dacron graft

Streptokinase
Known allergy
Recent streptococcal infection
Previous therapy within 6 months

fibrin degradation. It is also important to keep in mind that in conditions of health, fibrin formation and degradation occur in a continuous fashion through the activation of the intrinsic or extrinsic coagulation cascade and intrinsic tissue plasminogen activator. The balance between fibrin production, i.e. clot formation, and fibrin degradation, i.e. thrombolysis or clot degradation, is complex and regulated by multiple intermediaries that will promote or inhibit the formation of plasmin.[1–3]

The ultimate goal of fibrinolytic agents is to promote clot lysis by stimulating the conversion of the proenzyme plasminogen to the active enzyme plasmin (the final step of the fibrinolytic system). However, plasmin is a relatively non-specific protease, capable of hydrolyzing many proteins in addition to fibrin, such as fibrinogen, factors V and VIII, von Willebrand factor, kininogen, and prekallikrein, among others.[1] Consequently, the formation of plasmin may lead to hydrolysis, i.e. degradation, of multiple coagulation factors, potentially enhancing the risk for bleeding complications.

During the process of thrombosis, a large number of plasminogen molecules are incorporated into the clot. This is known as thrombus-bound (or fibrin-bound) plasminogen, to distinguish it from the circulating plasminogen in plasma. It is this fibrin-bound plasminogen which, after activation, leads to thrombus dissolution. Fibrin-specific agents such as tissue plasminogen activator (t-PA), and tenecteplase (TNK) preferentially activate the fibrin-bound plasminogen, whereas non-fibrin-specific agents such as streptokinase (STK), urokinase (UK), and reteplase (r-PA) do not discriminate between bound and circulating plasminogen, and may also cause degradation of circulating fibrinogen and other clotting factors, such as factors V and VIII (Table 6b.2).

Streptokinase

The discovery of streptokinase in 1933 brought about marked interest in the development of fibrinolytic agents that has spanned the past seven decades.[4] Streptokinase is a single-chain non-enzymatic protein produced by β-hemolytic streptococcus. Early clinical experience with this agent was complicated by frequent pyogenic and allergic reactions. Despite technical improvement in its production, streptokinase remains highly antigenic and has the potential for causing allergic reactions.[5] In 1999, the US Food and Drug Administration (FDA) warned of increasing life-threatening events associated with the use of streptokinase. Furthermore, patients with a recent exposure to streptococci and patients recently treated with streptokinase develop high levels of circulating antistreptococcal antibodies capable of neutralizing streptokinase. These individuals are resistant to standard doses of this fibrinolytic agent, requiring higher doses of the drug to exceed the saturation point of existing antibodies.[6]

Streptokinase needs to bind to a molecule of plasminogen before being able to become a plasminogen activator (i.e. requires plasminogen as a cofactor and as a substrate); consequently, fewer plasminogen molecules remain available to turn into plasmin and produce the desired fibrinolytic action, potentially shifting hydrolysis in the direction of other molecules such as fibrinogen and factors V and VIII, among others. These complex interactions of streptokinase make

Table 6b.2 Characteristics of the most commonly used fibrinolytics in peripheral interventions

	Streptokinase	*Urokinase*	*t-PA*	*Reteplase*	*Tenecteplase*
Source	β-Hemolytic streptococcus	Fetal renal cell cultures	Recombinant DNA technology	Plasminogen activator	Recombinant DNA technology
Metabolism	Liver	Liver	Liver	Liver	Liver
Half-life	23 min	16 min	4–5 min	14 min	20–24 min
Fibrin specificity	+	++	+++	++	++++
Advantages	Low cost	Direct activator	Fibrin selective; direct activator	Fibrin selective; direct activator	Fibrin selective; direct activator
Disadvantages	Allergic reactions. Complex interactions	Expensive	Expensive	Expensive	Expensive
Regional infusion doses	5000–10 000 U/h* 30 000–60 000 U/h**	2000–4000 U/min for 1–2 hours; then 1000–2000 U/min	0.05–0.1 U/kg/h	0.5 (0.25–1.0) U/h	0.25–1.0 mg/h
Approved indications	AMI, PE, DVT, arterial thrombosis/embolism	PE, venous catheter occlusion	AMI, stroke, PE, venous catheter occlusion	AMI	AMI

AMI, acute myocardial infarction; DVT, deep venous thrombosis; PE, pulmonary embolism; t-PA, tissue plasminogen activator.
*Low dose; **high dose.

the kinetics, half-life, and bioavailability highly variable and unpredictable.[6,7]

Despite the problem of antigenicity and unpredictable pharmacokinetics, many studies have shown clinical benefits of this agent for the treatment of acute myocardial infarction (MI),[5] or when catheter delivered for the treatment of acute arterial occlusions or deep venous thrombosis (DVT); however, bleeding complications occurred more frequently than with the use of urokinase (see below).[8–10]

A complex of streptokinase and anisoylated plasminogen-streptokinase activator complex (APSAC) or anistreplase was developed in an attempt to solve some of these problems, yet, clinical trials did not demonstrate any improvement in efficacy or decrease in antigenicity with this compound.[6]

Urokinase

This fibrinolytic agent is a serine protease that is normally present in urine as a product of renal tubular cells. Urokinase, in contrast to streptokinase, is a direct activator of plasminogen and is non-antigenic. The lack of circulating antibodies and its direct mechanism of action allow for a predictable dose–response relationship.[6,11]

During the 1990s, urokinase became the preferred fibrinolytic agent in the non-coronary circulation and a great deal of experience was gained with this drug. However, in 1999 Abbott laboratories discontinued its production due to FDA concerns regarding the potential for viral contamination. The safety issues were addressed and the drug was reintroduced in 2002.[12]

In phase I of the thrombolysis or peripheral arterial surgery (TOPAS) trial, three different doses of urokinase (2000, 4000, or 6000 IU/min for 4 hours, followed by 2000 IU/min for a maximum of 48 hours) were compared with surgery for the treatment of acute lower extremity ischemia. The patients who received the intermediate dose achieved comparable rates of complete thrombolysis compared to the low-dose and high-dose regimens (71% versus 67% and 60%, respectively; p = NS). However, the rate of hemorrhagic complications was significantly lower in the intermediate (2%), compared to the low (13%) and high-dose (16%) regimens ($p < 0.05$). In addition, the one-year mortality (14% versus 16%) and amputation-free survival (75% versus 65%) rates were similar in the intermediate dose and surgical patients.[13]

The incidence of major bleeding complications in patients treated for peripheral athero-occlusive disease ranges from 0 to 16%.[14,15] The Prourokinase versus Urokinase for Recanalization of Peripheral Occlusions: Safety and Efficacy (PURPOSE) trial, found a high (16.7%) incidence of major (no intracranial bleeding) and minor bleeding complications in the urokinase group using a maximum loading dose of 250 000 IU, followed by 240 000 IU/h for 4 hours, 120 000 IU/h for the next 4 hours, and 60 000 IU/h thereafter.[15] The incidence of intracranial bleeding with urokinase is in the range of 0 to 2.1%.[16–20]

Tissue plasminogen activator (t-PA)

A great deal of the clinical experience obtained with t-PA has been gained in the last few years, in the period when urokinase was withdrawn from the market.[12] Similar to urokinase, studies using t-PA for thrombolysis differ in dose, infusion length, infusion technique, weight-adjustment, and clinical condition, therefore relatively wide complication ranges have been reported. One study[21] reported an incidence of major bleeding complications and intracranial bleeding of 2.2% and 0%, respectively, compared to rates of 46% and 4% obtained for the same complications in a different report.[22] In addition, doses of t-PA have ranged from 0.25 mg/h to as high as 10 mg/h (40-fold increase). A report summarizing 12 published studies of 1291 patients receiving 13 different dose regimens found a mean incidence of major bleeding complications of 5.1% (range 0 to 17%), and a 0.54% incidence (range 0 to 2.2%) of intracranial bleeding.[23] The complication rates of this last study contrast with a British registry of 697 patients where an 11.9% incidence of major bleedings was observed.[24] When the catheter-directed infusion of t-PA was weight adjusted, in a small prospective study of 35 patients with acute occlusion of native and bypass grafts, no apparent decrease in bleeding complications was observed when compared with historical controls using urokinase; however, patients who received low-dose infusion (0.02 mg/kg/h) had a lower

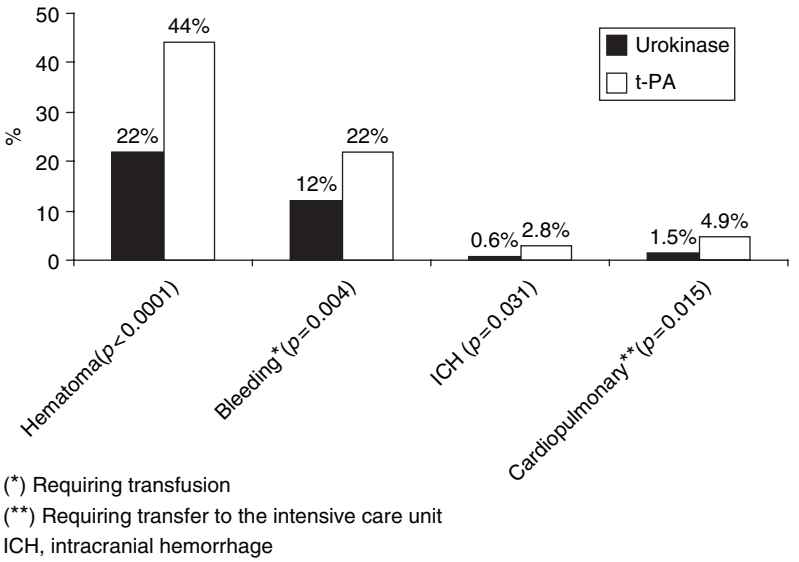

Figure 6b.1 Complication rates of urokinase versus t-PA.[18]

incidence of major bleedings compared to those who received a combined low-dose/high-dose (0.02–0.04 mg/kg/h) regimen (15% versus 46%; $p = 0.06$).[25]

In a consecutive series of 653 patients treated with arterial or venous thrombolysis, Ouriel et al[18] compared the complication rates between t-PA and urokinase. The complication rates were higher in the patients receiving t-PA (Figure 6b.1), but the mortality rate, although also higher in this group, was statistically not different (2.7% versus 6.2%; $p = 0.22$).

Reteplase (r-PA)

Before removal of urokinase from the US market in 1999, there were no data available on the use of r-PA for thrombolysis in the non-coronary circulation. Its introduction for catheter delivery use, in the non-coronary circulation, was supported by trials of acute myocardial infarction showing that this fibrinolytic agent had a similar safety profile to that of t-PA.[26] In a prospective study of 87 patients with three different doses of r-PA, complete lysis rates were similar in the three regimens (84 to 87%); however, bleeding complications were directly proportional to the dose (Figure 6b.2).[27]

In a small registry of 37 patients with acute arterial occlusion ($n = 26$) or DVT ($n = 11$), there

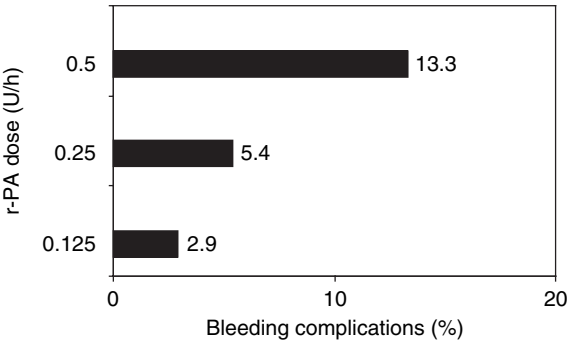

Figure 6b.2 Bleeding complications with three different infusion doses of r-PA in 87 patients with acute arterial occlusion.[27]

were no occurrences of intracranial hemorrhage; however, a similar direct relationship between r-PA dose and bleeding complications was observed in the arterial occlusion group (Figure 6b.3). In the DVT group, procedural bleeding occurred in three (27%) patients. The use of unfractionated heparin in subtherapeutic ($n = 18$) or therapeutic ($n = 8$) doses appeared not to affect the bleeding complications.[28] Reteplase has also been tested for the treatment of deep venous thrombosis with favorable results and a low bleeding complication rate (see below).[29]

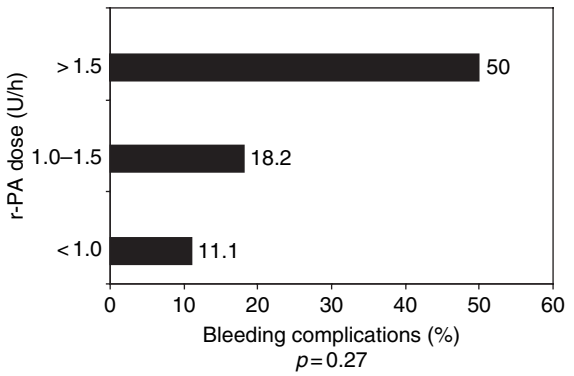

Figure 6b.3 Bleeding complications with three different infusion doses of r-PA in 26 patients with acute arterial occlusions.[28]

Tenecteplase (TNK)

Tenecteplase appears to have an improved safety profile compared to t-PA, in studies of acute myocardial infarction.[30] Compared to other fibrinolytics in the non-coronary circulation, there is still limited experience. In a study of 60 limbs with acute arterial occlusion ($n = 24$) or DVT ($n = 36$) using two different doses of TNK (0.25 or 0.50 mg/h) thrombolysis rates were similar for the arterial (83%) and venous groups (87%), and major bleeding complications occurred in only one case (1.8%).[31] In another small pilot study, 18 patients with arterial ($n = 13$) or venous ($n = 5$) occlusive disease were treated with infusions of 0.25 mg/h. Technical success was obtained in 100% and clinical success in 85% and 80% of the arterial and venous groups, respectively. Major bleeding complications occurred in only one patient (5.5%).[32]

Tenecteplase has also been used in conjunction with platelet IIb/IIIa inhibitors. In a pilot study in 16 patients with acute arterial ($n = 11$) or venous ($n = 5$) thrombo-occlusive disease, TNK was catheter delivered as a 5 mg bolus, followed by 0.25 mg/h in infusion of intravenous eptifibatide (180 μg/kg double bolus, followed by 1 μg/kg/min infusion). Clinical success was obtained in 82% of the arterial and 80% of the venous cases, and major bleeding occurred in only one case (6.3%).[33] In a larger study, 48 patients with acute limb ischemia were treated with TNK at doses of 0.5 mg/h ($n = 22$) or 0.25 mg/h ($n = 26$), in conjunction with periprocedural unfractionated heparin (500 U/h) and periprocedural and postprocedural tirofiban for 6 to 12 hours. Complete thrombolysis was obtained in 73% (mean infusion time of 7.5 hours and mean TNK dose of 4.8 mg). Major bleeding complications occurred in 10.4% without intracranial hemorrhage or deaths.[34]

Although the results of these small reports are promising, larger studies testing catheter delivered TNK are necessary to determine its clinical effectiveness compared to other fibrinolytic agents. Whether the addition of a platelet IIb/IIIa inhibitor will enhance the thrombolytic success of TNK or other fibrinolytic agents without increasing bleeding complications remains to be seen.

Complications related to specific clinical applications of thrombolysis

Acute arterial occlusion, limb ischemia

The use of fibrinolytic therapy for acute limb ischemia has emerged as the preferred treatment modality in selected patients. Candidates for thrombolysis must be able to tolerate ischemia for the duration of the infusion, which is one of the main limitations of this revascularization strategy.

The largest experience of intra-arterial fibrinolysis for the treatment of limb ischemia has been with urokinase and t-PA. Studies comparing the effectiveness of these two drugs have differed in the doses used and the sample sizes (Table 6b.3).[18,21,22,35–39] All but one study demonstrated that t-PA is slightly more effective than urokinase in achieving complete thrombolysis (Figure 6b.4), while t-PA carries a higher incidence of bleeding complications (Figure 6b.5).These results have been confirmed by a literature review of 48 studies comparing complications of 2226 urokinase-treated patients and 1927 t-PA-treated patients for peripheral arterial occlusions.[40] In this report the major amputation rate was similar in both groups (7.9% versus 7.2%; p = NS); however, the bleeding complications and mortality rates were significantly higher in the t-PA-treated patients (Figure 6b.6).

Despite evidence showing the efficacy of thrombolytic therapy in the treatment of acute arterial occlusion, it was not until lysis was

Table 6b.3 Doses used in eight studies comparing urokinase and t-PA

Study (reference)	*Type of occlusion*	*# of patients*	*Urokinase dose (IU)*	*t-PA dose*
Meyeroviz et al[35]	Leg occlusion	32	60 K bolus; 240 K/h × 2 h, 120 K/h × 2 h, then 60 K/h up to 20 h	10 mg bolus, then 5 mg/h
STILE trial[36]	Leg occlusion	249	250 K bolus; 240 K/h × 4 h, 120 K/h	0.05–0.1 mg/kg/h
Schweizer et al[37]	Leg occlusion	120	60 K/h	5 mg bolus, then 5 mg/h
Cina et al[22]	Leg occlusion	58	150 K bolus then 50 K/h	5 mg bolus, then 1 mg/h
Ouriel et al[18]	Leg occlusion/DVT	653	4 K/min	0.05–0.1 mg/kg/h
Mahler et al[38]	Leg occlusion	234	100 K/h*, or 20 K/cm of thrombus/h**	2.5 mg/h*, or 0.5 mg/cm of thrombus/h**
Shortell et al[39]	Leg occlusion/DVT	73	240 K × 4 h, then 120 K/h	2 mg/h
Sugimoto et al[21]	Leg occlusion/DVT	70	90 K/h–120 K/h	0.5–1.0 mg/h

*Hess technique; **Schneider technique. DVT, deep venous thrombosis; h, hour; K, 1000 IU.

compared to surgery, and showed comparable clinical benefits, that thrombolysis was accepted as a viable alternative treatment to surgery. In the Rochester trial, a non-randomized study, 114 patients with acute peripheral thrombotic arterial ischemia were treated with surgery or urokinase. The 12-month amputation rate was 18% for both groups, but the mortality rate in the thrombolysis group was only a third of the mortality rate observed with surgery (16% versus 42%; $p = 0.01$).[41]

Subsequently two prospective randomized trials compared thrombolysis versus surgical revascularization for thrombotic occlusion causing limb ischemia.[16,36] Both studies showed similar amputation and mortality rates in the thrombolysis and the surgical groups. However, major bleeding complications were higher in the thrombolytic group, in both the STILE trial (5.6% versus 0.7%; $p = 0.014$), and the TOPAS trial (13% versus 6%; $p = 0.005$).

Deep venous thrombosis

Anticoagulation with heparin (unfractionated or low-molecular-weight heparin) has been the standard treatment for deep venous thrombosis (DVT). This therapy is effective in preventing pulmonary embolism, but has limitations in preventing chronic postphlebitis in as many as 90% of the patients following DVT.[42] Studies using systemic fibrinolysis have shown that the use of these agents is as effective as heparin in preventing pulmonary embolism and mortality, but superior to heparin and warfarin in achieving early thrombus dissolution (~ 45%) and in decreasing postphlebitic syndrome.[43,44] In a study that pooled results from eight prospective randomized trials, comparing systemic streptokinase with heparin, it was found that patients treated with fibrinolysis achieved a rate of thrombus dissolution almost three times more frequently than those treated with heparin; however, the incidence of major bleeding complications was also nearly four times higher in the streptokinase-treated patients.[44]

The magnitude of early thrombus dissolution has been shown to be increased when the fibrinolytic agent is locally infused compared to when it is given systemically. In addition, catheter-directed therapy has a positive impact on patients' quality of life by preserving valve

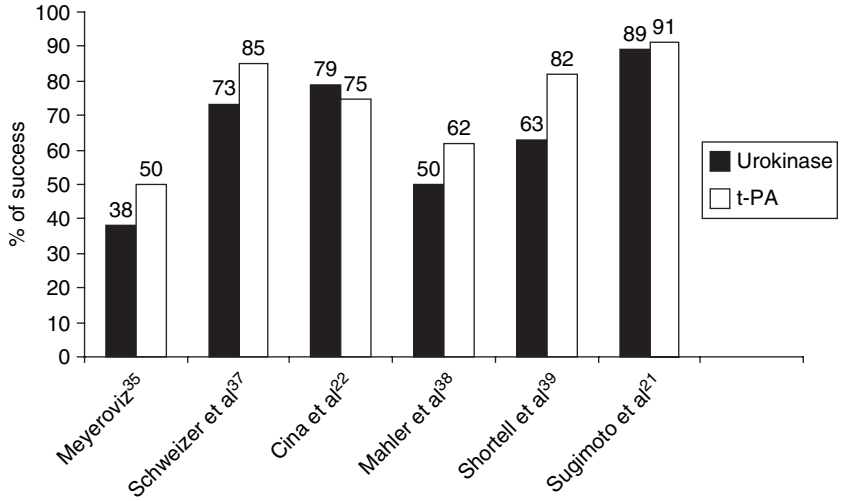

Figure 6b.4 Thrombolysis effectiveness: urokinase versus t-PA.[21,22,35–39]

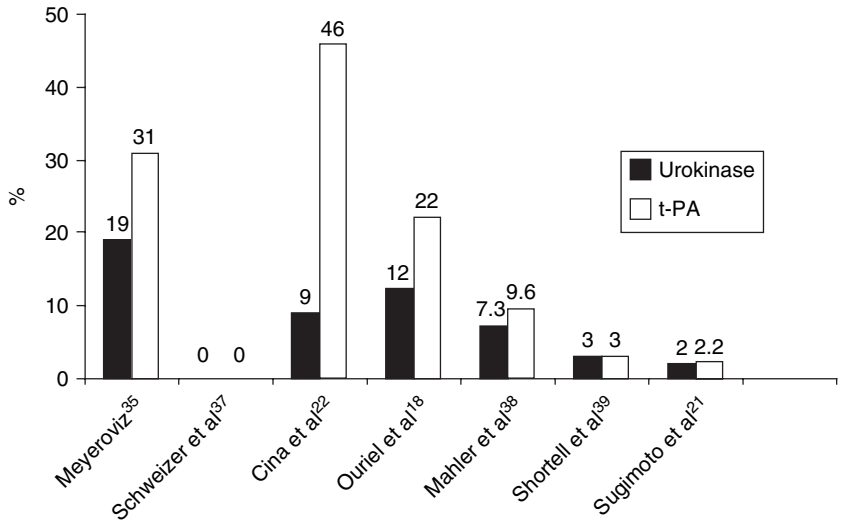

Figure 6b.5 Major bleeding complications: urokinase versus t-PA.[21,22,35–39]

function and decreasing the development of post-phlebitic syndrome.[45] In one multicenter registry of 473 patients treated with catheter-delivered urokinase, complete thrombolysis was obtained in 31% and substantial thrombolysis (50 to 99% thrombus resolution) in 83%. Complete thrombolysis was significantly higher in acute (≤10 days) than in chronic (>10 days) DVT (34% versus 19%; $p < 0.01$). Major bleeding complications occurred in 11% (the majority at the puncture site), and mortality was less than 1%.[46]

The experience with catheter-delivered t-PA or r-PA for the treatment of DVT is limited. In an early small study of 24 patients treated with t-PA (at 3 mg/h), the success rate was 75% but major bleeding complications occurred in 25%.[47] In a study comparing t-PA and urokinase for arterial occlusion ($n = 39$) and DVT ($n = 54$) in 93 limbs,

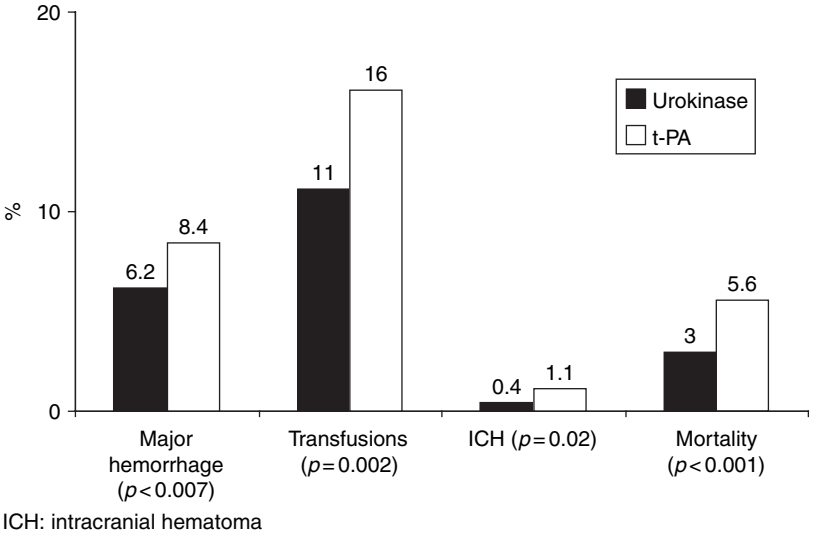

Figure 6b.6 Major bleeding complications and mortality: urokinase ($n = 2226$) versus t-PA ($n = 1927$).[40]

the efficacy (84% vs 88%; $p = 0.69$) and bleeding complication rates (4.4% vs 4.2%) were similar in the urokinase and t-PA groups.[21]

A pilot study tested catheter-delivered r-PA in 25 patients with DVT.[29] In this study 20 (80%) patients received 0.5 U/h, and five (20%) patients received 1.0 U/h of r-PA, in addition to subtherapeutic unfractionated heparin doses of 300–400 U/h. Thrombolytic success was obtained in 23 (92%) patients, and there was only one (4%) major bleeding complication. There were two patients in whom the nadir of fibrinogen was below 90 mg/dL, requiring transfusion of fresh frozen plasma. A retrospective analysis of 74 patients and 82 limbs with DVT compared catheter-delivered urokinase, t-PA, and r-PA.[48] Complete (71%, 66%, 50%; $p = 0.63$) and complete plus partial (97%, 97%, 100%, $p = 0.83$) resolution of thrombus, as well as major complication rates (5.3%, 3.1%, 8.3%, $p = 0.88$), were similar in the urokinase, t-PA, and r-PA groups respectively.

Pulmonary embolism

In the US pulmonary embolism (PE) is responsible for over 50 000 deaths annually, with a case fatality rate of 15% at 3 months.[49,50] However, the mortality rate more than doubles in patients who develop hemodynamic instability or right ventricular dysfunction.[51] The standard treatment for this condition has been anticoagulation with heparin followed by a 3 to 6 month course of warfarin anticoagulation.[52] Several randomized, controlled trials comparing thrombolytic therapy with heparin in patients with an acute PE have demonstrated more rapid clot resolution in those treated with fibrinolysis. [53–59] However, a beneficial effect of thrombolytic therapy on clinical outcomes, including the recurrence of PE and mortality, has been difficult to demonstrate. In addition, some investigators have suggested that treatment with fibrinolytic agents increases major bleeding complications and they therefore recommend a more conservative approach.[60]

A meta-analysis[61] involving 11 prospective randomized trials and 748 patients compared patients treated with fibrinolytic therapy versus heparin for the endpoints of mortality, recurrent PE, and bleeding complications. Compared with heparin, thrombolytic therapy was associated with a non-significant reduction in recurrent PE or death (6.7% versus 9.6%; OR 0.67, 95% CI 0.40 to 1.12), a non-significant increase in major bleeding (9.1% versus 6.1%; OR 1.42, 95% CI 0.81 to 2.46), and a significant increase in bleeding complications (22.7% versus 10.0%; OR 2.63, 95% CI 1.53 to 4.54) (Figure 6b.7). Thrombolytic therapy compared to heparin was associated with a significant reduction in recurrent PE or death in trials that enrolled patients with hemodynamically

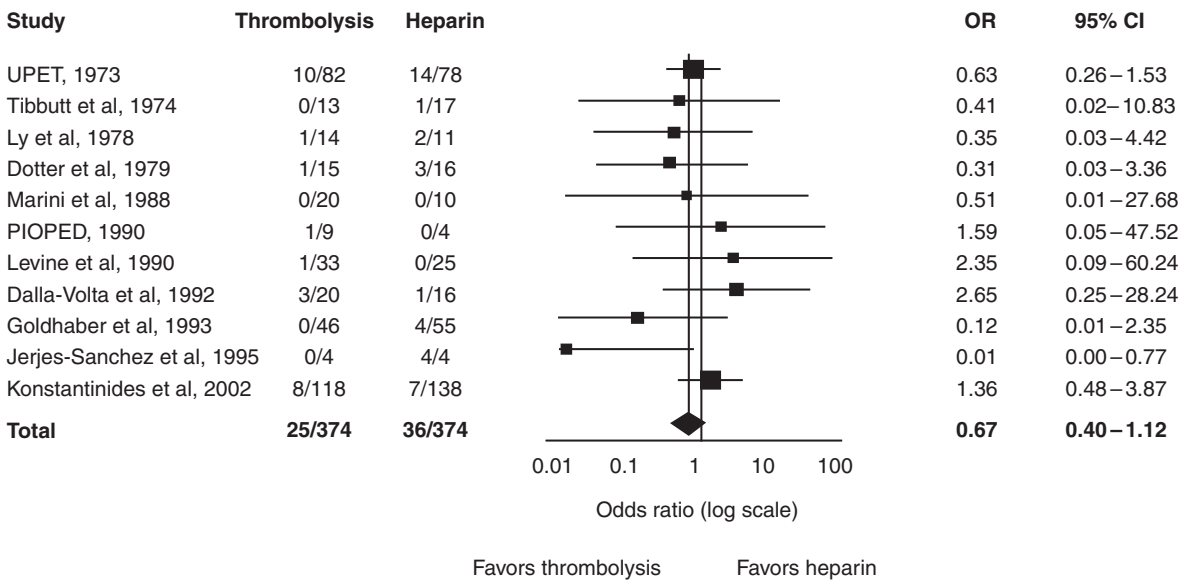

Figure 6b.7 Recurrent PE or death in trials comparing thrombolysis with heparin for initial treatment of acute pulmonary embolism.[61] Reproduced with permission from Wan et al. Circulation 2004; 110: 744–9.

unstable PE (9.4% vs 19.0%; OR 0.45, 95% CI 0.22 to 0.92) but not in trials that excluded these patients (5.3% vs 4.8%; OR 1.07, 95% CI 0.50 to 2.30). An earlier meta-analysis comparing fibrinolytic therapy versus heparin also showed a significant increase in major bleeding complications in the thrombolysis-treated patients (Figure 6b.8).[62]

Acute ischemic stroke

In 1996, the FDA approved t-PA for the treatment of acute ischemic stroke based on its safety and effectiveness when given within 3 hours of symptom onset.[63] Its approval was based on the results of the National Institute of Neurological Disorders and Stroke (NINDS) Recombinant Tissue Plasminogen Activator Stroke Study, in which 624 patients with ischemic stroke were treated with 0.9 mg/kg of t-PA within 3 hours of the onset of symptoms.[64] In the t-PA group, 31 to 50% had complete or near complete recovery at the 3-month follow-up, whereas in the placebo group this was achieved in only 38% ($p < 0.05$), and these differences persisted one year after the event. However, the mortality rate was similar in both groups, and the incidence of symptomatic brain hemorrhage was much higher in the t-PA treated group (6.1% vs 0.6%; $p < 0.05$). Interestingly, the benefits of intravenous thrombolysis for acute stroke were not duplicated in three other trials.[65–67] However, only 14% of the patients received thrombolysis within 3 hours of symptom onset, whereas in the NINDS, 99.7% did (48% within 90 minutes).

The use of intra-arterial thrombolysis in acute ischemic stroke with angiographically documented occlusion in the middle cerebral artery or a first-order branch was shown to yield even higher reperfusion rates. Using pro-urokinase, partial or complete reperfusion was achieved in 67% compared to 18% in the heparin alone group ($p < 0.001$), when therapy was given with 2 hours of symptom onset in the PROACT II study.[68] The primary outcome measure analyzed was the ability to live independently 3 months following the stroke and was much higher in the pro-urokinase group than in the heparin alone group ($p < 0.05$). However, this better clinical outcome in the pro-urokinase group was also achieved at the expense of a higher intracranial bleeding rate (10% versus 2%; $p < 0.06$). A higher NIHSS score, longer time to recanalization, lower platelet count, and hyperglycemia, have been found to be independent predictors for hemorrhagic transformation

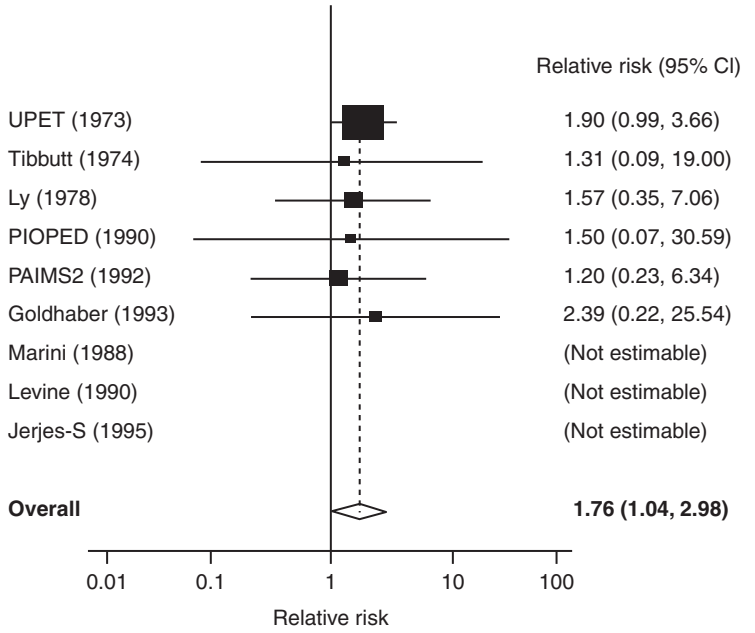

Figure 6b.8 Graphic representation of the relative risk (95% confidence interval [CI]) of major hemorrhage in the thrombolysis versus heparin groups.[62] Reproduced with permission from Thabut et al. J Am Coll Cardiol 2002; 40: 1660–7.

in patients receiving intra-arterial thrombolytic therapy.[69] There are no randomized data comparing intra-arterial versus intravenous thrombolytic therapy for the treatment of acute ischemic stroke.

Stent thrombosis

Percutaneous transluminal angioplasty with adjuvant stent placement has emerged as one of the best and most frequently used revascularization strategies in many vascular territories. However, stent thrombosis, although a relatively infrequent complication, may occur and frequently carries dire consequences. Stent thrombosis has been reported in essentially every vascular territory, with an incidence as high as 20% after femoropopliteal arterial revascularization in early series.[70] Although the true incidence of this complication is difficult to estimate, it appears to be significantly lower in more recent studies of femoro-popliteal, iliac, renal, mesenteric, or carotid circulation with a reported incidence of less than 2% in most series,[71–78] and it is often related to suboptimal stent expansion or vascular dissection adjacent to the stent.[79]

Fibrinolytic therapy has been reported to be successful in treating this complication in small case series and case reports.[70,76] However, there are no data addressing the systematic use of these agents for the treatment of stent thrombosis, consequently, the incidence of complications related to this form of therapy is unknown. It is reasonable to infer that bleeding complications will also depend on the dose, length, and type of fibrinolytic used.

METHODS TO DETECT POTENTIAL COMPLICATIONS

Bleeding is the most feared and most common complication of fibrinolytic therapy and is the result of the systemic effect of the thrombolytic agent. Although the use of local, catheter-directed thrombolysis may decrease systemic effects, major bleeding complications still occur in 5 to 15%. It is also important to mention that recent experience indicates that the incidence of bleeding correlates more with the duration of therapy than with the total dose of the agent infused. Consequently, it may be preferable to use higher-dose

protocols for a shorter period of time.[80,81] Although specific parameters of coagulation do not appear to correlate with the risk of bleeding during thrombolysis, a systemic lytic state increases this complication. Consequently, documentation of a decrease in fibrinogen of more than 50%, or prolongation of the thrombin time to more than two times normal, is important so that corrections are made should bleeding occur.

When systemic thrombolysis has been used and the development of a major bleeding complication such as gastrointestinal bleeding or intracranial hemorrhage is suspected, the infusion of the drug must be stopped immediately. If gastrointestinal bleeding is being considered but is not overt, serial measurements of the hematocrit as well as assessment of blood in stool must be carried out immediately while fluids are infused. If gastrointestinal bleeding is obvious, blood must be kept on hold for transfusion, particularly if the patient develops hemodynamic compromise (see below). The development of any neurologic manifestation such as confusion, stupor, seizures, or even mild changes in the mental status should be viewed as a possible intracranial hemorrhage, therefore, a CT scan of the brain must be obtained to confirm or rule out this complication. If bleeding is confirmed, neurosurgery consultation is indicated. The onset of eye pain or visual loss should also alert one to the possibility of intraocular bleeding.[82] Prompt consultation with an ophthalmologist must be obtained immediately to minimize ocular damage.

Endovascular, surgical, and medical techniques to resolve complications

In the case of catheter-delivered thrombolysis, the development of oozing around the catheter entry site without significant hematoma, during advanced or final stages of the treatment, can be controlled with local measures such as pressure dressings (although this rarely produces complete hemostasis) and close observation of the patient until the infusion is completed. On the other hand, the development of oozing in the early stages of therapy, when a long (12 to 24 hours) infusion is anticipated, deserves a different approach. The operator may be able to stop the oozing by exchanging the access sheath for a larger sheath (usually 1 French larger size); however, if this measure does not achieve hemostasis, and a hematoma is developing, it is likely that the treatment will have to be discontinued. The development of a hematoma or bleeding at a remote site warrants therapy cessation. Fibrinogen should be replaced with fibrinogen-rich components such as cryoprecipitate or fresh-frozen plasma, followed by blood transfusion if a significant drop in the hematocrit occurs.

Distal embolization probably occurs much more frequently than is clinically appreciated, but rarely requires discontinuation of therapy. If distal embolization of thrombus is recognized, an increase in the infusion rate is preferred to facilitate dissolution of the embolic particles. If severe or worsening of the ischemia occurs despite these measures, the infusion may be stopped to reassess the patency of the vessel with angiography. If profound ischemia is developing, the operator may consider the use of a mechanical thrombectomy device or surgical embolectomy. Several cases of embolization to the ipsilateral extremity have been reported during intra-arterial lytic therapy for occlusion of extra-anatomic (axillofemoral) grafts.[80] For this reason, several investigators consider lytic therapy unsuitable for the treatment of these bypasses due to their length, and choose a more traditional approach, such as surgical thrombectomy.

The treatment of bleeding complications depends on the severity and the time when they occur. In the case of systemic thrombolysis, if patients develop any evidence of major bleeding such as gastrointestinal bleeding or intracranial hemorrhage, the infusion of the drug must be stopped immediately, as mentioned previously. If gastrointestinal bleeding occurs, fluid replacement and transfusions may be given if hemodynamic compromise and/or significant decrease in the hematocrit are confirmed. The development of any neurologic manifestation should be viewed as intracranial bleeding until proven otherwise, so these patients must get a CT scan of the brain. If intracranial hemorrhage is confirmed, neurosurgery consultation must be obtained emergently. The occurrence of visual loss or eye pain should also alert one to the possibility of intraocular bleeding as mentioned before.[82] Prompt diagnosis and treatment is crucial to preserve function in the affected eye.

Vascular access complications such as hematoma, pseudoaneurysm, and arterio-venous fistula formation at the site of vascular access, or retroperitoneal bleeding (if the common femoral arterial access has been used), may occasionally occur. They are the most frequent site for bleeding complications following vascular access, with a reported incidence of 2 to 6%.[83–85] Only rarely do these complications require surgical repair and in the majority of the cases they may be managed conservatively or percutaneously.[86] These particular complications are addressed elsewhere in this book, hence we will not discuss them in this chapter.

Pulmonary embolism can occur during treatment for DVT, however its occurrence is low and appears to be similar to that seen with conventional heparin therapy. In the absence of other complications, continuation of lytic therapy is the treatment of choice. If recurrent emboli are observed, discontinuation of the fibrinolytic, heparin administration, and placement of a caval filter may prevent further morbidity or mortality. The development of fatal PE has been described during intra-arterial fibrinolysis of lower limb ischemia, as a result of venous stasis of the target limb, leading to DVT, partial thrombus lysis, and pulmonary embolization.[87] This is a very rare occurrence and treatment options include cessation of lytic therapy with heparinization or switching to intravenous fibrinolysis. If the latter option is chosen, the operator must remember to leave the arterial catheter/sheath in place to minimize risk of bleeding from the arterial puncture site.

Allergic reactions to streptokinase are not infrequent, however, most are minor febrile episodes that usually respond to aspirin or acetominophen. Serious allergic reactions are infrequent with the current streptokinase, and even more rare with t-PA.[88,89] They must be managed with intravenous steroids and conventional therapy for anaphylactic reactions.

SUMMARY

Fibrinolytic therapy is an important treatment modality for patients with thombotic stenoses or occlusions in the peripheral arterial and venous circulation. The first fibrinolytic agent available for peripheral vascular interventions was streptokinase, which at present is rarely used due to its frequent immunologic reactions, unpredictable pharmacokinetics, and relatively frequent bleeding complications. Most clinical experience has been obtained with the non-fibrin-selective urokinase and the fibrin-selective t-PA, which, overall, are equally effective for this condition, although t-PA may act more rapidly. Major bleeding complications appear to be slightly more frequent in t-PA treated patients. The experience with reteplase and tenecteplase is very limited, but potentially promising in terms of safety profile and effectiveness.

Recent randomized trials have shown that catheter-delivered fibrinolytic therapy is an alternative to surgical embolectomy in selected patients without profound ischemia. Intra-arterial fibrinolysis has been shown to decrease the long-term incidence of the postphlebitic syndrome and to increase the quality of life compared to anticoagulation. Thrombolysis should be offered to these patients, particularly those with extensive DVT affecting the iliofemoral venous system. Systemic fibrinolysis should be considered for patients with massive pulmonary embolism causing hypotension and right ventricular dysfunction. Recent meta-analyses have shown that in this group of patients, fibrinolysis decreases mortality as well as recurrent pulmonary embolism. Patients with acute ischemic stroke, presenting within 3 hours of symptom onset, should also be considered for fibrinolytic therapy.

Major bleeding complications occur in 5 to 15% of the patients undergoing this form of therapy. In patients with suspected gastrointestinal or intracranial bleeding, fibrinolytic therapy must be discontinued, and fibrinogen replaced. In patients with bleeding around the catheter entry site, the need to stop therapy must be individualized according to the severity of bleeding, length of infusion, and symptoms.

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7

Carotid stenting complications from the femoral artery to the intracranial circulation

Robert D Ecker, Horst Sievert, and L Nelson Hopkins

INTRODUCTION

Atherosclerotic carotid artery disease

With the introduction of distal embolic protection (DEP) devices and stents designed for the carotid circulation, several clinical studies have demonstrated the morbidity and mortality for carotid angioplasty and stenting (CAS) in high-risk patients with atherosclerotic carotid artery disease to be on a par with or better than for carotid endarterectomy (CEA).[1–12] High-risk CAS registries that included the outcome of myocardial infarction (MI), unlike the North American Symptomatic Carotid Endarterectomy Trial (NASCET)[13,14] and the Asymptomatic Carotid Atherosclerosis Study (ACAS),[15] have reported 30-day rates of MI, stroke, or death ranging from 3.9 to 8.2%.[4,5,7,8,10,11,16] The Stenting and Angioplasty with Protection in Patients at High-Risk for Endarterectomy (SAPPHIRE) trial had 5.8% 30-day and 12% 1-year event rates, also including MI.[12] A review of our series of patients at the University at Buffalo has demonstrated morbidity and mortality rates paralleling those of NASCET and ACAS, even in a group of patients undergoing CAS of whom 78% would not have qualified for enrolment in these studies due to anatomic or physiologic high-risk profiles.[17] Low-risk CAS trials are ongoing. Nevertheless, from femoral artery puncture to DEP device retrieval and final angiography, potential exists for complications during CAS that can be threatening to life, limb, or brain. Management of these complications can take the effort of a team that includes neuroradiologists, cardiologists, neurosurgeons, and vascular surgeons, depending on the clinical and technical skill set of the individual interventionists. Although delayed neurologic, cardiac, and peripheral complications can occur, an acute neurologic event often requires immediate intervention or the hope for meaningful salvage declines precipitously. Unlike CEA, CAS is usually performed while the patient is awake, which allows continuous neurologic and angiographic assessment and prompt recognition of potential problems.

Non-atherosclerotic carotid artery disease

Along with atherosclerotic disease, there are other arteriopathies that occur in the carotid artery that, when symptomatic, can be addressed with similar tools and techniques as atherosclerotic

carotid stenosis. These pathologies include dissection, fibromuscular dysplasia (FMD), carotid pseudoaneurysm, and true aneurysm. These four entities can also be faced in the context of atherosclerotic disease, either as secondary processes or as complications.

Dissection

Carotid artery dissections can occur spontaneously or after trauma, including seemingly minor events or more significant forces, like chiropractic manipulation or motor vehicle accidents with fracture dislocations. In some patients, both sides can be affected with or without vertebral artery involvement. The dissection flap can be associated with significant decrease in flow, or thrombus and occlusion, or can lead to subtle stasis of contrast material with essentially normal hemodynamics. Traditionally, carotid dissection has been treated with heparin and warfarin therapies for two reasons: the majority of patients in large retrospective series have done well and, until the maturation of techniques for carotid stenting over the last 10 years, little else was available.[18] However, what to do about the patient with a history of repetitive ischemic attacks or high National Institutes of Health Stroke Scale (NIHSS) score on presentation? In this subset of dissection, primary stenting can be performed safely.[19]

The most important aspect of treating a dissection is identifying the extent of the flap. Does it extend into the intracranial circulation? Is the dissection an extension of an aortic dissection? An aortic arch run with a 5 French (Fr) pigtail catheter can usually identify the proximal extent of the dissection. A soft navigable 0.014-inch microwire and microcatheter are generally chosen to attempt to gain initial access. The wire should easily pass through the dissection into the true lumen. Resistance suggests that the wire or catheter is in the false lumen. When this occurs, the microcatheter system should be brought well back into the proximal normal artery and then access reattempted. Once access to the distal true lumen is obtained, the distal anatomic boundaries of the dissection can be identified. For dissections extending into the intracranial compartment, only balloon-mounted cardiac stents were available until recently. Self-expanding nitinol stents (e.g., Neuroform™, Wingspan™; Boston Scientific, Natick, MA) are now available that have extended the application of stenting (albeit off-label) to the treatment of dissections within the tortuosities of the intracranial vasculature.

Acute aortic dissection with great vessel involvement carries a high mortality with medical and surgical management.[20] There are case reports of successful stenting of the great vessels to the level of the arch.[21] We have had one experience with this in an 84-year-old woman with an NIHSS score of 18 who presented with an acute right hemispheric stroke. Cranial computed tomographic (CT) perfusion imaging demonstrated significant hemispheric hypoperfusion (Figure 7.1a). Angiography demonstrated poor flow to the hemisphere, with initial filling of the external carotid artery (ECA) branches (Figure 7.1b). After access to the true lumen had been gained, the placement of overlapping Wallstents™ (Boston Scientific/Schneider, Minneapolis, MN) resulted in marked improvement in flow (Figure 7.1c). At the time of the 3-month follow-up evaluation, the patient was once again living independently. Suspicion for aortic dissection, based on the clinical history of chest pain prior to the onset of ischemic symptoms, led to the performance of a CT angiogram that demonstrated the dissection, which was managed conservatively (Figure 7.1d).

Fibromuscular dysplasia

Fibromuscular dysplasia (FMD) is a non-atherosclerotic, non-inflammatory arteriopathy of small and medium size arteries that often affects the renal and carotid arteries.[22] Angiographically, it is diagnosed by a distinct beading of the artery with alternating areas of dilatation and stenosis. Most often, this finding is of little clinical significance. However, patients can develop secondary dissections and symptomatic stenosis requiring treatment, often tracking high in the cervical segment of the carotid artery where filters are not easily used, but flow reversal might be possible. Soft, trackable self-expanding stents like the Xpert™ (Abbott Vascular, Inc, Redwood City, CA; off-label for this indication) can produce

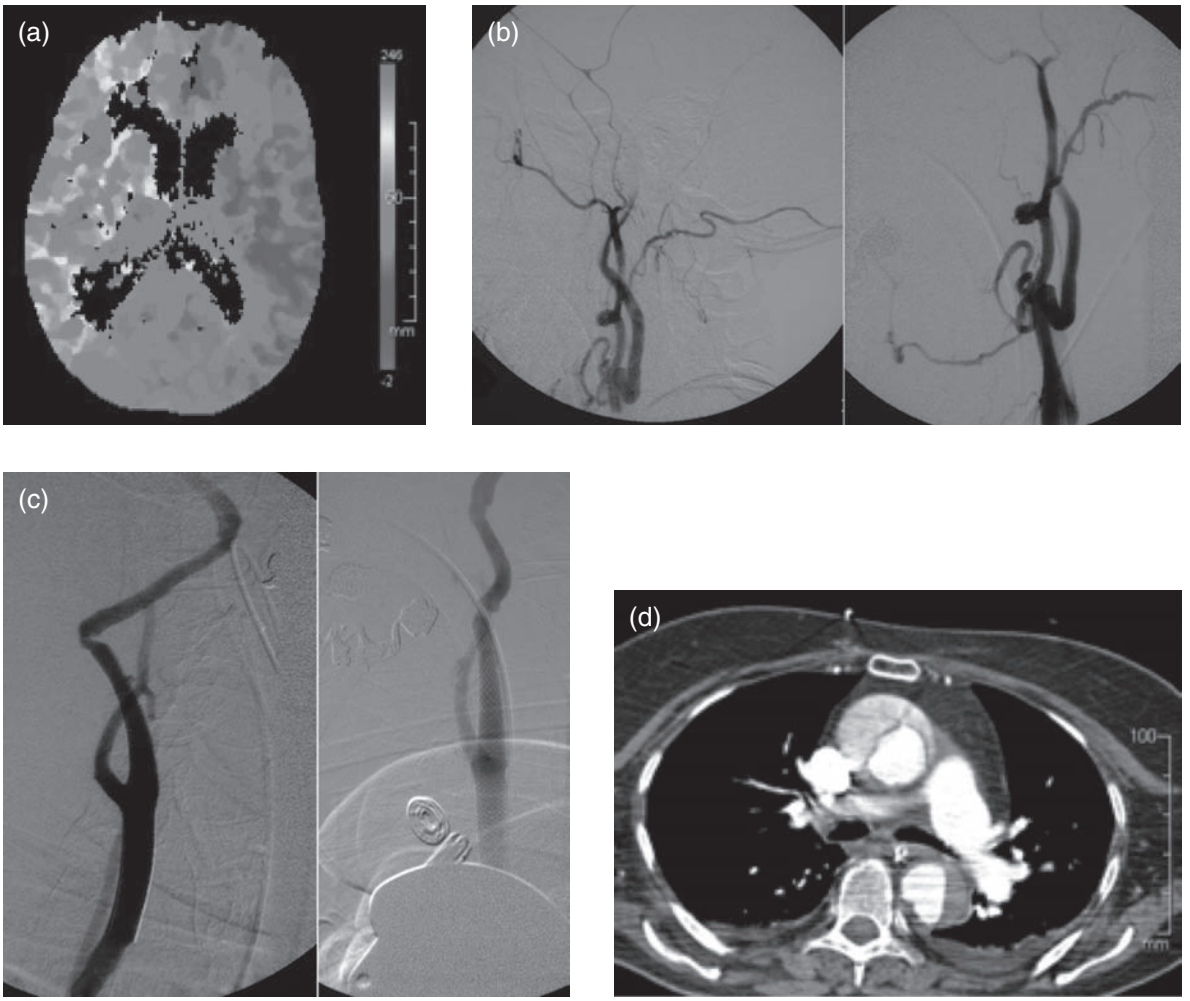

Figure 7.1 (a) CT perfusion image shows severe hypoperfusion of the right hemisphere. (b) Initial angiogram reveals filling of the ECA before the ICA (*left* and *right*: lateral views, at higher magnification on the right). (c) Angiographic images (*left*, oblique projection; *right*, AP projection) show improved flow after deployment of overlapping Wallstents™ (Boston Scientific/Schneider, Minneapolis, MN). (d) CT angiogram demonstrating an aortic dissection.

excellent results, and balloon angioplasty alone can often be effective without stenting for pure FMD. Patients with Ehlers–Danlos syndrome, especially type IV, as the underlying condition are a high-risk group for treatment-related morbidity and long-term failure, and the decision to treat such patients should be carefully weighed against the risks of further vessel dissection. One patient treated recently at the University at Buffalo had bilateral, chronic, symptomatic dissections of the carotid artery secondary to FMD (Figure 7.2a, *left*). The left-sided lesion was treated with an Xpert stent without DEP due to the high location and low risk for embolic phenomena; the right side was similarly treated with an Xpert™ stent (Figure 7.2a, *middle*). Proximal to the stented region, the artery developed significant pseudospasm overlying the pre-existing FMD (Figure 7.2a, *right*). Angioplasty of this region was performed with a fair result, and a follow-up angiogram performed the next day showed a remarkably normal artery (Figure 7.2b).

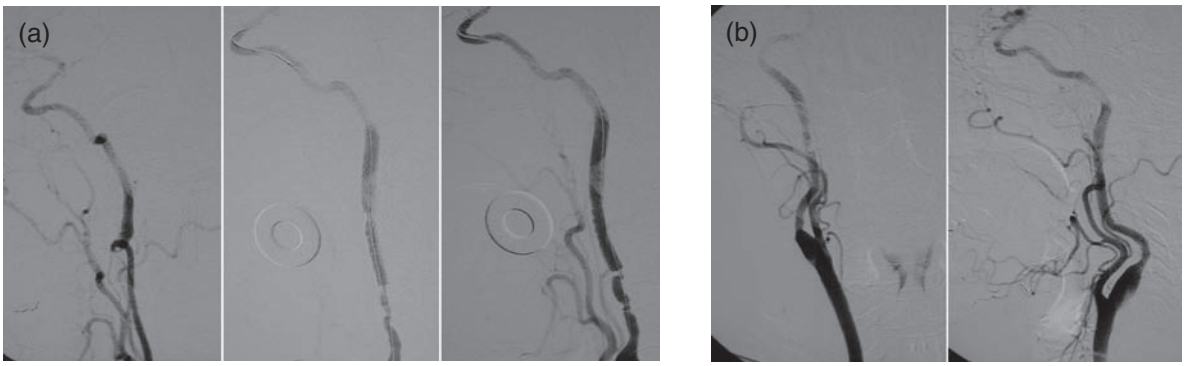

Figure 7.2 (a) *Left*, preoperative angiographic image shows right ICA with FMD and dissection. *Middle*, right ICA after stent placement (Xpert, Abbott Vascular, Inc, Redwood City, CA). *Right*, severe proximal pseudospasm post-stenting. (b) 12 hours after stand-alone angioplasty (*left*, AP view; *right*, lateral view).

Carotid pseudoaneurysm and aneurysm

Carotid pseudoaneurysms, or aneurysms that do not involve all three layers of the arterial wall, can be associated with dissection (acute and chronic) or FMD. Treatment is indicated in symptomatic patients and those with enlarging lesions. Low-porosity self-expanding stents including the Wallstent™, Magic Wallstent® (Boston Scientific), and Xact® (Abbott Vascular) can be deployed across the lesion, and the placement of one of these stents will often result in thrombosis of the lesion. Sometimes two stents are necessary. True aneurysms of the cervical portion of the carotid artery are uncommon, but can be dealt with similarly. The stent needs to bridge the aneurysm neck from the distal to the proximal segments of the non-diseased parent artery. As with pseudoaneurysms, two stents are sometimes necessary (Figure 7.3a–c).

IDENTIFYING PATIENTS AT HIGH RISK FOR COMPLICATIONS

Patient selection is the most important factor in minimizing complications associated with CAS.[23,24] Categories of major risk factors for CAS include medical, neurologic, anatomic, and genetic arteriopathy. Age is often listed as a risk factor, but it is the anatomic challenges and medical comorbidities that come with age that increase the risk for most patients.[25–27] Medically, the major risk factor in patients with carotid stenosis is MI. Patients with severe left main disease and severe triple vessel disease are at major risk for MI. A sudden decline in blood pressure and the onset of severe bradycardia present major risk for MI in patients with severe left main coronary artery disease and/or severe triple-vessel disease. In this group, if CAS before coronary intervention is necessary, minimal or no dilation of the stent after deployment will generally avoid major hemodynamic swings, and the patient can be sent for cardiac surgery, with a plan made for follow-up and retreatment as necessary. Neurologic risk increases with recent large infarction, crescendo transient ischemic attacks (TIAs), and stroke in evolution. Large infarctions present a significant risk for hemorrhage.[28,29] Traditionally, patients with large infarction are allowed to 'heal' their stroke for 6 weeks prior to intervention. Patients with active TIAs or stroke in evolution need to be treated but are higher risk for neurologic injury.

Patients with high-risk anatomy may include those with calcified tortuous aortic arches, tortuous and severe iliofemoral disease, and proximal or distal tortuosity of the common carotid artery (CCA) or internal carotid artery (ICA). Patients considered at high risk for CAS include those with long, irregular or concentrically calcified stenosis, pseudo-occlusion, string sign, carotid artery kinking, and intraluminal thrombus. Not all high-risk patients can be avoided. For example, treatment should likely be delayed

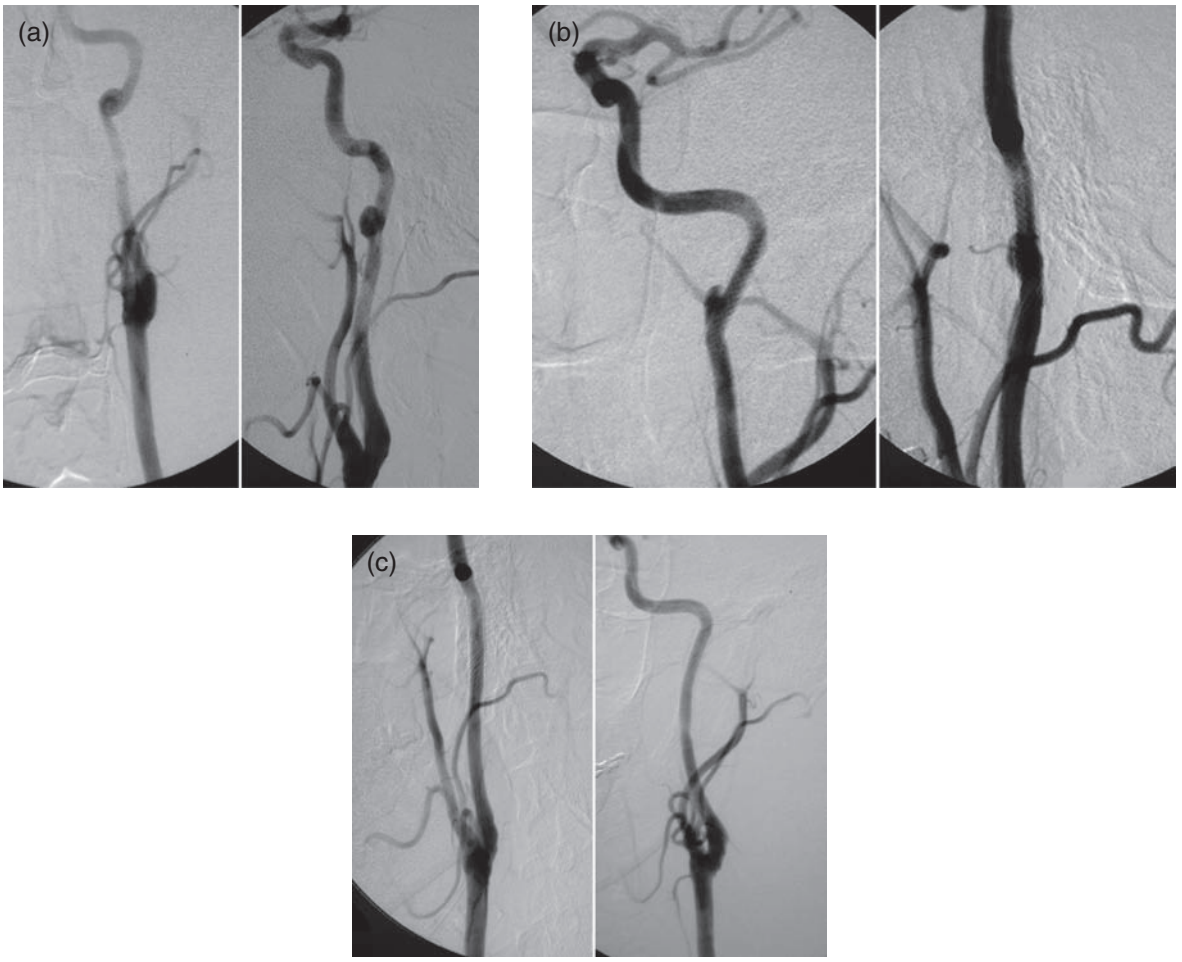

Figure 7.3 (a) True carotid aneurysm (*left*, AP view; *right*, lateral view). (b) Three months after the placement of a single Wallstent™ with persistent filling (*left*, AP; *right*, lateral). (c) The placement of overlapping Wallstents™ resulted in complete occlusion of the aneurysm (*left*, lateral; *right*, AP).

for 6 weeks in a patient who has a large completed infarction with territory still at risk. Conversely, treatment should promptly be undertaken in a patient in need of urgent coronary artery bypass grafting (CABG) who presents with crescendo TIAs and an MI. Each case should be evaluated on an individual basis. For patients who are candidates for carotid intervention, it should be remembered that CEA remains a safe and effective operation if CAS is thought to be too risky. In fact, CEA and CAS are amazingly complementary procedures; in those situations for which one is high risk, the other is usually feasible with acceptable risk. It is important to remember that backing out of a CAS procedure is rarely a problem for the patient, whereas persisting in the face of technical challenges may result in an avoidable stroke.

Creative endovascular solutions can be found even in high-risk patients when treatment is deemed necessary. For patients with intraluminal thrombus and symptomatic carotid disease, the traditional treatment has been heparin and warfarin therapy with re-evaluation in 6 weeks to 3 months. In four patients with multiple episodes of TIAs, we have used a trapping technique with proximal and distal balloon occlusion with good success (Figure 7.4a–e). Flow reversal devices,

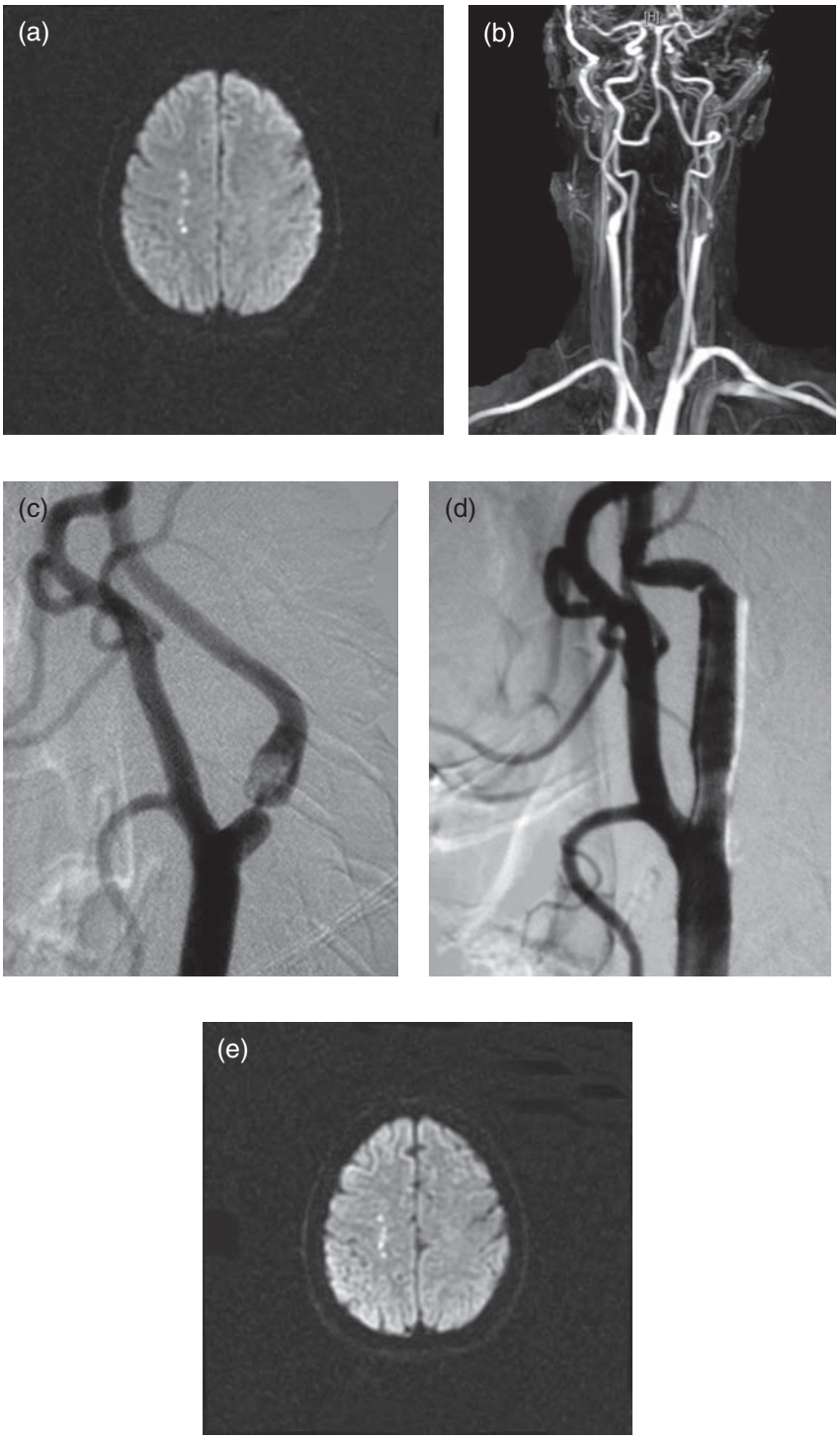

Figure 7.4 Internal trapping and stenting of symptomatic carotid stenosis with intraluminal thrombus. (a) MR image showing small left frontal infarction. (b) MR angiogram showing critical left ICA stenosis. (c) Angiogram with critical stenosis and flame-shaped intraluminal thrombus. (d) Post-stenting cervical angiogram. (e) Post-stenting MR image showing no new areas of stroke.

which are just becoming clinically available in the United States, may prove useful in this setting and in the context of kinks that make landing of a DEP unfeasible.[30] As reviewed earlier, patients with Ehlers–Danlos syndrome and FMD provide a great challenge because of the poor toleration of their vessel walls to manipulation with wires and balloons. The decision to treat such arteriopathies should be carefully considered.

Low-risk patients are those with either asymptomatic or single retinal or hemispheric TIAs with no previous cardiac history.[31] Anatomically, type I aortic arches with both straight proximal and distal anatomy provide the easiest anatomic substrate for CAS. Many of these patients have not been treated in the carotid stenting pool that has been reserved for 'high-risk' patients. Ongoing low-risk trials like the Asymptomatic Carotid Stenosis, Stenting versus Endarterectomy Trial (ACT I) will determine how these patients fare with CAS when compared with CEA.

COMPLICATIONS ASSOCIATED WITH INTERVENTIONAL STEPS AND TOOLS

Patient preparation for CAS

Many of the risks associated with CAS can be mitigated pre- and periprocedurally. Patients should receive a loading dose of aspirin and clopidogrel at least 72 hours before the procedure. Generally, the loading dose is 600 mg of clopidogrel and 650 mg of aspirin, with the daily doses being 75 mg and 325 mg, respectively. The interventional suite should have dedicated nursing personnel familiar with all the equipment, devices, and pharmacologic agents, critical care management, and the disease process treated. Guide catheters are flushed with normal saline (0.9% NaCl) with 5000 units of heparin in each pressure bag. The air will have been actively removed from each flush bag. Alternatively, the catheters should be flushed frequently. Lidocaine (1%) is percutaneously administered for local anesthesia, and midazolam (1 mg) and fentanyl (50 μg) may be intravenously administered for sedation. Femoral access is gained with a 19 gauge needle and a single-wall puncture technique and a 5 or 6 Fr groin sheath. A femoral artery angiographic run is then obtained. Heparin (50–60 units per kg body weight) is administered to obtain an activated coagulation time of >250 seconds. Alternatively, direct thrombin inhibitors such as bivalirudin may be used. Guide catheter access is gained directly with a 6 Fr guide catheter (for example: Envoy®, Cordis, Miami Lakes, FL) for lesions that can be treated in general with a stent that is 8 mm or less in diameter (for example, a Wallstent™); for 8 to 10 mm lesions, a 6 Fr guide sheath (Cook Shuttle select; Cook, Inc, Bloomington, IN) is brought into the CCA with an exchange maneuver or over slip catheter (Cook). Another option is to use an appropriate coronary guide catheter.

Overview of basic technique from the femoral artery to the common carotid artery

Femoral artery access

The femoral artery approach is most commonly used for CAS. As approximately 33% of patients have both significant carotid artery disease and severe symptomatic peripheral vascular disease,[32,33] the interventionist should also be familiar with radial and brachial approaches. In addition, femoral artery complications are likely more common in this population as many have femoral artery disease. Access site complications do not make the surface of primary or secondary endpoints in most of the major carotid stent trials, therefore the incidence is not clearly known. Other chapters of this book will focus on femoral artery access complications and their management.

Aortic or brachiocephalic access

In the process of gaining access to the CCA with a guide catheter, injury to any of the major aortic branches and brachiocephalic vessels can occur, resulting in dissection or thrombotic occlusion. Many patients with carotid stenosis have severe atherosclerotic debris throughout their arterial trees. Care should be taken when gaining access to the proximal carotid artery. Minor, nonflow-limiting dissections of the proximal brachiocephalic vessels can be observed, regardless

of whether the patient is receiving a heparin infusion. If concern exists, but the decision is made not to stent a dissection flap, repeated angiography within 24 hours may be indicated. In flow-limiting situations, the lesion should be stented. A microcatheter and soft wire can be used to locate the distal true lumen if wire access is lost, with angiography performed via the microcatheter to ensure that the distal wire is in the true lumen.

Stroke can occur at any point after femoral artery access. If a patient develops a sudden neurologic change, the diagnoses entertained should include hemorrhage and ischemia – most often due to embolism. Quick access should be gained to the vessel suspected of harboring the problem, based on the findings of the neurologic examination. If the patient's airway is compromised, intubation should be performed. If no vessel cut-off or slow flow is appreciated, hemorrhage must be ruled out, and the patient should undergo a cranial CT scan. The specifics of neurologic rescue will be discussed later.

Guide catheter placement: external carotid artery perforation and embolism

The ECA and its branches are often used to support a guidewire during the exchange of a diagnostic catheter for a guide sheath or catheter. This maneuver is felt to be safer than exchanging devices within the CCA because it prevents premature crossing of the lesion and showering of emboli. Additionally, it gives the purchase essential in the setting of a difficult aortic arch that might not be otherwise accessible. In our experience of more than 1500 stenting procedures, we have had five ECA branch artery ruptures secondary to wire perforations in four cases and a misdeployed PercuSurge embolic protection balloon (Medtronic, Minneapolis, MN) in an additional case.[34] The four wire perforations were secondary to advancement of the stiff exchange wire through the facial artery (two cases) and the lingual branch and artery to the sternocleidomastoid (one case each). A brief description of the management of these complications follows.

The first patient was electively intubated without endovascular intervention, and the hematoma tamponaded the bleeding spontaneously. The second patient required an emergent tracheostomy because of massive swelling of the tongue (Figure 7.5a). In the third patient, the artery to the sternocleidomastoid was accessed with a 0.014-inch microcatheter, and the branch artery was occluded with *N*-butyl-2-cyanoacrylate (NBCA). The fourth patient's hematoma was noted only at the conclusion of the procedure and hand pressure on either side of the cheek stopped the progression of the hematoma. In the fifth patient, a PercuSurge balloon was inadvertently placed in the ascending pharyngeal artery, which was aligned with the ICA and originated from the carotid bulb. Upon inflation, the artery ruptured and contrast extravasation could be seen (Figure 7.5b). A microcatheter was used to access this artery, and it was occluded with coils (Figure 7.5c).

Some lessons have been learned from these cases. First, large branches of the ECA, preferably the internal maxillary artery or occipital artery, should be used for exchange maneuvers. Second, carotid artery branch rupture can lead to life-threatening airway emergencies. A tracheostomy set should be available in the interventional suite. A physician who can intubate the patient or perform an emergency tracheostomy to establish an airway should be readily accessible. Third, carotid interventionists need to be comfortable with microcatheters and embolic agents like NBCA, coils, silk, gel foam, and even autologous clot, as a means to stop bleeding from perforations. Although a rare event, ECA branch artery perforation can quickly lead to airway compromise if not recognized and treated promptly.

An equally rare event is ECA embolism to carotid ophthalmic collaterals, which may lead to retinal embolism and blindness. Anatomically, embolization can occur through middle meningeal and superficial temporal collaterals to the ophthalmic artery and/or via direct ICA reconstitution associated with embolic phenomena or retrograde embolization through the ECA to ophthalmic and retinal branches. Wilentz et al studied 188 consecutive patients undergoing CAS with the Theron-type DEP system (in which debris is flushed into the ECA) or the PercuSurge system with careful funduscopy, fluorescein angiography, and visual field testing.[35]

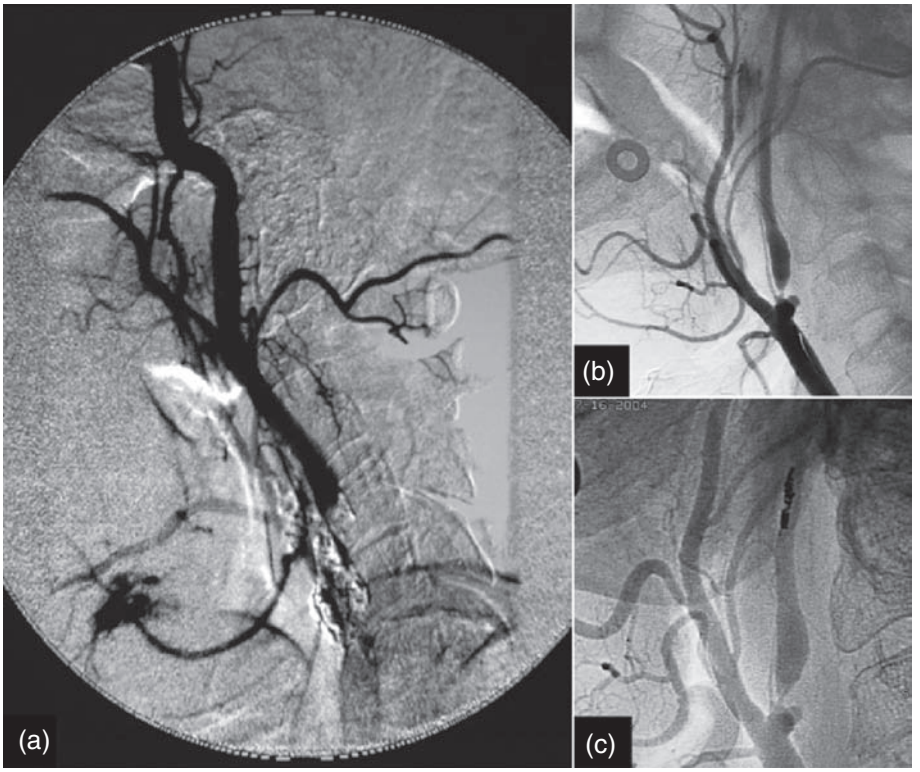

Figure 7.5 (a) Extravasation from the lingual artery caused by exchange wire. (b) Perforation of ascending pharyngeal artery from PercuSurge balloon (Medtronic, Minneapolis, MN). (c) Coils in ascending pharyngeal artery with no extravasation.

Overall, 6 of 118 patients had retinal emboli, which was symptomatic in 2 patients (1.7%). Looking at the two different systems, 13.2% (5 of 38 patients) treated with the Theron system had emboli, versus 1.25% of the PercuSurge group. In fact, in the setting of ICA occlusion, amaurosis fugax from the ECA collateral through the ophthalmic artery retrograde to the retinal artery can occur and responds well to carotid revascularization.[36] The predominance of the literature regarding ECA revascularization is from the CEA literature.[36–38] Embolic protection should be used if possible during ECA angioplasty and stenting.

Once visual loss has occurred, angiography should be obtained to determine the location of the occlusion. Central retinal artery occlusions can sometimes be opened with antiplatelet agents infused into the ophthalmic artery. If the ophthalmic artery is patent, the agent can be directly infused. If a shower of emboli is suspected, administration of eptifibatide as a bolus dose (180 μg/kg) and a 23-hour infusion (2 μg/kg for at least 12 hours) or other IIb/IIIa antiplatelet agent is indicated.

Distal embolic protection: from device deployment to retrieval

The technique of DEP has lowered morbidity and mortality rates associated with CAS. Additionally, DEP devices provide excellent platforms on which to perform CAS. However, each step of CAS from crossing the stenosis to retrieval of the DEP device has potential for complication. Transcranial Doppler (TCD) data have documented hits indicative of embolism at all stages of CAS; however, most TCD-detected emboli are clinically silent. On the basis of TCD data in which protected stenting with the PercuSurge device was compared to unprotected stenting, the highest-risk maneuvers for embolic

risk in unprotected stenting, in order from lowest to highest, were predilation angioplasty, stenting, and postdilation angioplasty.[39] In the PercuSurge-protected stenting group, guide sheath placement, guidewire manipulation, and deflation of the device were high embolic periods.[39] DEP significantly lowered the risk of hits documented by TCD imaging. Stenting performed in conjunction with filter devices for DEP (Filterwire EX®, Boston Scientific; Accunet®, Guidant, Santa Clara, CA) in a series of 10 patients was monitored with a multifrequency TCD imaging system.[40] The system utilized was capable of distinguishing between gaseous and solid emboli. During DEP deployment, more than 8000 microemboli were detected, with more than 40% being solid. During the stenting procedure, more than 7000 microemboli were detected, again with over 40% being solid. No patient developed clinical sequelae. Microemboli occur even in the gentlest hands, but with good patient selection and technique, the occurrence of symptomatic embolic phenomena can be kept low.

In the US market, five devices FDA approved for carotid use: the Fiterwire EX® and the Filterwire EZ™ (with the NexStert® [Boston Scientific]), the Accunet™ filter (with the Acculink™ stent)(Guidant), the EmboShield® filter (with the Xact® stent) (Abbott Vascular), and the Spider™ filter (ev3, Plymouth, MN). There are at least four other non-approved commercially made filters. Additional types of embolic protection devices include balloon occlusion catheters (PercuSurge; TriActive System, Kensey Nash, Exton, PA), proximal occlusion devices (MOMA, Invatec, Brescia, Italy), and flow reversal devices (Parodi Anti-Embolic System, WL Gore & Associates, Flagstaff, AZ).

The indication for proximal versus distal protection has not been determined. Logically, intraluminal thrombus, soft plaque, and poor distal landing zone would be indications for proximal protection. The results of the European Imaging in Carotid Angioplasty and Risk of Stroke (ICAROS) study showed that gray-scale median (GSM) scores of 25 or less (representing echogenic plaque) are associated with higher embolic potential.[41] The investigators created a prospective registry of 418 CAS cases from 11 centers and recorded GSM scores preprocedurally. Eleven of 155 (7.1%) patients with GSM of 25 or less had strokes versus 4 of 263 (1.5%) patients with GSM greater than 25 (p value of 0.005). Taking this one step further, the authors validated the use of DEP in patients with GSM greater than 25 ($p = 0.01$), but not in those with GSM of 25 or less. For those patients, stenting with proximal embolic protection devices or CEA may prove safer.

This portion of the chapter will focus on complications from filter DEP devices as they are used most often for embolic protection. In our practice, the PercuSurge device is the most often used alternative to filters, with the most common indications being ICA less than 2.8 mm in diameter, intraluminal thrombus, and acute occlusion (i.e., where clot burden is likely high and might potentially overwhelm a filter). When crossing a carotid lesion, plaque dissection and embolization can occur. In the case of dissection, the patient is already therapeutically heparinized, and if the true lumen can be entered with the DEP, it should be crossed and stented along with the stenosis. If the lesion cannot be crossed with the DEP, a microwire and catheter should be used to cross the lesion. The true lumen is identified with a microcatheter angiographic run, and the DEP is then brought into position. The EmboShield® and Spider™ filters are ideal for such situations. The EmboShield® platform is a microwire-based free-floating filter with the filter brought into place after passage with the microwire; the Spider™ filter is delivered through a microcatheter after passage of a lesion with a microwire and microcatheter. Embolic phenomena associated with crossing the lesion require quick completion of the cervical carotid stenting portion of the procedure in order to gain access to the distal intracranial circulation. Inability to cross a lesion should lead to reconsideration of the procedure and consideration of the feasibility of endarterectomy.

Ideally, the filter should be deployed in a straight segment distal to the stenosis, well opposed to the carotid wall. Predeployment of the filter can occur in the lesion inadvertently. Most often, this occurs secondary to the operator advancing the wire but not the housing sheath of the DEP. When unsheathing a filter, if the filter wire is not fixed as the sheath is retracted, the entire system can be dragged through the lesion.

In this case, the DEP should be recaptured and redeployed distally. With monorail delivery systems, such maneuvers are not always possible. Pushing the filter back into the ICA above the lesion is often a better choice than dragging the entire system through a lesion. A secondary strategy for retrieval is to exchange out the initial DEP sheath and to run a 4 Fr angled catheter up the wire and recapture the misdeployed device.

Loss of the filter device is rare, but possible. With the EmboShield®, which is a free-floating filter, the striped wire provided in the package must be used because it has a tapering segment that acts as a stop for the filter. Filter devices have been sheared off with recapturing. In these dire settings, the options include snare retrieval into the guide catheter, stenting the filter against the vessel lumen, or operative retrieval. If the DEP is in the bony segment of the skull base, operative retrieval may be impossible. Before any maneuvers are undertaken to retrieve a lost filter or other detritus, consideration should be given to arresting flow temporarily to avoid distal intracranial embolization.

In arteries in which a kink in the CCA or ICA has been moved cranially, with significant movement of the filter DEP device, and in some particularly sensitive arteries, carotid vasospasm can occur. Generally, this is not a clinically or an angiographically significant problem, but stroke has been described in conjunction with sudden severe spasm just after the deployment of an AngioGuard™ embolic protection device (Cordis).[42] Three patients in one of the initial series using the EmboShield® developed spasm, which was flow limiting in two patients.[43] In non-flow-limiting spasm, the case should be completed and the filter recaptured. Generally, the spasm clears after the passage of a few minutes. Contrast material remaining within the arterial wall should cause concern for dissection. In flow-limiting situations or if significant time has passed and the spasm persists, intra-arterial nitroglycerin (100–200 μg) is usually effective. Distal dissection at the level of the filter can occur, more commonly so with the PercuSurge device than with the filter devices. For cases of small, asymptomatic, and non-flow-limiting dissections, clinical observation is recommended. Stenting is warranted if the dissection is symptomatic or flow limiting. Spasm also occurs when a kink in the carotid artery is moved cranially by the DEP and guide catheter. This can be ignored as it will resolve with device retrieval and often resolves after stenting and postdilatation angioplasty.

Predilatation angioplasty, as mentioned earlier, is a low-risk portion of the procedure. Generally, a 3.0 or 3.5 × 30-mm balloon is used. Attention should be paid to blood pressure reduction due to carotid baroreceptor response. Patients who do not have pacemakers, are not undergoing CAS pre-CABG, and have initial baseline heart rates of less than 70 beats per minute may benefit from 0.75 mg of atropine given at least 2 to 3 minutes before balloon inflation. Postdilatation angioplasty is a high risk for both embolic phenomena and severe baroreceptor response. Balloon size is chosen based on the measurement of the stent in the distal ICA; the balloon is undersized by 0.5 mm. Angioplasty balloons in vessels in patients undergoing CAS pre-CABG are generally slightly underdilated to avoid a severe baroreceptor response. Dopamine or phenylephrine should be loaded at the start of the case for rapid administration if the patient's blood pressure drops significantly. It is important to remember that atropine may mitigate against severe bradycardia but will have no effect on hypotension.

Immediate complications associated with stenting are unusual. With dual antiplatelet therapy for 4 weeks and with arteries larger than 3 mm, acute and subacute thrombosis is uncommon. Subacute thrombosis has occurred twice at the University at Buffalo Neurosurgery practice when cardiac surgeons stopped the patients' antiplatelet medications within the first 2 weeks before CABG. Aspirin use was discontinued before urologic surgery in another patient 3 months after stenting of a carotid dissection with stents extending from the proximal segment of the ICA to the petrous segment of the ICA, and the stent became occluded; some degree of abnormal endothelialization was likely present in this case, and a hypercoagulation state may have been implicated. A dual antiplatelet regimen 4 weeks postprocedure and aspirin use for lifetime appears essential. Drawing on the cardiology literature, early stent thrombosis is likely due to a dissection unrecognized at treatment or an undersized or expanded stent; late thrombosis is likely due to stent mismatch to the artery, hypersensitivity,

abnormal endothelialization, or poor compliance with antiplatelet medications.[44] The stent should be sized to the CCA and the size of the postdilatation balloon based on the measurement of the stent in the ICA.

If arterial occlusion occurs acutely during the procedure, the diagnosis includes severe spasm, dissection, thrombosis from plaque and/or platelet aggregation, and a filter that is filled with embolic material. As long as there is no dissection, the spasm will resolve. Nitrates can be given, as mentioned earlier. Treatment is required for an occlusive dissection. A microcatheter and microwire need to be brought past the flap into the true lumen to accomplish this. If the clot has not embolized to the intracranial circulation and the patient is asymptomatic, consideration may be given to heparinizing the patient overnight, checking the angiographic collateralization, and performing stenting later. In the acutely symptomatic patient, stenting after the administration of a lytic agent and IIb/IIIa inhibitor may be necessary. If the filter is filled with embolic debris, a utility catheter can be used to perform a suction thrombectomy and the filter should be carefully captured and brought through the stent so as to not disturb the captured debris. Successful outcomes have been reported for a small series of patients undergoing operative rescue after acute or subacute stent thrombosis.[45] However, if the experience with emergency CEA for treatment of acute carotid occlusion is a guide, the associated morbidity and mortality is greater than 20%.[46] The hope is that with CAS, where we have the ability to visualize and access the entire cerebral vascular system, and with newly evolving techniques for treatment of acute stroke, we will have better salvage procedures and success with endovascular techniques.

Recapturing the filter device is the final technical step of CAS with DEP. When this step goes smoothly, it is effortless; however, when accessing the filter with the recapturing sheath proves difficult, dissections, stent movement, and shearing of the filter device can occur. The most common setting for difficulty in recapturing the filter is with an open-celled stent on a significant curve or with the DEP parked in a tortuous distal vessel. A systematic approach to recapturing maneuvers will generally lead to successful recapture:

1. Advancing the guide catheter into the stent will bias the wire away from the stent wall, allowing the recaptured sheath to pass.
2. Having patients inhale deeply or turn their heads opposite the direction of the vessel curve can help straighten the curve or elongate the artery enough for passage of the sheath. More aggressively, pressing on the stent in the patient's neck will also change the bias of the wire.
3. If the sheath is impeded by a stent tine, redilatation with a larger balloon or spinning the sheath with forward pressure will help flatten the tine or allow passage of the sheath.
4. If other maneuvers fail, a 4 or 5 Fr angled glide catheter can be passed over the DEP wire and used to capture the filter.

Intracranial complications

The intracranial complications of carotid stenting can be grouped into large vessel occlusion, shower of emboli, and hemorrhage. In any patient with an acute or delayed neurologic change not explained at the cervical level, all three sources should be entertained. In the acute setting, a cerebral angiogram should be performed to look for vessel cut-off or slow flow and emptying. If a clear large vessel cut-off can be seen, an immediate attempt should be undertaken to recanalize the occluded vessel. A microcatheter (0.014-inch lumen or larger) should be brought through the lesion to confirm patency of the distal vessel and confirm the length of the occlusion. In cases of acute stroke at the University at Buffalo, we have been using the 021-ID microcatheter for the Merci® device (Concentric Medical, Mountain View, CA) as the initial catheter to obviate the necessity for additional exchange maneuvers. One or two passes with the Merci® retriever should be attempted (Figure 7.6a,b). If this device is not available, thrombolytics can be used initially. There is some evidence that IIb/IIIa inhibitors give additive benefit.[47] Other devices that can be used to open occlusions of large intracranial vessels (M1 segment of the middle cerebral artery, A1 segment of the anterior cerebral artery, P1 segment of the posterior cerebral artery, basilar artery, carotid artery) include balloon angioplasty,

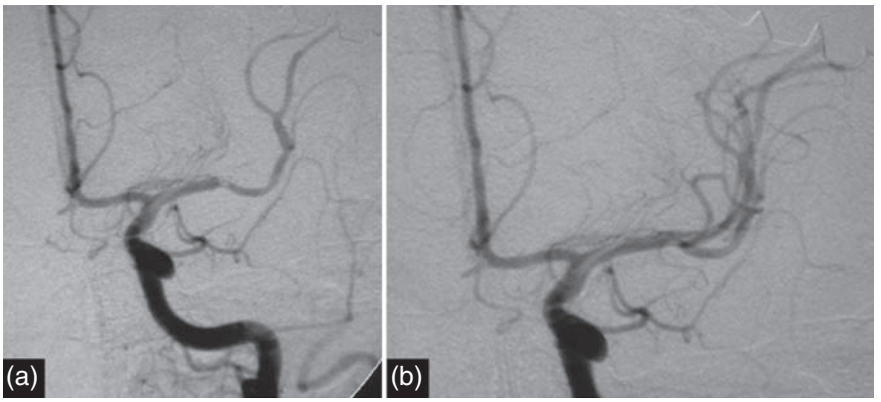

Figure 7.6 (a) M1/M2 embolus after endarterectomy. (b) Opening of middle cerebral artery with Merci® retriever (Concentric Medical, Mountain View, CA).

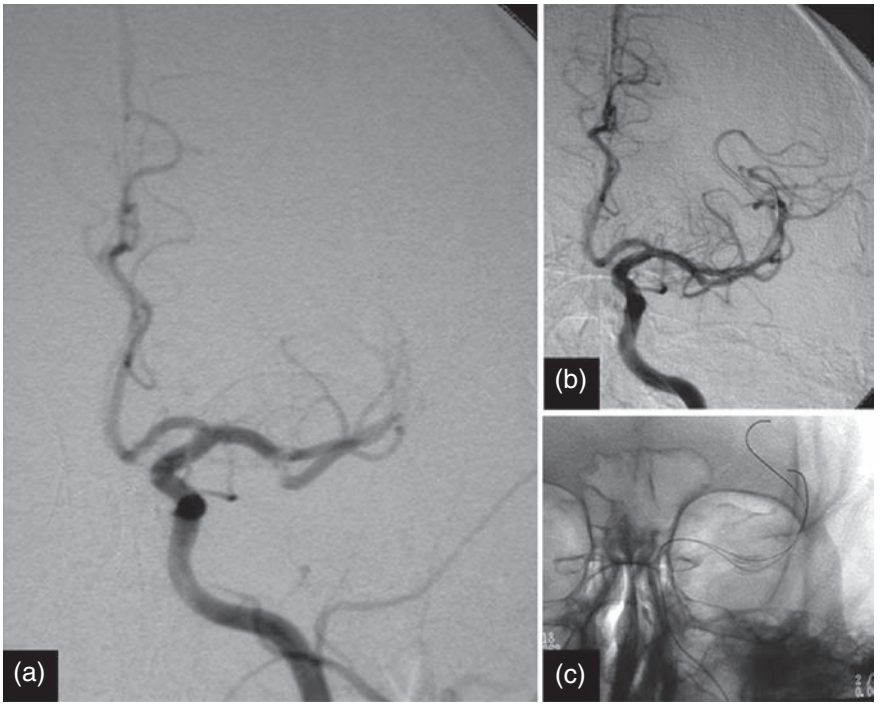

Figure 7.7 (a) Superior and inferior M2 occlusion. (b) Opening of M2 divisions with stents. (c) Wires in M3 branches and unsubtracted view demonstrating both stents.

snares, large microcatheters, and stents[48] (Figure 7.7a–c).

In settings other than clear large vessel cut-off, if the DEP has already been deployed, the procedure should be completed and a cranial CT scan obtained. Intracranial hemorrhage (ICH) can present as slow flow and, prior to expansion of the hematoma and development of significant mass effect, it may appear as a shower of emboli. If an angiogram documents slow flow and the CT is negative for hemorrhage, IIb/IIIa antiplatelet agents are administered as a bolus dose followed

by a 23-hour infusion. The patient's blood pressure should be controlled tightly, with a systolic blood pressure of less than 160 mmHg. If a hemorrhage is identified (Figure 7.8a–c), the systemic heparin anticoagulation should be reversed with protamine, the blood pressure tightly controlled, and a repeat CT scan obtained in 6 to 12 hours. Life-threatening hematomas in neurologically salvageable patients can be evacuated. In the setting of hematoma expansion but no operative indication, factor VII can be given to stop the progression of the hemorrhage. According to the trauma literature, most ICHs expand within the first 12 hours.[49] Strong consideration should be given to stopping the patient's dual antiplatelet therapy. The source of reperfusion hemorrhage remains debatable; some advocate a hyperperfusion origin, whereas others have suggested hemorrhagic conversion of a shower of emboli. In different cases, both sources are likely possible. However, once the hemorrhage has occurred, the treatment is identical.

Occasionally, a patient will present with an intracranial aneurysm ipsilateral to a critically severe carotid stenosis. In a review of NASCET data, 1 of 90 patients with aneurysms known before the performance of CEA experienced aneurysm rupture (at 6 days post CEA).[50] On the basis of the findings of the International Study of Unruptured Intracranial Aneurysms (ISUIA),[51] the following approach seems rational: for patients with unruptured, asymptomatic aneurysms smaller than 6 mm, CAS can be performed prior to any aneurysm treatment; and for patients with unruptured, symptomatic aneurysms 6 mm or larger, the aneurysm should likely be treated before CAS is performed.

Systemic complications

Systemic complications of endoluminal carotid intervention include seizures, MI, contrast material nephropathy, and contrast material allergy. If a patient has a seizure during angiography,

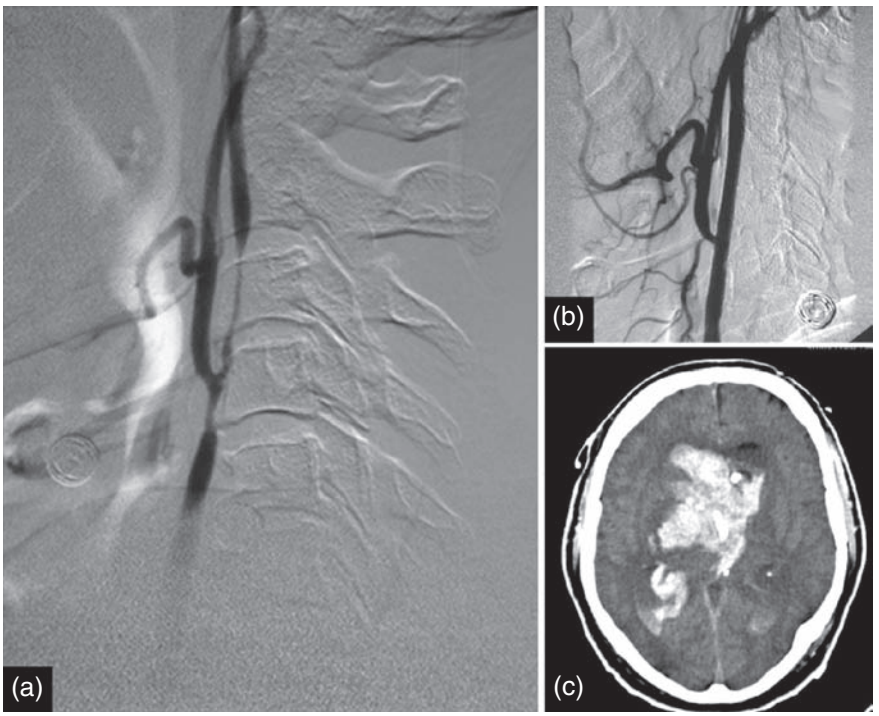

Figure 7.8 (a) High-grade symptomatic carotid restenosis. (b) Good revascularization with angioplasty and stenting. (c) Massive reperfusion hemorrhage.

attention should first be paid to basic life support and pharmacologic seizure control consisting of the establishment of an airway and administration of lorazepam (2 mg) and a phosphenytoin load (18–20 mg/kg body weight). The differential diagnoses include embolism (air, necrotic debris), ischemia from vessel occlusion or vasospasm, ICH, hyperperfusion, and contrast sensitivity (which is less common with lower osmolar load agents). After the seizure has been aborted and control of the airway established, angiography should be performed and a CT scan obtained and the differential diagnosis worked through until a source is identified. An electroencephalogram is performed if necessary.

The rate of MI in the SAPPHIRE trial was 2.5% at 1 year, which was statistically lower than the risk for MI during CEA.[12] One of the major benefits for CAS in the major studies completed is the lower incidence of intraprocedural and postprocedural MI. However, MI still occurs in the CAS population. Standard measures that include nitrate infusion, beta blockade, and heparin administration should be initiated if MI is diagnosed by obtaining cardiac enzymes and electrocardiogram. A cardiologist should be consulted early, because those patients with Q-wave infarction seen on the electrocardiogram usually will require acute coronary revascularization.

Acute allergy to contrast material is another setting in which airway safety is ensured. The patient should be intubated if necessary. Methylprednisolone (120 mg given parenterally) and epinephrine (1 mg) are administered as necessary. Patients with known contrast media allergies are treated with 30 mg of prednisone at 12 hours and then 1 hour before the procedure, along with 50 mg of benadryl.

The exact incidence of contrast nephropathy is not clear. In one study of patients with creatinine levels less than 1.5 mg per deciliter, only 8% of patients had an increase in their level of 0.5 mg per deciliter, and none had rises greater than 1.0 mg per deciliter with angiography. Other data suggest that contrast nephropathy is the third most common cause of renal failure in hospitalized patients.[52] Certainly, the state of a patient's renal function prior to angiography is the greatest determinant of post-treatment renal failure. A recent exhaustive review of contrast nephropathy[52] gives a few practical guidelines for renal prophylaxis in patients with pre-existing elevated creatinine levels. Hydration with normal saline (0.9% NaCl) for 2 to 12 hours at a level of 1 ml/kg/h before contrast administration is recommended. Low doses of low osmolar contrast agents like iodixanol should be given. Doses greater than 5 ml/kg of body weight divided by serum creatinine level are associated with higher risk.

METHODS FOR DETECTING COMPLICATIONS

As reviewed in the previous section, the physiologic and neurologic examination of the patient while on the angiography table is the first step taken to detect a complication. Comparison of the initial control cervical and intracranial angiographic images with the final angiographic images obtained, with the patient still on the table, is the second step. Angiographically, vessel cut-off and slow intracranial flow during the capillary phase can suggest a shower of emboli or focal embolic occlusion. When there has been neurologic change and no clear vessel cut-off, CT scanning is required to rule out intracranial hemorrhage. All patients should undergo repeat carotid duplex imaging within 24 hours postprocedure as a baseline measurement; however, this has rarely, if ever, been the means for identifying a complication. If CT scanning is negative for hemorrhage, any patient experiencing TIA or stroke systems during the periprocedural period is brought to the angiogram suite for a repeat study. For systemic complications, these should be identified and the usual pathways followed as described above, i.e., electrocardiogram, enzymes for suspicion of MI, CT scan, anti-epileptic agents, and electroencephalogram for seizure activity.

TREATMENT OF COMPLICATIONS

The site- and equipment-specific complications have been reviewed earlier. However, some general comments can be made regarding management of complications by frequency. A recent review of the data for more than 300 patients who underwent CAS at the University at Buffalo Department of Neurosurgery has shown morbidity

and mortality in line with the NASCET and ACAS standards of <6% major morbidity and mortality for symptomatic lesions and <3% for asymptomatic lesions.[17] Among those complications that occurred most commonly, shower of emboli, reperfusion hemorrhage, and MI were responsible for the major morbidity and mortality. One patient had femoral artery shut down caused by the placement of a closure device that required open vascular repair.

Embolic showering is generally detected by a change in the patient's neurologic examination on the angiography table including, but not limited to, hemiplegia, neglect, or speech difficulty. Angiographically, there will be slowing in the capillary phase. If CT scanning demonstrates no hemorrhage, these patients are brought back to the angiogram suite and a bolus dose of eptifibatide or another IIb/IIIa inhibitor is infused into the appropriate hemisphere, and a drip is hung for a 23-hour infusion. Most patients will improve. Frank vessel drop-out has not often occurred, but would require microcatheter access of the lesion and either thrombolysis, Merci® retrieval, or stenting, as mentioned.

The diagnosis of intracranial hemorrhage requires heparin reversal and is often a fatal event. Severe hypoperfusion and hemorrhagically converted stroke are the most common causes. Hemorrhage may necessitate intracranial pressure monitoring, drainage of CSF, or operative removal. One interesting case at the University at Buffalo occurred in a 45-year-old man with a symptomatic left carotid artery dissection and no significant infarction on preoperative imaging. After loading doses of aspirin and clopidogrel had been administered, the patient was brought to the angiography suite (Figure 7.9a). After femoral artery access was obtained, sufficient heparin was administered to produce an activated coagulation time of >250 seconds. A 6 Fr Cook shuttle was then brought into the left ICA. The lesion was crossed with a PVS wire (Boston Scientific/Precision Vascular Systems, West Valley City, UT) and s110 catheter (Boston Scientific) and then an Allstar™ 14-inch wire (Guidant) was brought into the petrous segment of the carotid artery. Overlapping Xpert™ stents were placed across the dissection flap with excellent angiographic results (Figure 7.9b). The patient did well until 8 hours postprocedure when he complained of sudden worsening of his pretreatment headache and quickly progressed to clinical herniation. After CT scanning revealed nonconfluent temporal, paracentral, and basal ganglia hemorrhages (Figure 7.9c), the patient was brought to the operating room and underwent a craniotomy with removal of temporal clot. He made a fair recovery after several weeks of rehabilitation therapy. Because of his mild preoperative symptoms, repeat magnetic resonance (MR) imaging was not obtained before the procedure, which may have demonstrated larger areas of ischemic injury with petechial hemorrhage than clinically suspected.

METHODS TO AVOID COMPLICATIONS

The best way to avoid complications of CAS is to predict in the preoperative setting who is not a good candidate. Patients with asymptomatic disease who have concurrent severe medical comorbidities (i.e., ejection fraction <30%, active cardiac ischemia, severe chronic obstructive pulmonary disease, or severe peripheral vascular disease) are best left alone. Although there are many techniques to gain access to type III arches, e.g., Simmons 2 or 3 guide catheters (Terumo Medical, Somerset NJ), wire obturator combinations like a Vitek (Cordis) or slip catheter (Cook) with a guide catheter, and balloon purchase followed by guide catheter placement, if the operator is inexperienced or there is no clear indication for CAS, these patients are generally better with medical management or CEA. Severe calcific stenoses with proximal and distal kinks are well treated with CEA and can provide a great challenge for CAS.

After the decision has been made to treat with CAS, appropriate guide catheter choice is critical. In a challenging proximal arch, a 6 Fr angled Envoy® catheter can be a good choice, so long as a stent longer than 8 mm is not needed for adequate coverage of the lesion. For short CCAs or tight stenoses with kinks, a stiffer guide catheter like a Cook shuttle is an excellent choice. Appropriate dosing of heparin and loading of antiplatelet medications is essential. Use of platelet aggregometers, although these devices are relatively new, may well help to lower the embolic risks of

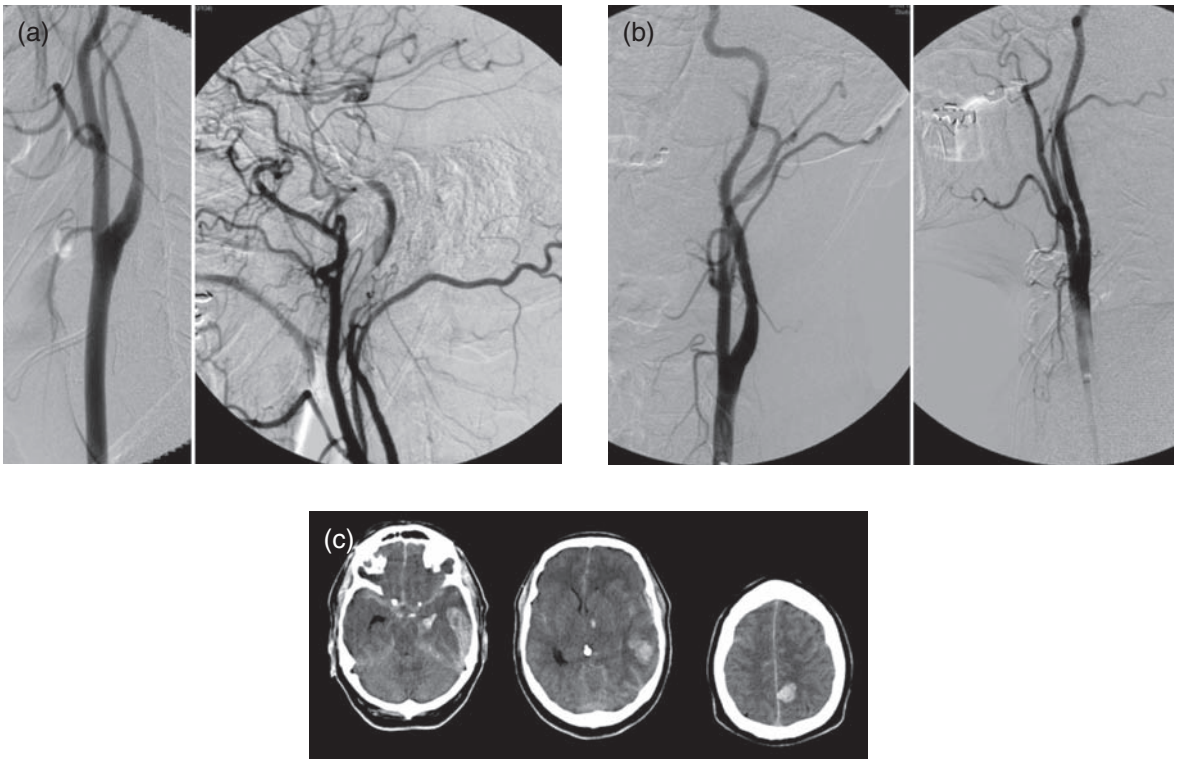

Figure 7.9 (a) Angiogram demonstrating the extent of the flow-limiting dissection. *Left*, lower cervical (AP view); *right*, higher cervical (lateral view). (b) Immediately after the deployment of overlapping Xpert™ stents (Abbott Vascular, Inc, Redwood City, CA). *Left*, AP view; *right*, lateral view. (c) CT images demonstrating non-synchronous, non-confluent ICHs. *Left*, left temporal ICH and subarachnoid hemorrhage; *middle*, left temporal and left basal ganglia hemorrhages; *right*, left parietal ICH.

stenting by identifying those patients who will not benefit from standard antiplatelet regimens. Technical problems with filters and stents can be best avoided by understanding the mechanics of all the devices before performing stenting procedures. Most often, technical problems relate to guide catheter access, and the inability to cross a lesion with a stent or to recapture a filter device can often be solved by simply bringing the guide catheter higher. The details of bailout techniques have been reviewed earlier in this chapter.

SUMMARY

Carotid artery angioplasty and stenting can be performed with low morbidity and mortality. However, complications can occur that can quickly take a patient from normal health to severe neurologic impairment or death. Unlike CEA in which a few simple tools are used, a detailed understanding of the complexities of the CAS systems is necessary. Furthermore, as many of the patients have blood vessel disorders and multisystem disease, systemic complications like MI and renal failure are possible. Good mentoring by an experienced operator, careful patient selection, an understanding of the limitations and benefits of each device, and meticulous care before, during, and after the procedure will maximize the potential for excellent clinical results.

CHECK LIST FOR EMERGENCY EQUIPMENT FOR INTERVENTIONS IN THIS SPECIFIC VESSEL AREA

The following is a list of emergency supplies for CAS complications in our interventional suite:

- protamine; reteplase, eptifibatide
- epinephrine (for allergic reactions)

- nitroglycerin (for catheter-induced spasm, angina)
- atropine (for treatment of bradycardia or asystole)
- lorazepam and phosphenytoin (anti-epileptic agents)
- tracheostomy set
- emergency crash cart
- 0.014- to 0.021-inch microcatheters and wires
- detachable or pushable coils
- liquid embolic agents: NBCA, Onyx®
- MERCI® retriever
- stents appropriately sized for the intracranial circulation: e.g., Neuroform™, MiniVision (Guidant).

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8

Complications in percutaneous subclavian and vertebral artery interventions

Julio A Rodriguez, Francisco Guerrero-Baena, Dawn M Olsen, and Edward B Diethrich

Introduction to the frequency and type of complications • Factors identifying high-risk patients for complications • Complications of specific interventional steps and complications of specific interventional tools • Methods to detect potential complications – which diagnostic steps are needed routinely to rule out or identify complications • Endovascular, surgical, and/or medical techniques to resolve complications • Methods to avoid complications • Summary • Check list for emergency equipment for interventions in this specific vessel area

INTRODUCTION TO THE FREQUENCY AND TYPE OF COMPLICATIONS

More and more, clinicians rely on angioplasty and stenting to correct flow abnormalities. Subclavian artery stenosis and occlusions have traditionally been managed with classic, open surgical repair via a transthoracic or cervical approach. This involved carotid–subclavian bypass or subclavian artery transposition. Introduction of extra-anatomic surgical techniques allowed for satisfactory long-term patency and decreased incidence of serious complications related to aortic inflow.[1–4] Unfortunately, though the minimally invasive approach reduced mortality, there was an increase in local complications.[5,6] Percutaneous revascularization has become popular in the management of upper extremity claudication and subclavian steal syndrome,[7,8] coronary steal syndrome,[9,10] and treatment of pathologic atherosclerotic lesions of the subclavian artery (SCA) including Takayasu's arteritis,[11–13] Behcet's disease,[14] fibromuscular dysplasia,[15] radiation-induced stenosis,[16] true aneurysms,[17] mycotic aneurysms,[18] post-traumatic pseudoaneurysms, arteriovenous fistulae, bleeding,[19–21] and spontaneous[22] or iatrogenic dissections[23] (Table 8.1).

Management of extracranial vertebral disease has been a controversial issue because, although operative and follow-up results reported were promising, reported experience in this field represented only a few centers,[24–26] and most vertebral occlusive disease has been managed with medical treatment. Once thought to be benign, posterior cerebral disease was shown in the New England Medical Center Posterior Circulation Registry to increase the risk of stroke, causing major disability in 18% and death in 3.6%.[27] A growing literature of case series suggests endovascular intervention with percutaneous transluminal angioplasty (PTA) and stenting is a safe and effective treatment for extracranial vertebral artery atherosclerotic stenosis of >50% at the vertebral artery origin[28–33] and promotes a favorable hemodynamic response after angioplasty.[34] Some early reports of angioplasty alone for vertebral artery origin stenosis cited a marked incidence of restenosis.[33] Primary deployment of stents to stenotic lesions in the extracranial vertebral arteries, however, has shown high levels of technical success (98–100%),[28–33] making primary stenting at the origin of the vertebral artery the therapy of choice.

Table 8.1 Clinical indications for endovascular interventions

Clinical indications for endovascular procedures

1. Chronic upper limb ischemia
   a. distal embolization
   b. limb claudication with no response to conservative management
2. Neurologic symptoms
   a. subclavian steal syndrome with vertebrobasilar symptoms
   b. contralateral vertebral and/or multivessel supraortic disease
   c. unstable plaque/dissection with embolization or high risk
3. Acute upper limb ischemia
4. Acute vertebral occlusion (dissection and/or thrombosis)
5. Myocardial risk
   a. subclavian – coronary steal syndrome – IMA (symptomatic or asymptomatic)
   b. prior to CABG in subclavian artery stenosis
   c. subclavian artery patency protection in coronary disease patient who may need coronary revascularization in future
6. Failing or rescue of an acute occlusion of an extra-anatomic bypass graft
7. Failing dialysis AV fistula
8. Arterial access for another procedure (heart catheterization)
9. True aneurysms
10. Traumatic arterial injury
    a. pseudoaneurysms
    b. AV fistula
    c. bleeding
11. Spontaneous rupture
    a. aneurysms
    b. other non-traumatic entities – cerebral fibromuscular dysplasia

IMA, internal mammary artery; CABG, coronary artery bypass graft; AV, arteriovenous.

Although randomized trials to assess endovascular management of posterior cerebral circulation atherosclerotic occlusive disease are lacking,[35] there are many case reports documenting satisfactory results. However, given the small numbers and variations in type of procedures, it is difficult to determine the true incidence of complications and long-term patency. The complications cited in our review have been experienced by most of the readers dedicated to endovascular therapy. Endoluminal procedures are less commonly performed in the subclavian and vertebral arteries as compared to lower-limb revascularization, and there are no reported standards for treatment and management of potential complications. Potential complications are shown in Table 8.2, and key points to consider in preventing them are listed in Table 8.3. Tables 8.4 and 8.5 provide information from the literature about common complications of subclavian and vertebral interventions, respectively. Our experience with these types of intervention has led to the following comments about technical management of the procedures and their complications.

FACTORS IDENTIFYING HIGH-RISK PATIENTS FOR COMPLICATIONS

Disease in the subclavian is most commonly found at the arch origins, and there often remains a 1–2 cm stump of subclavian artery from the aortic lumen, allowing adequate access for angioplasty and stenting. Normally, subclavian and innominate artery lesions are concentric, although the proximal aortic stump may present some asymmetry secondary to flow disturbances caused by plaque formation, particularly at the 90° origin of the left subclavian artery. In general, lesions are not associated with loose debris, but ulcerated plaques may be seen in the vertebral artery and are sometimes associated with upper limb embolization. Although subclavian lesions are quite often calcific in nature, most are easily crossed, ballooned, and stented. Lesions in the second part of the subclavian artery, however, should be evaluated very carefully to ensure that stent placement will not interfere with patency of the vertebral artery or the internal mammary artery. Subclavian lesions frequently affect the left side more often than the right because of the intrathoracic segment, and are generally limited to the proximal segment. Overall, endovascular manipulation of the subclavian is relatively safe.

In the innominate artery, elongation may occur with age. Access by a retrograde femoral approach may be difficult, and there may be an increase of risk of right carotid events secondary to manipulation. Other anatomic considerations

Table 8.2 Subclavian and vertebral artery complications

Complications

1. Related to the puncture site
   a. thrombosis
   b. bleeding
   c. pseudoaneurysm
   d. AV fistula
   e. arterial injury
   f. peripheral nerve injury
2. Related to aorto-iliac navigation
   a. peripheral atheroembolism: *to limbs*, *visceral*, *cerebral*
   b. arterial injury
3. Related to the use of contrast
   a. allergies
   b. renal failure
   c. metabolic problems
4. Related to target vessel manipulation
   a. spasm
   b. peripheral embolism (microembolic, atheroembolism) *to upper limb, cerebral, IMA*
   c. wire tip injury
      i. *subintimal dissection*
      ii. *perforation*
   d. postballooning injury
      i. *dissection*
      ii. *plaque rupture*
   e. damage to arteries in close proximity: *vertebral, right common carotid, IMA*
   f. 'in situ' vessel rupture
   g. 'in situ' thrombosis
   h. aortic dissection
5. Related to hemodynamic response to the angioplasty
   a. cerebral hyperperfusion syndrome
   b. upper limb hyperperfusion syndrome (hyperemia, swelling)
   c. compartment syndrome
6. Delayed complications
   a. dissection
   b. pseudoaneurysm
   c. mycotic aneurysm
7. Failure
   a. in-stent restenosis
   b. occlusion
   c. persistence of symptoms

IMA, internal mammary artery; AV, arteriovenous.

that increase embolic risk with a femoral approach are a bovine arch (10%), type II or III arch, right-sided lesions, an arch origin of the left vertebral artery (5%), or an ostial lesion that must be crossed during arch navigation. Lesions of the aortic arch and brachiocephalic artery may be associated with extensive atherosclerosis.[36–38] Accurate diagnostic assessment that includes careful imaging with angiographic studies (conventional angiography, CTA, and MRA) and hemodynamic explorations via cervical duplex ultrasound are important in reducing the risk of procedure-related emboli[39] and global ischemia. Indeed, ischemic neurologic symptoms may be a consequence of aortic arch navigation with hemispheric embolization or innominate artery and right common carotid manipulation.[40–42] Jaeger et al[43] reported that 94% of asymptomatic lesions detected in 8 patients who underwent angioplasty or angioplasty plus stenting of brachiocephalic arteries by diffusion-weighted MRI were located in territories irrigated by the target vessel. Although MRI is not a routine study in the preoperative work-up of the brachiocephalic vessels, it is useful for identifying thrombus and plaque characteristics that may increase the risk of embolization.[44] Calcific atherosclerotic plaques affecting either the subclavian or vertebral arteries are also prone to dissection (Figure 8.1), which is probably the most common complication related to angioplasty, and a potential cause of extensive damage and procedural failure.

The left vertebral artery is dominant in 50% of individuals, whereas right dominance occurs in 25%. Dominance may be clinically significant in occlusive disease and related to the trend toward left-sided lesions in the subclavian territory. Anatomically, the vertebral artery measures 3–5 mm and can be divided into four different segments – three extracranial and one intracranial portion (Figure 8.2). The first portion corresponds to the origin of the vessel to the level where it enters the transverse foramen of the cervical vertebral body. The extracranial portion of the vertebral artery can be affected by numerous etiologic factors, athererosclerotic disease being the most common. Other conditions include fibromuscular dysplasia, dissection, vasculitis, or extrinsic compression – this is particularly true in the intervertebral segment and is mostly due to trauma or an osteophyte. The most common extracranial location is ostial, where the lesions may have fibrous characteristics that make them less prone to ulceration.[45] Symptoms related

Table 8.3 Key points to consider to minimize endovascular complications

Minimizing complications in subclavian and extracranial territories

1. Indication
   a. accurate case selection
2. Characterize disease at the target vessel
   a. approach: aorta, arch anatomy
   b. for subclavian artery
      i. stenosis vs occlusion
      ii. proximal subclavian stump
      iii. vertebral artery and LIMA
      iv. vertebral retrograde flow
      v. extension towards axillary artery
   c. for vertebral artery
      i. stenosis, dissection
      ii. location proximal/distal (segment involved V1–V4)
      iii. single/tandem
3. Anticoagulate the patient
   a. antiplatelets prior to procedure
   b. heparinization during the procedure; maintain ACT above 250
   c. ESR normalized in arteritis, steroid therapy if needed
4. Choose access site
   a. associate complementary techniques if needed (aorto-iliac procedure, brachial cutdown)
   b. antegrade access requires a subclavian stump on aortic side
   c. retrograde access requires careful 'crossing technique' of the lesion
5. Obtain an optimal view of the extension of the artery to treat
   a. unfold the subclavian artery to see branch ostium over the aorta
   b. same for ostial vertebral artery over subclavian artery
6. Protective techniques to avoid embolization and neighboring vessel injury if needed
   a. vertebral and internal mammary artery (wire catheterization, kissing balloon technique)
   b. right common carotid artery protection in right subclavian – innominate artery procedures
7. Rule out technical defects after procedure
   a. visible defects on angiographic imaging
      i. flow defects (dissection, occlusion, residual stenosis)
      ii. extravasation (perforation, rupture)
   b. invisible defects on operative angiographic imaging
      i. hemodynamic evaluation of flow (pressure gradient across the lesion)
      ii. IVUS (stent apposition to arterial wall, dissection, residual stenosis)
8. If selective stenting is preferred
   a. innominate and subclavian artery stenting is recommended after suboptimal angioplasty and occlusion
   b. ostial vertebral artery stenting is recommended
   c. antiplatelet therapy
9. Follow-up
   a. in-stent restenosis has a silent evolution; close follow-up is mandatory
   b. in patients with mammary–coronary bypass grafting, subclavian patency follow-up becomes important.

LIMA, left internal mammary artery; ACT, accelerated clotting time; ESR, erythrocyte sedimentation rate; IVUS, intravascular ultrasound.

to vertebral artery stenosis are part of the vertebrobasilar insufficiency constellation, including brief TIAs, dizziness, difficulty with visual focus, and loss of balance. These symptoms are related to ischemia of the vestibulocerebellar structures in the medulla and cerebellum.[46] Associated intracranial and bilateral disease may increase cerebral ischemia.[47]

The natural tortuosity of the vertebral artery at V1 and V3 segments makes this vessel prone

Table 8.4 Complications in subclavian artery interventions

Author	*Total (#)*	*PTA/stent*	*Success in occlusions (%)*	*Complications*	*Death*
Henry et al[132]	113	57/46	9/19 (47)	3 (2.7%) access complications, 1 (3.1%) brachial thrombosis, 4 (3.6%) dissection, 1 (0.9%) vessel occlusion, 1 (0.9%) TIA, 1 (0.9%) stroke	0
Schillinger et al[130]	115	89/26	13/27 (48)	7 (6.1%) minor complications, 3 (2.6%) visceral embolization, 1 (0.9%) TIA	0
deVries et al[42]	110	43/59	13/20 (65)	3 (2.7%) dissections, 2 (1.8%) TIA, 2 (1.8%) stroke	1 (1.8%)
Martinez et al[56]	17	0/16	17/17 (100)	1 (6%) stent migration, 1 (6%) thrombosis (residual stenosis)	0
Huttl et al[41]	89	89/0	Not specified	2 (2.3%) groin hematoma, 2 (2.2%) residual stenosis, 4 (4.5%) TIA, 1 (1.1%) stroke	0
Brountzos et al[84]	49	0/49	Not specified	2 (5%) groin hematoma, 1 (2%) brachial-axillary thromboembolism, 2 (4.1%) residual stenosis, 1 (2%) vessel thrombosis, 1 (2%) TIA	0
Bates et al[131]	94	0/91	13/15 (87)	8 (8.5%); 2 (2.1%) access hematoma, 2 (2.1%) embolism, 1 (1.1%) peripheral arterial thrombosis, 1 (1.1%) stent migration (spasm), 1 (1.1%) heart failure episode	0
Sullivan et al[58]	73	0/69	6/10 (60)	1 (1.4%) brachial embolization, 3 (9.7%) brachial hematoma, 1 (3.2%) brachial AV fistula, 1 (3.2%) brachial pseudoaneurysm, 1 (2%) femoral pseudoaneurysm, 2 (2.9%) VA origin coverage, 1 (1.4%) LIMA embolization	0
Amor et al[40]	89	0/83	7/13 (54)	5 (5.6%) minor access complications, 2 (2.2%) limb embolization, 1 (1.1%) LIMA embolization, 1 (1.1%) TIA, 1 (1.1%) stroke	1 (1.1%)
Al-Mubarak et al[134]	38	0/35	1/4 (25)	no complications	0
Tyagi et al[53]	61 (32 T.A.)	59/0	3/5 (60)	2 (3.3%) dissection, 1 (1.6%) thrombosis, 1 (1.6%) residual stenosis	0
Rodriguez et al[10]	110	5/105	25/30 (83)	4 access thrombosis, 5 (4.5%) dissection, 4 (3.6%) residual stenosis, 3 (2.7%) thrombosis, 1 stent migration (0.9%), 1 (0.9%) TIA	0
Sadato et al[135]	7	0/7	7/7 (100)	1 (20%) brachial thrombosis, 1 (14.3%) residual stenosis and thrombosis (14.3%), 1 stroke	1 (14.3%)

continued

Table 8.4 Complications in subclavian artery interventions – continued

Author	*Total (#)*	*PTA/stent*	*Success in occlusions (%)*	*Complications*	*Death*
Erbstein et al[75]	24	24/0	2/2 (100)	5 (20.8%) dissection, 5 (20.8%) residual stenosis, 1 (4.2%) TIA	0
Insall et al[133]	37	33/0	2/2 (100)	1 (2.7%) groin hematoma 1 (2.7%) peripheral artery thrombosis, 3 (8.1%) residual stenosis, 1 (2.7%) stroke	1 (2.7%)
Wilms et al[136]	23	21/0	—	1 (4.3%) peripheral embolism 1 (4.3%) peripheral artery thrombosis	0
Motarjeme[36]	93	84/2	6/13 (46)	1 (1.1%) peripheral embolism	0

Ath, atherosclerotic; CCA, common carotid artery; LIMA, left internal mammary artery; PTA, percutaneous transluminal angioplasty; TA, Takayasu arteritis; TIA, transient ischemic attack; VA, vertebral artery.

to injury during endoluminal intervention.[48] Dissection or perforation is a risk, particularly with interventions at distal territories of the vertebral artery, V3 and V4 (Figure 8.3). These segments are subject to wire tip injury during navigation that may result in life-threatening intracranial bleeding and can be difficult to control.[49] Postoperatively, patency has been related to reference vessel diameter.[50]

Some differences in the distribution of atherosclerotic posterior circulation occlusive disease may be related to gender and race. Caucasians tend to have lesions at the origin of the left vertebral artery and high-grade lesions of the extracranial vertebral arteries. African-American patients tend to have lesions of the distal basilar artery, high-grade lesions of intracranial branch vessels, and symptomatic intracranial branch disease.[51,52] Other etiologies such as fibromuscular dysplasia or Takayasu's arteritis affect younger patients, particularly women. In treating Takayasu's arteritis, high rates of dissection and suboptimal dilatation and restenosis are often seen in long lesions.[53] When acute inflammation is suspected, preoperative steroid treatment that normalizes the ESR may improve outcome.[12,54,55]

COMPLICATIONS OF SPECIFIC INTERVENTIONAL STEPS AND TOOLS

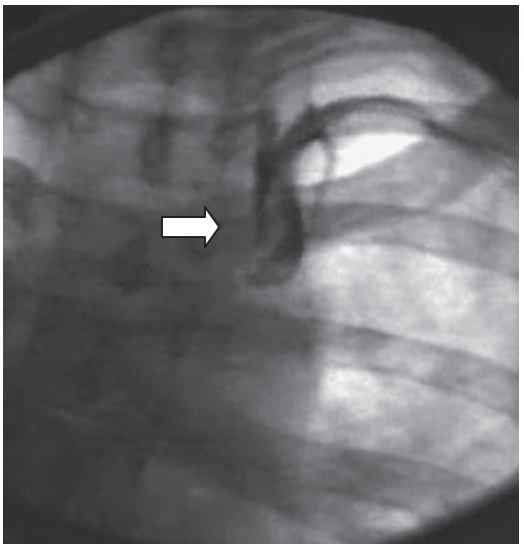
Oral antiplatelet therapy is used in stenting procedures in the subclavian and vertebral arteries and may be given preoperatively, or once the vessel is accessed. Local anesthesia with mild sedation allows the assessment of neurologic episodes, but there are disadvantages to using local anesthesia, as patient movement during the procedure can be problematic when 'roadmapping' is being used to guide balloon angioplasty or stent deployment.

Endovascular management of subclavian artery occlusions was initially associated with failure rates as high as 54%.[36] However, in other series, mid-term patency rates of up to 84% were reported.[56,57] The best way to access the target lesion is still controversial, and the risks and benefits of different approaches (femoral, brachial) have to be assessed on a case-by-case basis. Our preference, especially in a tight lesion, is the

Table 8.5 Complications in vertebral artery interventions

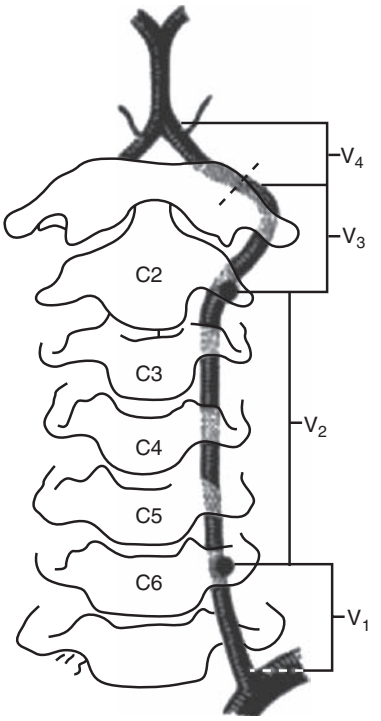
Author	*Total (#)*	*PTA/stent*	*Success*	*Complications*	*Death*
Albuquerque et al[61]	33 (proximal VA)	33/0	32 (97%)	1 (3%) dissection, 1 (3%) stent maldeployment	1 (3%)
Chastain et al[48]	55 (proximal VA)	0/55	54 (98%)	1 (1.8%) dissection	2 (3.6%) non-related
Cloud et al[101]	14 (proximal VA)	4/10	14 (100%)	1 (7.1%) residual stenosis, 1 (7.1%) 72 h postoperative TIA, 1 (7.1%) brachial hematoma	0
Hauth et al[49]	16 (11 proximal, 1 cervical, 4 distal V4)	9/3	14 (87%)	1 (6.25%) dissection with vessel occlusion	0
Higashida et al[28]	41 (34 proximal, 5 distal VA, 3 BA)	41/0	—	1 (2.4%) vessel rupture, 2 (4.9%) spasm, 2 (4.9%) TIA, 2 (4.9%) stroke	0
Janssens et al[137]	19 (proximal VA)	19/0	17 (89%)	4 (21%) residual stenosis, 4 (21%) dissections, 1 (5.2%) groin hematoma, 1 (5.2%) access dissection (bilateral iliac artery)	0
Jenkins et al[29]	38 (34 proximal, 4 cervical VA)	0/38	38 (100%)	1 (2.6%) TIA	0
Malek et al[31]	13 (10 proximal, 3 cervical VA)	0/13	13 (100%)	5 (38%) dissections, 1 (7.7%) TIA	0
Motarjeme[36]	39 (35 proximal, 1 cervical and 2 distal VA)	0/36	36 (92%)	1 (2.6%) bilateral blindness, (bilateral severe VA stenosis PTA)	0
Piotin et al[100]	7 (proximal VA)	7/0	7 (100%)	no complications	0
Weber et al[70]	38 (proximal VA)	0/38	38 (100%)	2 (5.3%) dissections, 1 (2.6%) TIA	0

CA, carotid artery; PTA, percutaneous transluminal angioplasty; TIA, transient ischemic attack; VA, vertebral artery.



white arrow – prevertebral dissection

Figure 8.1 Angiogram of a subclavian artery dissection.



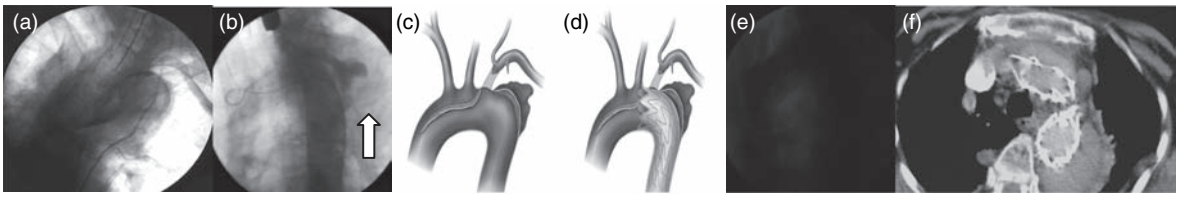
Vertebral Artery: V1 – extends from the arterial ostium to the level where it enters at C6 transverse foramen, V2 – "intraoseum" from C6 to C2, V3 – extracranial but high in posterior neck at level of C1, V4 – intracranial from C1 to basilar artery

Figure 8.2 Anatomical classication of vertebral artery segments.

percutaneous brachial approach through a 5–6 Fr sheath because proximity to the site of the lesion allows better 'pushability' of the device. In general, the closer the puncture site is to the area of therapy, the easier it is to maneuver and access the area of interest. Accurate lesion cannulation is required to prevent plaque rupture and retrograde dissection to the thoracic aorta. Such complications have the potential for severe consequences.[58,59]

Femoral puncture sites are a considerable distance from lesions of the upper extremity and may be problematic when the arch configuration is tortuous or the great vessel origins are anomalous in their take-offs. A coaxial technique incorporating a diagnostic catheter may increase the strength of the guiding catheter, and placement of a long 7–8 Fr sheath in the vicinity of the target can also be helpful, providing better angiographic views closer to the lesion and offering better support for guiding a stent through a tight channel. A long sheath allows more placement options if navigation complications necessitate implantation of a stent in other territories (such as the iliac artery).[60]

Wire selection may be dictated by therapist experience and the target vessel and its characteristics. In our experience, an angled 0.035-inch hydrophilic guidewire and a straight 5 Fr angiographic catheter are adequate for most procedural approaches. In occlusions, if the initial maneuver is unsuccessful, a straight 0.035-inch stiff wire through a 45° angled catheter can enable cannulation of the core of the plaque (Figure 8.4). Predilatation with a 4 mm balloon can accommodate a stent device. From our point of view, lower profile wires (0.014 to 0.018-inch) can be considered in extraordinary cases for subclavian and innominate lesions, mainly when predilatation with a low-profile balloon is necessary. Different views (left/right oblique with cranial angulation) are recommended to obtain optimal visualization of the origin of the vessel to treat.



Aortic dissection complicating a subclavian occlusion angioplasty attempt. (a) dye staining both the ascending and descending aortic wall. (b) Two weeks later patient returns with chest pain. A pseudoaneurysm of the aorta is noted (white arrow). (c) schematic demonstrating the extension of the problem, (d) thoracic endograft placement to exclude the SCA and the pseudoaneurysm, (e) post-endograft angiogram demonstrating adequate seal. (f) chest CT-scan 1 month after the onset, free of endoleak.

Figure 8.3 Subclavian artery dissection that involves the descending thoracic aorta. New pseudoaneurysm develops and is treated with an endograft.

(a,b) Crossing technique in a subclavian artery total occlusion. (c,d) Use of an angulated catheter and a straight wire to stay within the core of the plaque. (e) "zig-zagging" of the wire usually leads to subintimal space, and ultimately to a dissection.

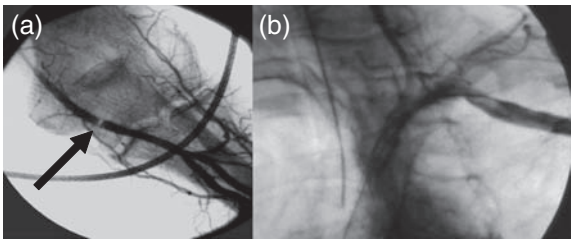
Figure 8.4 Crossing technique in subclavian artery occlusion.

The identification of the origin becomes paramount at the time of stent deployment, since one of the well-known causes of in-stent restenosis can be the inadvertently missed arterial ostium.

Routinely, balloon-expandable stents are the device of choice in an ostial location because of their radial strength and ease of deployment. Selection of stent size is based on the adjacent normal vessel and the length of the lesion. In general, the diameter of the balloon is 1 mm smaller than the balloon the stent is mounted on. In subclavian territories, self-expanding stents are useful in tortuous settings or in treating lesions at points of flexion. In these cases, the diameter of the stent may be 1–2 mm larger than the native vessel. The small diameter of vertebral arteries makes the use of short, low-profile balloon-expandable coronary stents ideal here.[61] This is an area in which stiff devices (wires, balloons, stents) can cause technical difficulties that have the potential to lead to major complications. Although we do not favor the use of stents in V2 and V3 segments due to the bony encasement of the vessel, others have placed stents here successfully.[62–64] If stenting is necessary in these segments, a flexible stent is advisable.

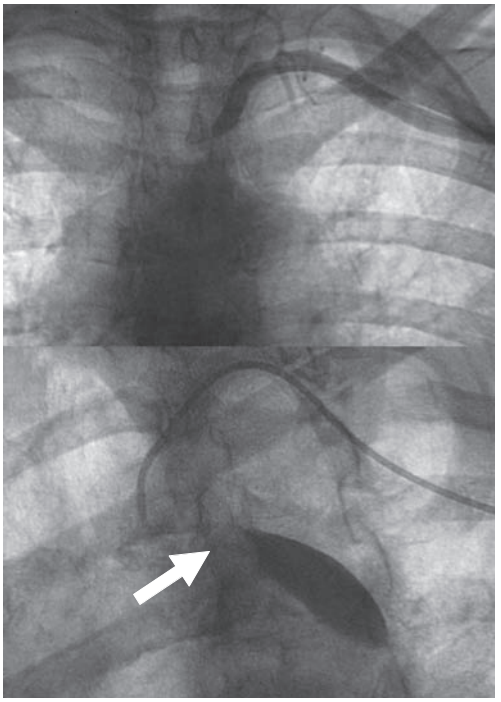
Local complications can occur with attempted percutaneous recanalization of the subclavian and vertebral arteries, including dissection, perforation, disruption, thrombosis, and embolization. In addition, complications such as the dissection of the arch aorta or vertebral artery may occur. Subintimal wire penetration or a catheter crossing against a rigid plaque can create a dissection plane, and this is a common complication in subclavian artery interventions. Though entering *under* a plaque in high-grade lesions and reentering into the true lumen may be a successful strategy, it is not always possible, especially in an occluded subclavian artery. While it is tempting to proceed in a subintimal plane, balloon angioplasty and stenting here may result in perforation of the vessel.

Plaque fracture related to angioplasty or stent maldeployment can create a flap (Figure 8.5). Dissections of brachiocephalic vessels may extend into adjacent territories including the aorta[58] (Figure 8.6) or vertebral arteries (Figure 8.7),



(a) intimal flap (arrow) with subsequent thrombosis, after brachial approach, (b) subclavian artery intraluminal thrombus secondary to a suboptimal angioplasty

Figure 8.5 Angiogram demonstrating brachial artery flap and subclavian artery thrombus.



Aortic dissection secondary to attempt of subclavian stenosis. The white arrow indicates the area of dissection on the proximal descending thoracic after attempting crossing the stenosis.

Figure 8.6 Aortic dissection secondary to attempt of subclavian angioplasty.

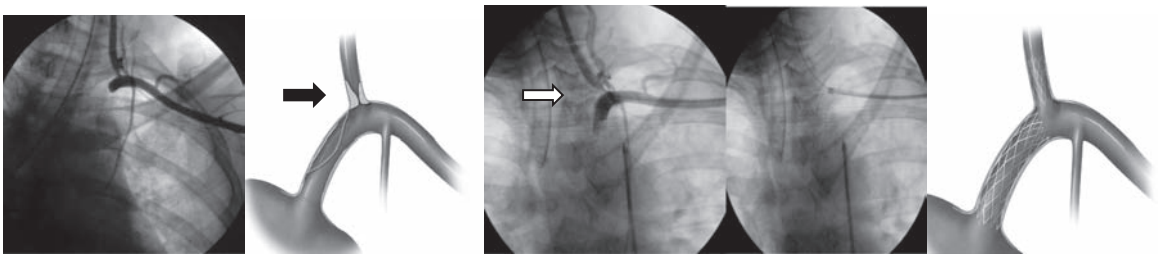
extending toward the upper limb and including the LIMA such that there is compromise of myocardial revascularization.[65] Persistent dissection beyond the stented area can result in procedure failure due to flow disturbance and, in some cases, development of a pseudoaneurysm.[66] Dissection at the ostium or prevertebral subclavian is likely to extend into the aortic arch, descending thoracic aorta, or vertebral artery, with sequelae that may be quite severe and include pseudoaneurysm development, rupture, or vertebrobasilar symptoms. If a dissection occurs and involves the descending thoracic aorta, its extension needs to be evaluated to determine the necessity of further treatment such as thoracic stenting or endoluminal grafting (Figure 8.3).

The subclavian artery is a thin-walled vessel compared with the carotid. The subclavian is susceptible to close trauma and operative injury even during conventional procedures and, though rare, perforation due to direct wire injury has been reported in endovascular intervention.[67–69] Tortuousity in subclavian and vertebral arteries may contribute to the potential for wire injury when there is an attempt to maneuver the lesion or manipulation occurs inadvertently at the level of the branches.[70] Iatrogenic arterial wall disruption can also be caused by balloon angioplasty or stent deployment. Both procedures transmit increased radial force from non-compliant devices to the vessel wall, and may produce a tear in a weakened area or in an underlying calcific lesion.

Vessel rupture is rare in the subclavian, and vertebral artery manipulation is more often associated with wall injuries[71,72] (see Table 8.5). Broadbent et al presented two cases of supra-aortic vessel rupture (one carotid and one subclavian) in a heterogeneous series of 180 patients.[72] Careful vessel diameter evaluation and device selection is of the utmost importance in avoiding overdilatation and arterial injury.

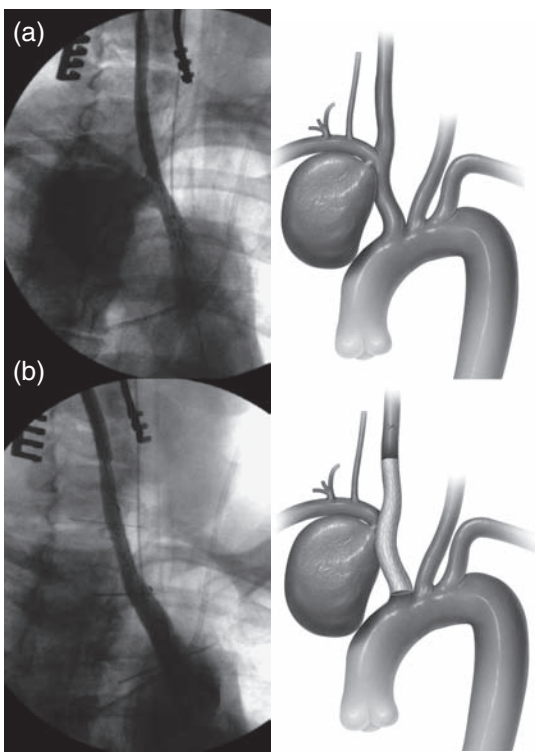
Manifestations of wall injuries due to perforation and rupture may present early or be delayed. Early presentation can range from a simple operative finding that can be managed in the same session, or one that results in a neck hematoma, pseudoaneurysm, or an active, life-threatening bleed in the thorax. Delayed presentation may be seen as a pulsatile mass secondary to pseudoaneurysm formation[73] (Figure 8.8).

The incidence of thrombosis is limited with the use of systemic periprocedural anticoagulation. The majority of the time, acute thrombosis is associated with the brachial artery access site. It can also occur due to an untreated iatrogenic dissection from wire advancement or balloon angioplasty. Subacute events may occur secondary to persistent stenosis. Incomplete dilatation was



Post subclavian angioplasty a dissection develops that extends into the ostium of the vertebral artery. (black & white arrows) The origin of the VA has to be stented to correct the dissection and the compromised lumen. The subclavian artery was treated following the VA intervention.

Figure 8.7 Dissection in the subclavian artery extended to the vertebral artery.



(a) Traumatic pseudoaneurysm arising from the ostium of the right subclavian artery, (b) Pseudoaneurysm excluded with a Gore endograft from distal common carotid approach

Figure 8.8 Pseudoaneurysm of the innominate artery, treated with endoluminal graft.

initially described as a potential source of thrombotic and embolic complications.[74] Causal factors may include suboptimal high-grade lesion angioplasty, a persistent dissection at the target lesion after balloon angioplasty (or in areas that might remain uncovered by the stent), unrecognized or ineffectively treated disease, maldeployed stents, and diseased axillary or brachial arteries that affect 'run-off'.[75] We experienced a case of dissection distal to the deployed stent in our series[10] (Table 8.4).

Embolization during endovascular management of subclavian and vertebral artery stenoses is also possible. There are two main sources of emboli. Debris can be liberated from the intimal arterial surface as endovascular devices advance to the target lesion. The other possibility is embolization from the target lesion itself. This is particularly concerning in subclavian–vertebral procedures due to the associated risk of stroke. Some series have shown a potential protective mechanism of direct vs selective stenting in reducing the incidence of embolic events.[40] There is, however, a well-known mechanism of physiologic protection during the angioplasty of the subclavian artery as described by Bachman, who evaluated vertebral flow after subclavian artery balloon angioplasty in patients with vertebral flow reversal secondary to subclavian steal syndrome.[76] Ultrasound monitoring of the homolateral vertebral flow patterns has also been described by Ringelstein,[77] who documented antegrade flow in 10 successfully treated patients with delay longer than 20 seconds after dilatation. This unexpected hemodynamic behavior provides physiologic protection that contributes to the low rate of neurologic events in patients treated for subclavian steal syndrome. MRI of ischemic lesions before and after brachiocephalic angioplasty also suggests the safety of subclavian

procedures.[43] Supra-aortic occlusive disease is related to extensive atherosclerosis, and neurologic symptoms may be a consequence of aortic arch navigation. Atherosclerotic plaque can be fragmented after balloon angioplasty and liberate debris to the circulation; the same plaque offers a thrombogenic surface to platelets. Potential affected end organs are the upper limb and brain (via the posterior circulation and the right carotid artery).

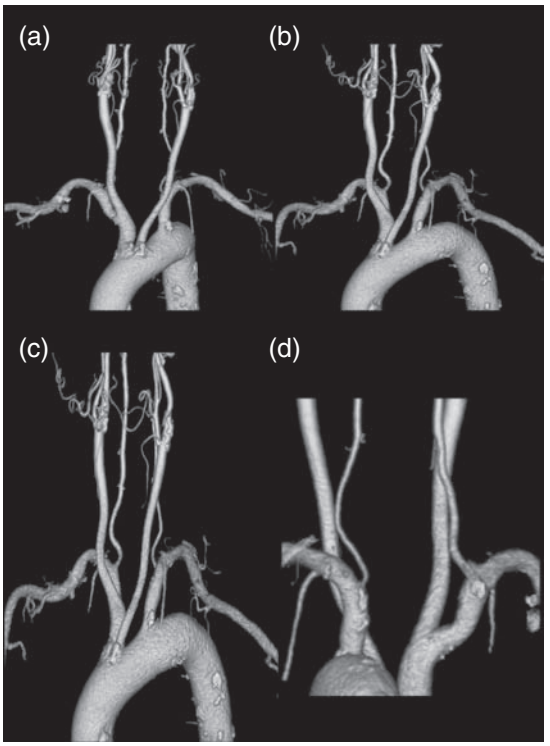
After completion of an endovascular procedure, patients should be transferred to the intensive care unit and monitored. The sheath is withdrawn when the ACT is below 150 seconds. The patient is usually discharged the following day. In our experience, implantation success nears 100% for stent placement in the subclavian and innominate arteries, and we have had good success in the vertebral artery as well.

METHODS TO DETECT POTENTIAL COMPLICATIONS – WHICH DIAGNOSTIC STEPS ARE NEEDED ROUTINELY TO RULE OUT OR IDENTIFY COMPLICATIONS

Preoperative assessment

Preoperative study is vital in determining the indication, approach, and technique for endovascular intervention in the subclavian and vertebral arteries. Clinical findings (access pulses or bruits, upper limb pulses, asymmetry and pressure gradients, cervical bruits or palpable pulsatile masses or thrill) and global brachiocephalic imaging must be part of the routine preoperative work-up.

Although useful in determining subclavian flow changes, carotid disease, and most cases of vertebral origin stenosis,[78,79] duplex ultrasound is less useful for morphologic study of lesions because of the intrathoracic location of left subclavian artery origin. Nevetheless, it can reveal hemodynamic patterns of subclavian steal in its later stages.[80,81] In vertebral stenosis, duplex ultrasound is less specific than for other occlusive entities (i.e., hypoplasia, aplasia, dissection). It is useful in establishing the flow pattern in vertebral artery for preoperative evaluation of procedural embolic risk. Coronary embolization in patients with prior myocardial revascularization has been well described with antegrade flow in the vertebral artery; retrograde internal mammary artery (IMA) flow may also be problematic, but is relatively rare.[80]



64 slice CT-scan with 3D reconstruction of the arch and carotids. (A, B) right vertebral artery difficult to visualize on the AP and right lateral view, its origin is easily appreciated on the rotational left lateral view. (C ,D) A posterior view is required to fully evaluate the ostium of the left vertebral artery.

Figure 8.9 64-slice VCT axial view of the vertebral artery.

Angiography is the gold standard for diagnosis of cerebrovascular occlusive disease.[82,83] However, newer techniques such as angioCT or MRI offer satisfactory non-invasive target lesion imaging and three-dimensional (3D) reconstruction (Figure 8.9). Careful aortic arch study may detect atherosclerotic sources of emboli and wall-attached vessel thrombus.[44,84]

Operative assessment

Angiography is the main imaging method during endoluminal procedures, and roadmapping allows satisfactory views of the target lesion and angioplasty and stenting sites. However, the ostial

location of most of the subclavian or vertebral artery lesions may be difficult to visualize using standard arch views because of superimposed images of the subclavian artery origin over the aorta and of the first segment of the vertebral artery over the subclavian artery. Additional oblique views are of the utmost importance for accurate diagnosis. Angiographic information also remains very useful for visualizing active bleeding secondary to perforation or vessel disruption, spasm, thrombosis, or embolic phenomena, but it is less helpful in determining cross-sectional plaque volume, the extent of the lesion, and the morphology of plaque composition,[85] distribution or wall defects.[86,87]

Assessment of flow restoration may be obtained by determining the pressure gradient between the upper limbs or on either side of the target lesion vessel in the vertebral artery.[88] Such determinations allow accurate evaluation of underlying remnant flow defects (residual stenosis, elastic recoil, dissection) that can threaten early outcome and impair long-term patency. Flow defects secondary to suboptimal angioplasty stenting can be missed using angiography alone. In 100 patients with a residual intra-arterial mean pressure gradient higher than 10 mmHg, Tetteroo et al[89] found angiography sensitivity and specificity to be 45% and 63%, respectively, for postprocedural diagnosis of residual stenosis following iliac angioplasty.

The 360° tomographic imaging provided by intravascular ultrasound (IVUS) is extremely useful in endovascular intervention in the subclavian and innominate arteries. Serial images are stacked by the computer during a single 'pull-through' and reassembled into a 3D reconstruction that allows the whole length of the artery to be displayed at one time. Lesions may be examined from any angle, slice, or rotation – an advance we have found particularly helpful in peripheral interventions. In one series of thoracic outlet syndrome cases, subclavian vein IVUS imaging results were comparable to those obtained by venography.[90] Postprocedural IVUS studies in coronary and femoropopliteal arteries have been used to assess stent attachment, maldeployment, dissection, and luminal irregularities caused by plaque rupture.[91] They may also determine the presence of calcification and residual stenosis <70%,[86,87] which can be missed by angiography,[89] and increase the risk of in-stent thrombosis and procedural failure. Although the IVUS literature for subclavian angioplasty is lacking, experiences reported in equivalent diameter vessels such as the iliac arteries indicated in vitro IVUS sensitivity was 74% for dissection and 59% for media rupture.[92] Clinical use of IVUS has revealed visible defects in 45% of patients undergoing endovascular intervention (including dissections, inadequate stent dilatation, migration, and thrombus entrapment) that were not seen using uniplanar angiography.[93]

Transcranial Doppler ultrasound has been used successfully to detect procedure-related embolic signs during and after vertebral angioplasty[94] and to evaluate hemodynamic response to vertebral angioplasty. This non-invasive technique is useful for operative monitoring[94,95] and postoperative evaluation of posterior cerebral procedures, though standardized protocols are lacking. Diffusion-weighted MRI is another non-invasive means of diagnosing cerebral infarction.[96]

ENDOVASCULAR, SURGICAL, AND/OR MEDICAL TECHNIQUES TO RESOLVE COMPLICATIONS

Prevention of complications through the use of the appropriate technique is an important goal. Following stent deployment, an angiographic control image should be taken, and the gradient recorded. As described above, IVUS may be superior to angiography in detecting inadequate stent deployment and, when the IVUS images suggest suboptimal deployment, a larger balloon should be used to expand the stent.

Perforation occurs more commonly during treatment of total rather than partial occlusions of the vessel and may be caused by creation of a subintimal dissection (as above) or following overdilatation of the balloon before or after the stent has been deployed. Location of the perforation is relevant when it comes to management. If it is a large perforation, the patient will exhibit hypotension. Delayed identification of a perforation usually results in hypotension, tachycardia, shortness of breath, or even chest pain. A postoperative chest X-ray will demonstrate a hemothorax.

Management of a perforation may be difficult to resolve percutaneously. Simple balloon angioplasty may tamponade the bleed, but more than

one inflation may be necessary, and reversal of the anticoagulation may be helpful. If the decision is made to reverse the heparin, an endograft should be available in case balloon dilatation alone is unsuccessful. The location of the perforation, however, can limit the use of an endograft.[45,74,97] Angiography may be the most useful method to determine if the lesion is amenable to endovascular repair.[98] If the right subclavian artery ostium is involved, the endograft may extend proximally and compromise the right common carotid artery. If the pre- or postvertebral artery is the site of perforation, then a short endograft must be selected so as to avoid coverage of the vertebral artery. If the perforation is located at a region unsuitable for deployment of a covered stent, then the decision to convert to open repair should be made early on. A balloon can remain inflated while exposure is obtained.

When intimal injury is caused by arterial cannulation, local thrombosis of the vessel and occlusion may be treated with thrombolytics. Acute thromboses or emboli presenting within 24 hours are most amenable, and thrombolysis is our preferred option to restore patency of grafts occluded less than 14 days. Acute stent thrombosis in the vertebral artery has been reported to cause transient diplopia and ataxia[99] spasm, dissection, restenosis, and TIA.[28,100,101] The use of a stent at the origin and proximal segment of the vertebral artery will help to prevent the potential complications of dissection and early restenosis. This is important because spasm and dissection have been linked to immediate occlusion and transient or permanent neurologic complications.

In treating chronic occlusion, or in situations where severe acute ischemia is present, surgical intervention is generally preferred over thrombolysis. Typically, thrombosis is most often associated with the access site. It can be related to the target vessel as well, primarily due to the disruption of a plaque and creation of a dissection. Diagnosis may be made intraoperatively with evidence of slow flow through the brachial artery. It may also be recognized based on dampened waveforms in the arterial line of the involved upper extremity. In addition, upper extremity pallor or coolness may be apparent perioperatively. Arterial duplex is helpful in documenting the extension of the acute arterial occlusion. Management of thrombosis includes prevention with adequate anticoagulation. Choose stents that can be delivered via small caliber sheaths (5 or 6 Fr sheath), and use the methods previously described to avoid dissection. Usually, thrombosis occurs in the early postoperative period, while the patient is being recovered. If the caliber of the brachial artery is a concern, early sheath removal should be considered in order to prevent early thrombosis.

Local thrombosis in the subclavian is best prevented by adequate anticoagulation. Percutaneous treatment may include thrombolysis if the sheath remains in place; the newest lytic agents offer better management due their shorter half-life. However, in order to revascularize local thrombosis and avoid bleeding risks associated with fibrinolysis, the dose and duration of treatment may be reduced, and direct suction and thrombectomy[102] or mechanical thrombectomy procedures may be tried.[103,104] Results of such interventions in other vascular territories,[105,106] either as a single therapy or followed by fibrinolysis, have been satisfactory. It should be noted that experience and knowledge about prevention of vertebral or coronary embolization are lacking. Indeed, embolization is a complication that has been related to rotational (Rotarex-Straub Medical, Switzerland)[107] and hydrodynamic (AngioJet-Possis Medical Inc, Minneapolis) atherectomy devices.[106]

Embolization is usually identified postoperatively. As a consequence of embolization, neurologic deficits ranging from mild to profound may be evident. A CT scan or MRI of the head will document the territory involved and any evidence of bleed. Thrombolytics can be considered when there is early recognition of symptoms. Upper extremity embolization can occur with discoloration or pain in the digits. If the embolus occludes the distal circulation of the upper extremity and acute thrombosis occurs, the symptoms will likely become more severe, necessitating heparinization and embolectomy.

Conventional anti-aggregation methods and procedural heparinization should be considered standard in cerebral procedures.[28] Abciximab is a glycoprotein (GP) IIb/IIIa antagonist which diminishes platelet aggregation and thrombus formation and may have anticoagulant[108] and throm-

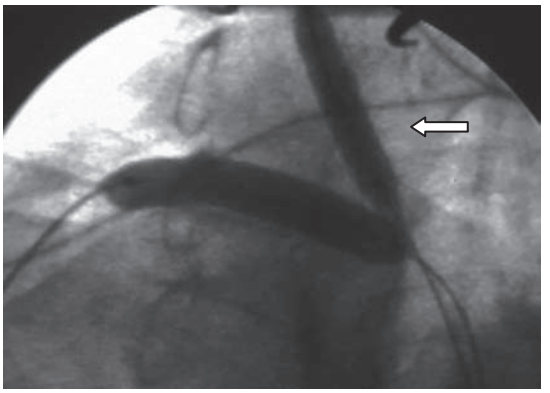
bolytic effects.[109] Periprocedural abciximab has been shown to decrease ischemic complications and late clinical events after coronary angioplasty,[110] but these results have not been reproduced in the carotids to prevent neuroembolic events.[28,111,112] However, satisfactory results with GP IIb/IIIa antagonists have been reported, whether used for pharmacologic thrombolysis,[62,113] angioplasty, and stenting[109,114–117] or other neurovascular endovascular procedures.[118] Intravenous and/or intra-arterial abciximab has been used alone or as an adjuvant thrombolytic therapy[119–121] and may be a useful tool for managing thromboembolic episodes without cerebral hemorrhage.

Mechanical reperfusion has been adapted to smaller coronary and intracranial vessels to treat thromboembolic episodes of diverse origin in high-risk patients. Intra-arterial thrombectomy devices, snares for clot retrieval,[122,123] and direct suction thrombectomy[124,125] cause mechanical disruption that may increase the penetration of fibrinolytic agents. Similarly, micro-guidewire passage, laser photoacoustic emulsification, and primary intracranial angioplasty or endovascular ultrasound may potentiate fibrinolytics or GPIIb/IIIa antagonists.

Spasm and dissection have been linked to immediate occlusion that leads to transient or permanent neurologic complications. Arterial spasm is a common response to guidewire tip and catheter manipulation in the brachiocephalic vessels. Although reversible, it may threaten cerebral ischemic status. Intra-arterial vasodilators, papaverine, nitroglycerin, or calcium-channel blockers, can alleviate spasm. Nifedipine by mouth or sublingually may prevent and treat vertebral spasm.[126]

METHODS TO AVOID COMPLICATIONS

Avoiding complications requires good judgment. Do not be overly aggressive. Watch the behavior of the wire – if the wire does not travel without resistance, or if it begins to 'buck' and follow a 'zig-zag' pattern, it is likely in a subintimal plane. Pristine technique that includes *gradually* crossing the lesion is advocated. Avoid creating dissections. Avoid angioplasty in subintimal planes even if the true lumen is re-entered. The force of the inflation or overinflation may result in perforation. Careful vessel diameter evaluation is of the utmost importance in order to avoid overdilatation and arterial injury secondary to device selection.



Double balloon technique for cerebral protection(arrow) when treating lesions at the ostium of the subclavian or those that extend into the innominate artery.

Figure 8.10 Double balloon technique as protection for right carotid artery.

The best management is prevention of embolization. Gentle manipulation of the wires, catheters, and sheath is key. As cited above, direct stenting is less likely to cause embolization, probably because the procedure is simpler and target lesion manipulation is reduced.[40] Symptomatic cerebral embolization is more likely when treating the right subclavian or innominate artery. If the stenosis or occlusion involves either of these vessels, then each movement (even simply crossing the lesion with a wire) risks embolization to the common carotid artery, which is in close proximity. If a lesion at either of these vessels appears highly calcific or difficult to cross due to high-grade occlusion, a temporary occlusion of the common carotid artery[126] can be performed using a dual brachio-femoral approach in a kissing-balloon fashion to access the target vessel from the brachial artery (Figure 8.10). In addition, aspiration of any debris prior to deflation of the occluding balloon may be accomplished using a long femoral sheath placed at the ostium of the common carotid artery. At present, sizes of the carotid protection devices, such as filters, limit their use in the subclavian and vertebral arteries; however, alternative pro-

tection devices, like the Parodi system, have been successfully applied in this territory.[127] Double-balloon techniques are also recommended when there is concern of vertebral artery compromise (via occlusion or dissection) secondary to subclavian manipulation.[40,128] This is especially important when there are vertebral ostial plaques, distal or long lesions in the subclavian, or antegrade vertebral flow. Myocardial protection in patients with prior coronary revascularization can be performed by balloon occlusion of the LIMA.[129]

Follow-up

Although restenosis is not as common in the subclavian and vertebral arteries as in the vessels of the lower extremities, Przewlocki et al[128] have identified three independent restenosis risk factors in the subclavian and innominate arteries:

1. the implantation of more than one stent
2. low stent diameter, and
3. difference in systolic blood pressure between the arms after the procedure.

Similarly, Schillinger et al reported three independent predictors of restenosis as follows:

1. lesion length more than 2 cm
2. residual stenosis greater than 30%, and
3. stent implantation.[130]

Female gender has been proposed as a risk factor for restenosis as well.[131] deVries et al[42] compared 102 cases of PTA alone in 43 patients vs selective stent placement for suboptimal dilatation and procedural dissection in 59 patients. Overall, there was a 5-year patency rate of 89% and, after a mean follow-up of 34 months, there was no difference in long-term outcome, even in cases treated for an arterial occlusion. All cases of restenosis were attributed to hyperplasia and were seen during the first 26 months of follow-up, leading the authors to recommend limited follow-up. Conversely, Przewlocki et al[128] noted restenosis as late as 2–3 years after angioplasty in these regions and suggested a longer follow-up period to assess the potential for complications. Lin et al performed angiographic evaluation of 32 lesions at a mean 11.0 ± 9.6 months following stenting and reported restenosis in 8 (25%) vessels; all patients were asymptomatic. Reference vessel diameter was the only predictor of restenosis in vertebral artery ostial stents.[50]

SUMMARY

Angioplasty and stenting have been used successfully in a number of vascular territories to correct flow abnormalities and restore patency, and may reduce the incidence of serious complications as compared to open surgical intervention. An expanding literature suggests endovascular therapy is safe and effective and promotes a favorable hemodynamic response, though data from randomized trials are not yet available. The complications associated with endovascular therapy are often preventable. The use of appropriate technique is one of the most important means of eliminating complications. Avoiding technical difficulties requires good judgment, and preoperative study is vital in determining the indication and optimal approach for endovascular intervention in the subclavian and vertebral arteries. Clinical findings and global brachiocephalic imaging must be part of the routine preoperative work-up.

Angiography remains the gold standard for diagnosis of cerebrovascular occlusive disease, though newer techniques such as angioCT or MRI offer satisfactory non-invasive target lesion imaging. Three-dimensional reconstruction imaging via IVUS is extremely useful for determining the presence of calcification and residual stenosis, dissections, inadequate stent dilatation, migration, and thrombus entrapment not visualized with uniplanar angiography. Transcranial Doppler ultrasound is also helpful in operative monitoring and postoperative follow-up. Careful vessel diameter evaluation is of the utmost importance in order to avoid overdilatation and arterial injury secondary to device manipulation. Gentle manipulation of the wires, catheters, and sheath is imperative as each movement (even simply crossing the lesion with a wire) risks embolization to the common carotid artery. Although restenosis is not as common in the subclavian and vertebral arteries as in the vessels of the lower extremities, it has been reported to occur as late as 2–3 years after angioplasty; clinical follow-up and imaging remains extremely important in patients who have undergone endovascular intervention.

CHECK LIST FOR EMERGENCY EQUIPMENT FOR INTERVENTIONS IN THIS SPECIFIC VESSEL AREA

Angiographic catheters

- Quick-Cross® Catheter (The Spectranetics Corp, Colorado Springs, CO)
- Soft-Vu® Berenstein (AngioDynamics, Queensbury, NY)
- Impulse® IM Angiographic Catheter (Boston Scientific Corp., Natick, MA)

Low-profile balloons

- Savvy® PTA Dilatation Catheter® (Cordis Corp, Miami Lakes, FL)
- OPTA™ PRO PTA Balloon Dilatation Catheter (Cordis Corp, Miami Lakes, FL)
- Sterling™ Monorail® Balloon Dilatation Catheter (Boston Scientific Corp, Natick, MA)

Cutting balloons

- Flextome™ Cutting Balloon® Device (Boston Scientific Corporation, Natick, MA)
- AngioSculpt™ Scoring Balloon Catheter (AngioScore, Inc, Fremont, CA)

Guiding catheter and long sheath shuttle

(For selective angiographic imaging, increased strength of distal access, and accurate delivery of balloon expandable stent by sheath retrieval)

- VISTA BRITE TIP® Guiding Catheter (Cordis Corp., Miami Lakes, FL); shapes: IM, MPA1, Hockey Stick
- Flexor® Check-Flo® Introducers (Cook® Vascular, Inc, Vandergrift, PA)

Covered stents

(For subintimal wire dissection, post predilatation dissection or possible wall injury, perforation, or disruption)

- iCast™ Covered Stent (Atrium Medical Corp, Hudson, NH)
- VIABAHN® Endoprosthesis Stent-Graft (WL Gore & Associates, Inc, Flagstaff, AZ)

Snares

(Many uses, including thrombectomy)

- Expro® Elite (CoMed Medical Specialties, Littleton, CO)
- EN Snare® Intravascular Retrieval Devices (InterV, Gainesville, FL)

Thrombolysis systems

- Uni*fuse® Infusion Catheter (Angiodynamics, Queensbury, NY)
- EKOS LysUS® Infusion System (EKOS Corp, Bothell, WA), for ultrasound-enhanced thrombolysis

Aspiration thrombectomy

- Diver CE™ Clot Extraction Catheter (Ev3, Inc, Plymouth, MN)

Rheolytic thrombectomy

- AngioJet® Thrombectomy System (Possis Medical, Inc, Minneapolis, MN)

Stents for crossing vertebral artery or LIMA

- Bridge® Assurant Stent (Medtronic, Inc, Minneapolis, MN), a modular design less likely to jail these vessels

Protection devices

- PAES® Parodi Anti-Embolic System (WL Gore & Associates, Inc, Flagstaff, AZ)

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9

Aortic aneurysmal disease

Joe T Huang, Takao Ohki, and Frank J Veith

INTRODUCTION TO THE FREQUENCY AND TYPE OF COMPLICATIONS

The most devastating complication of aortic disease is hemorrhage, resulting in death. Thoracic and abdominal aortic aneurysms have a natural history of expansion and inevitable rupture, if left untreated. Aortic dissections and penetrating aortic ulcers are other major aortic disease processes with serious consequences.

Abdominal aortic aneurysms (AAAs) are responsible for 15 000 deaths in the United States annually.[1] They represent the third leading cause of death in men over 60 years of age. Thoracic aneurysms occur less frequently than AAAs, with an incidence of 10.4 cases per 100 000 person-years.[2] Acute aortic dissection is the most frequent catastrophe of the aorta. It has an incidence of 5 to 30 cases per 1 million people per year.[3–6] Untreated, the mortality of acute dissection is 50% within the first 24 hours.[7]

Traditional open surgical repair of AAAs and dissections has consisted of transperitoneal or retroperitoneal incision, followed by aortic cross-clamping, and transposition of the diseased segment with a tube graft. The 30-day mortality of open abdominal aortic aneurysm repair stands at 3.8 to 8.2%.[8] The more common complications of open repair include hemorrhage, cardiac ischemia, hypotension from aortic declamping, sexual dysfunction, iatrogenic ureteral injury, renal failure, distal embolization, visceral ischemia, and paraplegia. Late complications include aorto-enteric fistula (0.9%), pseudoaneurysm (1.3%), and graft infection (0.4%).[9]

Open repair of thoracic aortic aneurysms and dissection is an invasive procedure that includes thoracotomy, aortic cross-clamping, left heart bypass, and transposition of the thoracic aorta with a tube graft. Mortality rates for patients undergoing open thoraco-abdominal and descending thoracic aortic aneurysm repairs range from 4 to 21%.[10–13]

The first endovascular abdominal aortic aneurysm repair (EVAR) in a human was described by Parodi in 1991.[14] The first EVAR was completed in the United States in 1995.[15] Since then, advances in the endovascular treatment of thoracic and abdominal aortic diseases have accelerated with breathtaking speed. It is now reported that 45 to 80% of patients with AAAs are candidates for EVAR.[16–18] This phenomenon is primarily due to increasing experience, newer technology, and increasing referrals.

EVAR has the advantage of avoiding major abdominal or retroperitoneal incisions and bowel manipulation, as well as decreasing postoperative pain and fluid requirements.[19] EVAR also obviates many of the cardiac, respiratory, and renal complications that frequently accompany open repair, with reductions from 11 to 5% in cardiac

complications and 5 to 3% in pulmonary complications.[20] EVAR is thus associated with faster recovery times and shorter intensive care stays.

In patients with diseases of the descending thoracic aorta, up to 57% of these patients are potential candidates for endovascular grafting.[21] Indications for endovascular therapy of thoracic aortic disease are constantly expanding. Diseases treatable by endovascular techniques now include chronic dissections, pseudoaneurysms, degenerative aneurysms, mycotic aneurysms, traumatic aortic dissections, type B aortic dissections, intramural hematomas, and penetrating aortic ulcers.[22] Endovascular repair of thoracic aortic disease is particularly appealing to patients who would normally be considered poor surgical candidates. It is considerably less invasive than open surgical options and avoids complications associated with open thoracotomy, aortic cross-clamping, and left heart bypass. Perioperative mortality rates of 3 to 12% have been reported for endovascular treatment.[23]

COMPLICATIONS AFTER ENDOVASCULAR AORTIC ANEURYSM REPAIR

While there are distinct advantages to endovascular repair of thoracic and aortic diseases, there are also disadvantages of endografting for these diseases. By undergoing an endovascular aortic repair, the patient is committing to lifelong imaging surveillance because of a host of complications specific to endovascular therapy. Endovascular repair is also potentially more costly than open surgery, with the graft device comprising 52% of total costs.[24]

Initial experience with EVAR saw conversions to open repair secondary to limited operator experience, patient selection, and early generation devices. However, the rate of early conversion (defined as any open repair within 30 days of initial EVAR) has fallen to 0.7%.[25] In one series by Verzini et al, causes for early conversion to open repair included significant vessel calcifications, aortic neck rupture, and inability to catheterize the contralateral limb of the graft.[26] Treatment included open repair with tube grafts or bifurcated grafts. Rates of late conversion range widely, from 4 to 50%.[14] The recently published EVAR 1 trial, with an average follow-up of 3.3 years, reported a cumulative conversion rate of 2.6%.[27]

While actual rates of secondary intervention after EVAR range from 10 to 20% per year, there is a higher number of observed complications.[28–30] According to the EVAR 1 trial results at 4 years, 41% of patients experienced at least one complication after EVAR, compared with 9% in the open repair group. The most common complications in this study were type II endoleaks (42%), type I endoleaks (14%), graft thrombosis (6.5%), and graft migration (6.5%).[27] Similarly, the Dutch Randomized Endovascular Aneurysm Management (DREAM) trial had a rate of secondary intervention for EVAR that was three times the rate of open repair in the first 9 months.[31]

In the DREAM trial, the acute benefit of EVAR translated into lower cumulative rates of aneurysm-related deaths. At 2 years, the aneurysm-related death rate was, 2.1% for EVAR and 5.7% for open repair. There was, however, no difference in cumulative survival between open repair and endovascular repair at 2 years (89.6% vs 89.7%). Four-year results from the EVAR 1 trial also demonstrated a small but a significant reduction in aneurysm-related deaths with EVAR (4% versus 7%), with no difference in all-cause mortality between the two groups of patients randomized to EVAR versus open repair.

In one series by Cao et al, 1119 patients treated with either open repair or EVAR were followed over a minimum of 7 years.[32] The overall risk for secondary procedures after EVAR was reported at 49.4%, compared with 7.1% in the open repair group. Despite the higher rate of re-intervention, freedom from aneurysm-related death at 84 months showed minor differences (97.5% in the EVAR group and 95.9% in the open repair group).[32,33]

TYPES OF COMPLICATIONS

Endoleaks

Endoleaks are complications unique to endovascular aneurysm repair. An endoleak is defined as persistent blood flow outside the graft and within the aneurysm sac.[34] Positive predictors of endoleak include large proximal aortic neck diameter, large aneurysm size, severe angulation of

the proximal infrarenal neck, patent inferior mesenteric artery (IMA), and lack of thrombus or small amounts of thrombus in the aneurysm sac. Twenty percent of patients will present with endoleak at some point during follow-up. Seven percent of these patients present one month postoperatively and the remaining 13% are found later.[35–38] There are four major types of endoleaks, as listed in Table 9.1. Types I and III are termed graft-related endoleaks, while type II is referred to as a collateral endoleak. Approximately 70% of early endoleaks disappear within 30 days, with the majority being type II endoleaks.[39–41]

Diagnosis of endoleaks is accomplished primarily through computed tomography (CT) scanning with iv contrast. It is useful for detecting contrast flow in the sac and for measuring aortic diameters. The imaging protocol should include delayed phases in order to visualize any vessels that may be supplying type II endoleaks. Biphasic CT scanning improves rates of detection by 11% when compared to CT scanning with arterial phase only.[42] CT angiography with three-dimensional (3D) reconstruction is also useful, but not as widely available. Color duplex ultrasound is also frequently used, with a sensitivity of 95% and specificity of 97% for detecting endoleaks.[43] Duplex imaging is better at detecting limb outflow disturbances than CT. Ultrasound also has the advantage of being non-invasive, non-irradiating, and more repeatable. However, it is highly operator dependent and artifacts such as bowel gas and body fat can obscure findings. Magnetic resonance arteriography (MRA) and selective arteriography are other diagnostic modalities. Angiography is an invasive procedure with inherent risks, but offers the possibility of simultaneous endoleak treatment at the time of diagnosis. Plain abdominal films are also very helpful to evaluate for stent fracture, stent migration, limb disassociations, and graft kinks.

Type I endoleak

The incidence of type I endoleak is approximately 10%.[44] It is defined as an inadequate seal between the endograft and native aorta at the proximal or distal attachment sites, which results in continued blood flow and pressurization into the aneurysm sac. Proximal type I endoleaks necessitate intervention as they are likely to persist and can lead to aneurysm rupture.

Endovascular treatment modalities include balloon angioplasty of the proximal and distal

Table 9.1 Endoleak classification system

Classification	*Alternative terms*	*Forms*
Type I	Graft-related endoleak Peri-graft leak Attachment endoleak Peri-graft channel	A Proximal graft attachment site B Distal graft attachment site C Iliac occluder
Type II	Retrograde endoleak Branch endoleak Collateral flow	A Simple or to-and-fro (1 patent branch) B Complex or flow-through (≥2 patent branches) Patent branches lumbar, IMA, intercostals, internal iliac, subclavian, etc.
Type III	Fabric tear Modular disconnection	A Junctional leak or modular disconnect B Fabric disruption Minor (<2 mm; e.g. suture holes) Major (≥2 mm)
Type IV	Fabric porosity (<30 days after graft placement)	Graft wall fabric porosity or suture holes
Endotension	Type V endoleak Endopressure Pseudo-endoleak Pressure leak	See Table 9.2

ends, the placement of additional bare stents (usually balloon-expandable stents), and the placement of additional aortic cuffs.[45] If endovascular intervention cannot be carried out, early or late conversion to open repair may be necessary. Options include banding of the proximal or distal attachment sites, suturing of the endoleak under direct visualization, or open surgical repair with a conventional graft.[19] The key to preventing type I endoleaks is appropriate oversizing of the proximal and distal ends of the graft.[46] However, one should note that excessive oversizing (>30%) will also lead to increased rates of migration (Figure 9.1a–c).

Type II endoleak

Type II endoleaks are defined as flow from patent side branches, e.g. inferior mesenteric arteries, lumbar arteries, visceral vessels, and hypogastric arteries. The incidence of this complication ranges from 10 to 25% and comprises the majority of endoleaks.[44] Those identified via angiography upon completion of endograft deployment are often managed conservatively, because most type II endoleaks are considered to be low flow and resolve spontaneously.

Vigilant monitoring of these endoleaks, as well as measurement of the AAA diameter utilizing CT, has been advocated, with an increase in diameter of 5 mm representing a significant value.[47] However, the association between type II endoleaks and aneurysm sac enlargement is unclear. While some studies have shown a higher incidence of aneurysm growth in the presence of type II endoleaks, others have not demonstrated a significant change in aneurysm size despite the presence of type II endoleaks.[38,48–50] It is important to note that type II endoleaks are not entirely benign, as they have been associated with cases of aneurysm rupture, albeit anecdotal.[51–54] There is continued debate about the significance of this type of endoleak and the timing of intervention. Some groups advocate conservative management for all type II endoleaks while others intervene in all type II endoleaks. Others recommend treatment if the aneurysm sac is observed to be expanding.[50,55–57] It is also important to exclude in these patients the possibility of type I or type III endoleaks that should be fixed more promptly.

Treatment methods for type II endoleaks include coil embolization of the responsible branch, either via a transarterial approach (femoral or brachial) or direct translumbar puncture of the aneurysm sac. The inferior mesenteric artery can be approached through the superior mesenteric and meandering collaterals, while the lumbar arteries can be accessed through hypogastric and the ilio-lumbar artery. These treatment options, however, are technically challenging.[58–62] Other methods include laparoscopic clipping of side branches, injection of thrombin polymer, and thrombogenic sponge placement within the sac to facilitate thrombosis of the excluded aneurysm.[63]

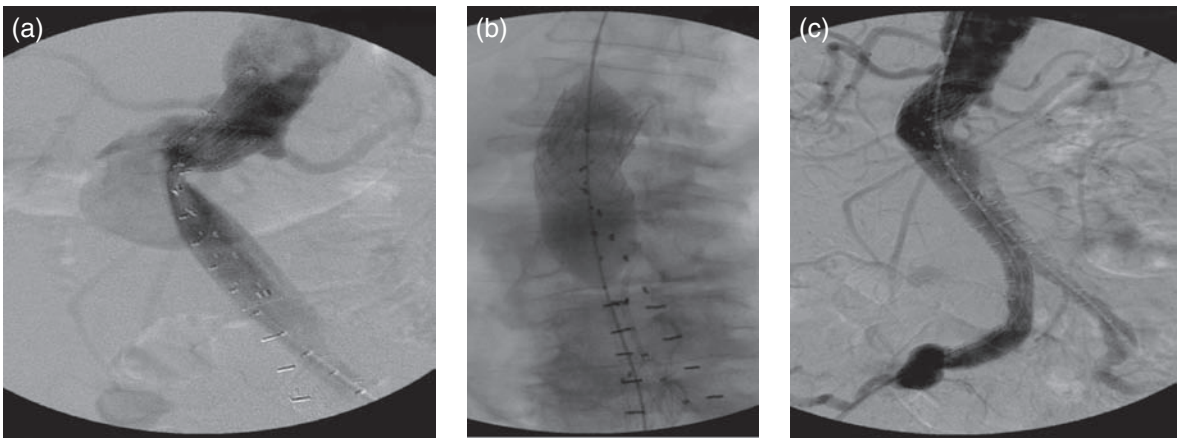

Figure 9.1 (a) Type I endoleak. (b) Type I endoleak with proximal aortic cuff placement. (c) Type I endoleak; completion angiogram.

In one study by Baum et al, 92% of patients treated with translumbar embolization of the aneurysm sac were successfully treated, while 80% of patients who underwent transarterial embolization of the inferior mesenteric artery failed therapy.[58] The study concluded that transarterial techniques to embolize aneurysm sacs may not be durable methods of treating type II endoleaks.

Various studies have also examined the practice of preoperative embolization of patent side branches to prevent type II endoleaks. Results indicate that the presence of patent lumbar and inferior mesenteric vessels is a poor predictor of the formation of type II endoleaks. Therefore, such preventive measures should not be taken[44] (Figures 9.2 and 9.3).

Type III endoleak

A type III endoleak is persistent blood flow from a tear in the graft fabric or from component separation. It is subcategorized as a minor disruption when the fabric perforation is less than 2 mm and as a major disruption when the perforation is greater than 2 mm.[63] Grouped with type I endoleaks, type III endoleaks occur in approximately 12% of patients undergoing EVAR.[19] This type of complication increases the risk of rupture nearly 9-fold.[51] Therefore, discovery of a type III endoleak necessitates prompt therapy, especially if it appears late during follow-up. Endovascular management of type III endoleaks consists of deploying additional stent grafts over the graft defects. If the damage to the stent graft is severe, then conventional open repair is necessary (Figure 9.4).

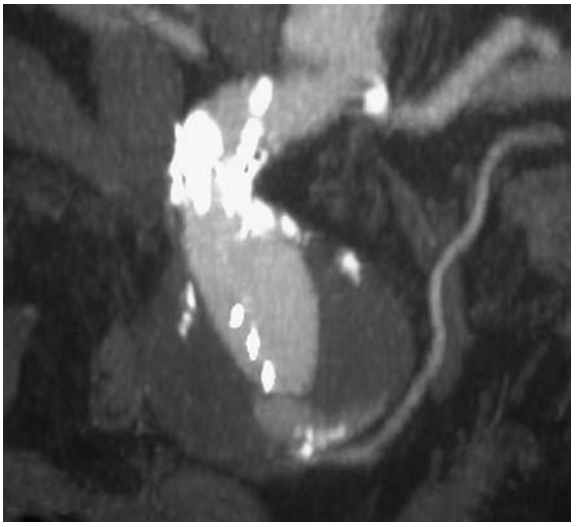

Figure 9.2 Type II endoleak on CT scan.

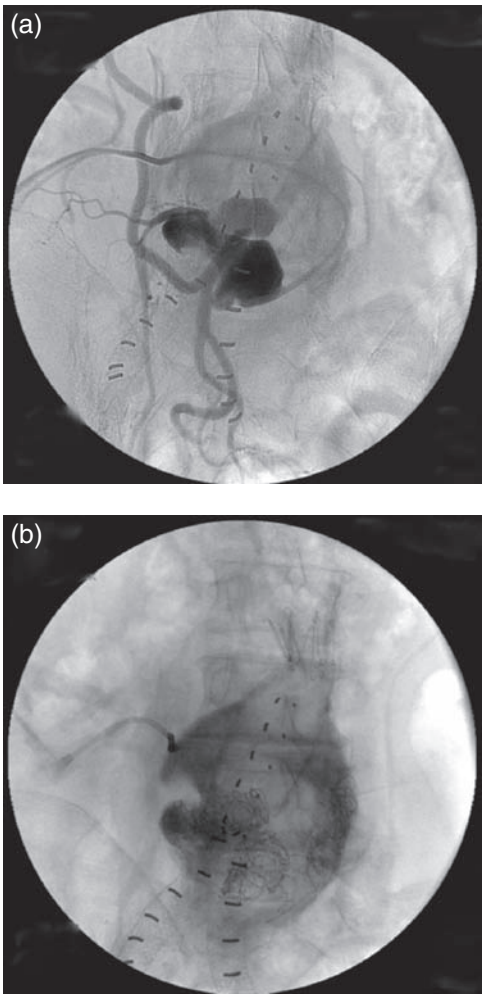

Figure 9.3 (a) Translumbar angiogram of type II endoleak. (b) Translumbar catheterization with coil embolization of type II endoleak.

Type IV endoleak

Type IV endoleaks are due to graft porosity and suture holes that permit the leakage of blood through the graft. Approximately 30% of grafts will allow contrast into the aneurysm sac in the first few days after EVAR. However, most resolve

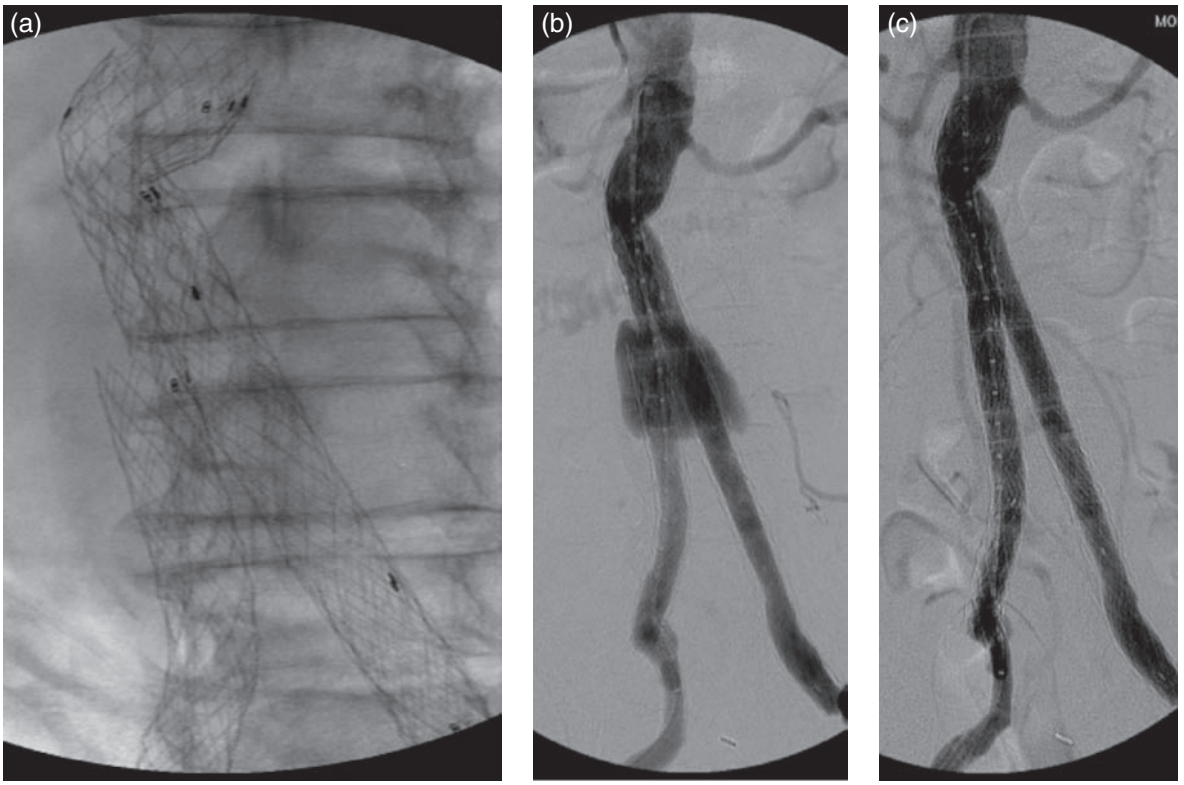

Figure 9.4 (a) Type III endoleak due to component separation. (b) Type III endoleak on angiogram. (c) Type III endoleak; completion angiogram after additional cuff placement.

spontaneously within one month.[64] Earlier devices, which utilized thinner graft material, encountered higher rates of type IV endoleak than current devices. Type IV endoleaks are believed to be limited in their nature.

Endotension

Endotension, also referred to as type V endoleak, is defined as persistent or recurrent pressurization of the aneurysm sac after EVAR in the absence of endoleak.[22] An alternate definition is pressurization of the aneurysm sac, regardless of the presence of a detectable endoleak. As described by Gilling-Smith et al, this broader definition states that increased sac pressure is the causative factor for aneurysm rupture, rather than blood flow.[65,66] Possible causes of endotension are listed in Table 9.2.

The presence of endotension is suspected when there are observed increases in aneurysm diameter on radiographic imaging. The next step in diagnosis involves aneurysm sac pressure measurements, either through direct intra-arterial catheterization or translumbar puncture of the aneurysm sac. These options are invasive by nature. As a result, there has been an impetus to develop newer non-invasive methods for monitoring direct sac pressures. Recently approved for commercial use is a wireless, battery-less, radiofrequency-activated pressure sensor that can be implanted in the excluded aneurysm sac at the time of EVAR. The advent of this device makes it possible to non-invasively detect endotension and potential endoleaks[67] (Figure 9.5).

Treatment for endotension includes open surgical repair, especially if the aneurysm becomes extremely large and causes a mass effect (Figure 9.6). Symptoms may include abdominal or back pain and constipation. However, in a report from the EUROSTAR registry on 2463 patients, endotension was identified in 97 patients (3.7%),

Table 9.2 Mechanisms of endotension

Possible mechanisms of endotension[134]

Pressure transmission to aneurysm sac around the ends of graft

- Layer of thrombus between the graft and aortic wall[135,136]
- Graft displacement exposing thrombus layer at aortic neck
- Endoleak channel sealed by thrombus
- Undetected endoleak
- Intermittent endoleak channel[136]
- Very low flow endoleak channel

Pressure transmission through graft wall

- High graft porosity
- Microleak through graft interstices[137]
- Transudation/exudation of fluid through graft fabric[138]
- Graft pulsatility/wall movements

Pressure transmission from branch vessels

- Thrombus over orifice of internal mesenteric or lumbar arteries

Pressure build-up from fluid accumulation in situ

- Graft infection
- Thrombus fibrinolysis/hygroma[139]
- Genetic modulation
- Enzymatic activity
- Others

of whom only 3 (3.3%) underwent open repair.[68] Other treatment options include conservative management with an increased frequency of clinical and radiographic monitoring and secondary endograft procedures.[69] Our policy is to treat endotension conservatively until the patient complains of symptoms related to the presence of a large aneurysm sac. Endotension may also be treated endovascularly by placing a second layer of endograft within the first one. This relining method is effective in decreasing the porosity of the first endograft (Table 9.2).

Stent migration

Graft migration is defined as movement of the graft more than 5 mm distally. Movement occurs when the displacement forces on the graft exceed the strength of the endograft at its proximal and distal attachment sites. Displacement from the proximal site poses the greatest risk of danger. Stent migration can lead to endoleak, graft kinking, rupture, and graft thrombosis.[70] Ouriel et al reported a migration rate of 3.6% at one year after EVAR.[71] Reported migration rates vary widely, with Conners et al reporting a 7% rate of migration at 1 year, 20% at 2 years, and 42% at 3 years.[72] In the AneuRx clinical trial, migration was reported in 94 of 1119 cases.[73] Freedom from migration was 98.6% at 1 year, 93.4% at 2 years, and 81.2% at 3 years by Kaplan–Meier analysis (Figure 9.7).

One risk factor for stent migration is dilation of the proximal aortic neck after EVAR and resultant dislodgement of the stent. The incidence of proximal neck dilatation has a range of 10 to 36%.[72–80] It is known that patients with larger aneurysms are at higher risk for neck dilatation.[72,75] Univariate and multivariate analysis of the study by Zarins et al revealed that renal artery to stent graft distance and proximal fixation length are also significant predictors of migration, with each millimeter increase in distance below the renal arteries increasing risk for subsequent migration by 5.8% and each millimeter increase in proximal fixation length decreasing risk for migration by 2.5%.[73]

Mohan et al studied 2862 patients using a mathematical regression model for blood flow to identify variables associated with stent graft migration.[81] Ninety-nine (3.5%) patients developed stent graft migration, which was clinically relevant in 85 (3.0%) patients. Hypertension, smoking, maximal aortic diameter, and distal transverse aortic diameter correlated with migration in their univariate analysis. Analysis of graft characteristics revealed that increasing proximal graft size was associated with migration, with each increase of 1.0 mm in graft diameter elevating the risk of migration by 1.13. Patients with a proximal graft diameter greater than 30 mm were found to have 2.5 times the risk of migration compared to patients with a graft diameter of less than 24 mm in multivariate analysis. Likewise, for patients with a distal transverse aortic diameter greater than 30 mm, the risk was 2.54 times greater compared to patients with a diameter of less than 24 mm. The risk of stent graft migration was also increased for longer aneurysms (longer than 12.6 cm) and for those with iliac artery diameters larger than 1.6 cm. On multivariate analysis, current smoking, hypertension,

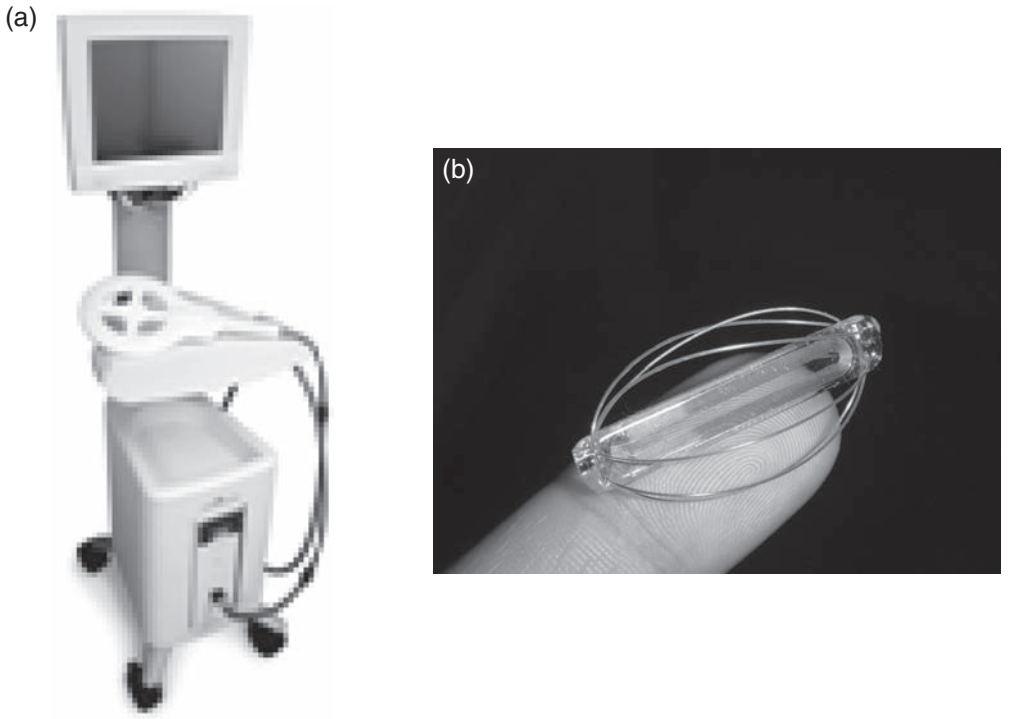

Figure 9.5 (a) CardioMEMS antenna. (b) CardioMEMS wireless pressure sensor.

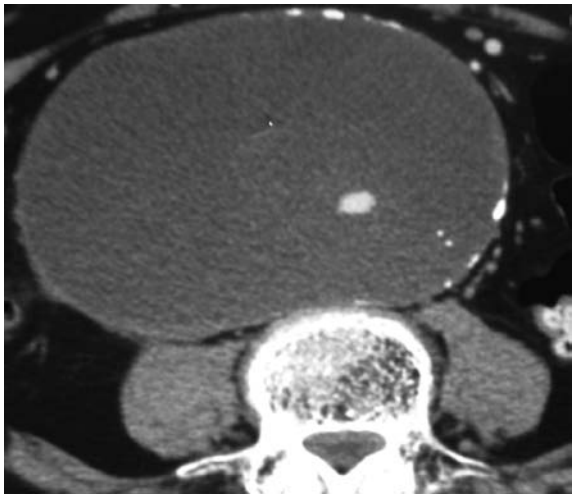

Figure 9.6 Endotension; enlarging aneurysm without evidence of endoleak.

distal transverse aortic diameter, maximum common iliac diameter, and increasing proximal graft size were significantly associated with stent graft migration.

Graft migration can be reduced through strict adherence to a particular stent graft's instructions for use (IFU) when selecting patients. Aneurysms that have adequate and less angulated proximal aortic necks also decrease the likelihood of graft migration. Precise graft placement adjacent to the renal arteries as well as the hypogastric artery distally is equally important.[19,37,72] Conservative management may be acceptable if there is no evidence of endoleaks, aneurysm expansion, or signs of ongoing migration. Interventions for migration include the placement of balloon-expandable stents, endograft cuffs, or open surgical repair. The practice of oversizing stents by 20% relative to the proximal neck diameter is also aimed at preventing graft migration.[46] Balloon expansion of the proximal aortic neck may also improve proximal graft fixation. We examined 41 patients who underwent EVAR with a balloon-expandable endograft and were followed for an average of 31 months.[82] Aortic neck diameters were measured at the level of the lowest renal artery and 5 mm distally. Proximal neck dilatation was

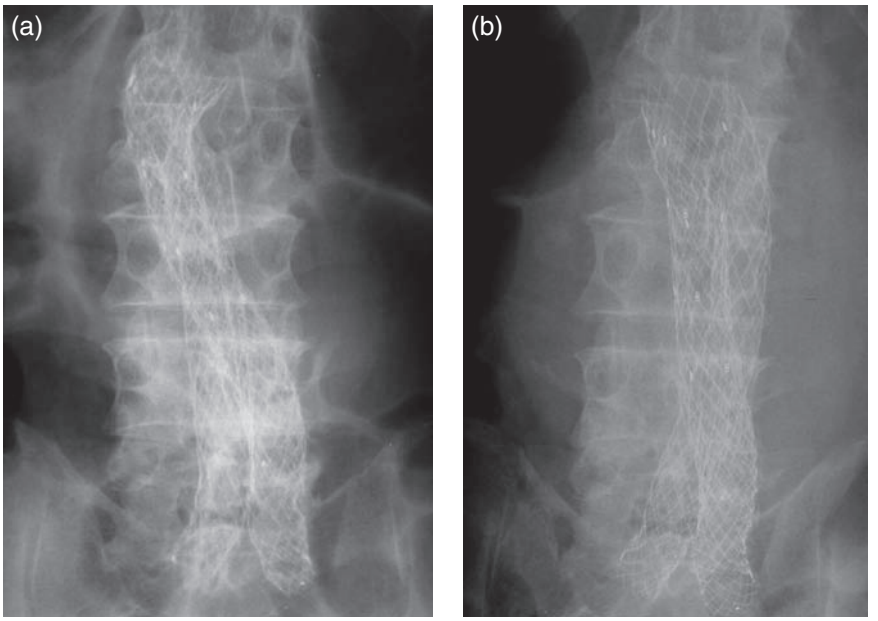

Figure 9.7 (a) Stent graft. (b) Stent graft with migration.

defined as neck enlargement of 2.5 mm or more. To assess endograft migration, the distance between the superior mesenteric artery and the proximal end of the stent was measured. Stent migration was defined as a change of 5 mm or more. The maximum aneurysm diameter was unchanged or decreased in 85% of this group of patients who had balloon-expandable endografts. The immediate postoperative proximal neck diameter was 19 to 29 mm and was unchanged during follow-up. None of the patients had significant proximal neck dilatation and none of the patients developed significant endograft migration. This study concludes balloon expandable stents are superior as a means of fixation.

Endografts with hooks, barbs, or supra-renal fixation devices have a lower rate of migration. For example, Malina et al reported that the addition of suprarenal stents, hooks, and barbs on grafts enhanced proximal fixation 10-fold, while stents that rely on radial force and friction had no impact on fixation, with the most secure proximal fixation device being pararenal barbed stents.[70,83,84] An additional method of minimizing migration is to increase the columnar strength of the endograft by adding longitudinal bars, although the efficacy of this method is less clear.

A vascular endostapling device has been developed to attach the graft to the aortic wall. This device is introduced through a 13 Fr sheath. An optic fiber and endostaple are used to penetrate the endograft and aortic wall at a desired location. The endostaple is inserted, assumes its preformed shape, and behaves like a wire suture.[85] Possible applications of this device include prevention of graft migration, sealing or preventing graft migration, and expansion of EVAR to aneurysms with 'unfavorable' necks. Other devices include an endostapling device which utilizes a motor driven nitinol screw to secure the endograft to the aortic wall.[86]

Stent fracture

The endograft prosthesis comprises a fabric and a metallic skeleton. Graft materials on the market today include polytetrafluoroethylene (PTFE) and Dacron®. Some grafts have metallic stents only at the proximal and distal ends. Others have a metallic exoskeleton throughout the graft. The metal compounds used include nitinol, Elgiloy, and stainless steel. Nitinol is an alloy that is 55% nickel and 45% titanium. Stents made from this alloy have shape memory and are self-expanding.

Elgiloy (Elgiloy Limited Partnership, Elgin, IL) is 40% cobalt, 20% chromium, and 15% nickel. The remaining components include iron manganese, molybdenum mohybian nolinium, carbon, and beryllium.[87]

Stent fractures occur due to stress fatigue on the metallic stents. Sites where the graft is sutured to metallic stents are points of stress and can fracture. Kinking or sharp angulation of the stent can subject the stent graft to micromotion with each cardiac cycle and place it at increased risk for stent fracture.[88,89] Some stents possess endoskeletons held together by sutures. These sutures have the potential to break or become untied. The endoskeleton can buckle and the tips can come into contact with the graft, with resultant graft erosions and type III endoleaks.[90] Many stent fractures can be diagnosed through plain abdominal films. Treatment options include placement of additional bare stents, additional stent grafts, or open surgical repair.

Rupture

Rupture is the most devastating complication of aortic aneurysms.[53,91–93] The incidence of rupture after EVAR ranges from 0.2 to 1.0%.[29,51,94–97] Analysis of EUROSTAR data concluded there are three independent predictors of aneurysm rupture after EVAR: history of continuing aneurysm expansion, proximal stent migration, and type III endoleak.[98] Causes of rupture include migration, component separation, fabric erosions, and endoleaks. Rupture after EVAR is usually treated with emergency open conversion, but secondary endografting has also been reported (Figure 9.8).

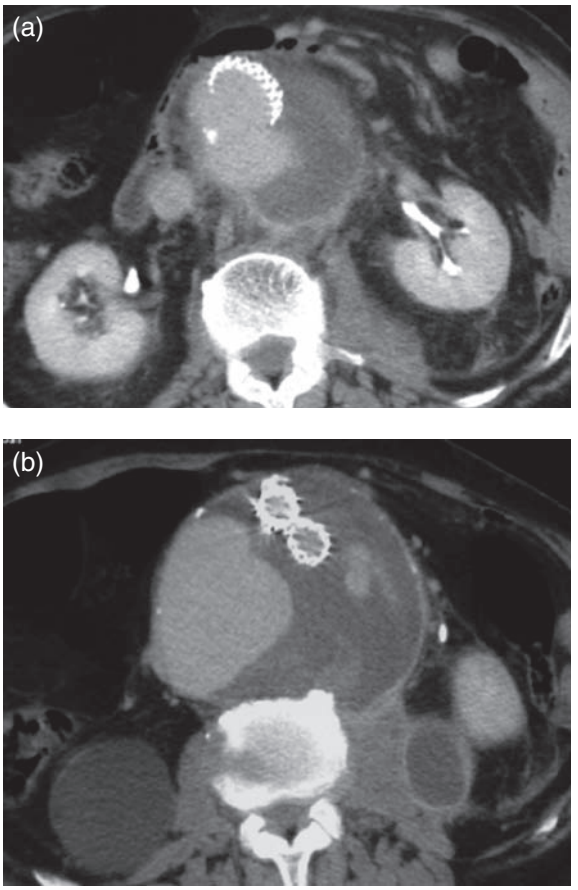

Figure 9.8 (a) CT scan demonstrating type I endoleak. (b) Type I endoleak and posterolateral aneurysm rupture.

Thrombosis

Graft limb occlusions after EVAR have been reported to have an incidence of 0 to 15%.[99–101] In a series by Sampram et al, involving 703 patients of a single institution, there was a graft limb occlusion incidence of 2.8%. Risk was determined to be 2.7% at 1 year, 4.1% at 2 years, and 5.5% at 3 years postrepair.[102] Etiologies of graft limb occlusion include compression of the graft in the proximal neck, compression of the limb in a narrow distal aneurysm neck, kinking or compression of the limb, peripheral vascular disease causing poor run-off, and limb twisting during deployment. Kinking can be due to excessive graft oversizing, tortuous iliac vessels, or the use of an unsupported endograft.[19,103]

To prevent thrombosis, narrow proximal aortic necks should be preferentially treated with long bodied grafts. In cases of tortuous iliac arteries, fully supported flexible grafts should be used. If an iliac limb kinks, it can be stented to prevent subsequent occlusion. If one graft limb thromboses, a possible solution is the creation of a femoral–femoral graft.[19]

Hip and buttock claudication

Hip and buttock claudication can occur from the occlusion of one or both hypogastric arteries. It can manifest as pain in the region or as impotence. Occlusion can be inadvertent, such as covering

by the graft limbs. Extension of the iliac limbs to exclude aneurysmal common iliac arteries and intentional coil embolization of the hypogastric arteries during graft deployment is another etiology. With the occlusion of these vessels bilaterally, the collateral circulation for the left colon can be compromised, with left colon ischemia arising as a potential complication. There is a reported incidence of 26 to 41% of hip and buttock claudication after coil embolization of the hypogastric artery.[104–109] In this situation, a surgical bypass from the external iliac artery to the internal iliac artery can be created, although rarely indicated.[110]

Renal compromise due to the use of suprarenal stents

The development of endografts capable of suprarenal proximal fixation is a welcome addition to the arsenal of devices at the disposal of endovascular specialists. Kalliafas et al observed a lower rate of graft migration in suprarenally fixated grafts versus infrarenally fixated grafts (2.1% versus 10.9%).[112] Suprarenal fixation is accomplished by having bare stents cross the orifices of the renal arteries, which permits blood flow into these vessels. While there have been concerns about the bare stents causing renal artery occlusion or emboli to the kidney this concern has not been validated. Studies have demonstrated minimal flow disturbances.[113–115] In one study by Burks et al, 192 patients underwent EVAR with additional long (15 mm) uncovered Parodi/Palmaz or Talent-LPS stent segments placed at the proximal attachment sites.[116] Based on postoperative imaging follow-up, 95 patients (49%) showed the uncovered stent at or above the level of the superior mesenteric artery. In 23 patients (12%), the stent extended to the celiac artery. After an average of 25 months of follow-up, serum creatinine levels were unchanged. Contrast-enhanced CT scans demonstrated no stenoses or occlusions in the celiac, superior mesenteric, or renal arteries. In addition, there was no evidence of renal, hepatic, splenic, or intestinal infarctions. The most important aspect regarding this potential complication is deployment of the fabric-encased portion of the stent graft as close to the level of the lower renal arteries as possible without vessel occlusion. Accuracy of placement thus hinges on operator experience, the delivery system, and the resolution of imaging equipment.

Access artery injury

The delivery of large endografts through diseased iliac arteries can lead to perforation and dissection. Prompt recognition and treatment with covered stents is essential for perforations. For dissections of access arteries, the use of self-expandable or balloon-expandable stents has been highly effective. Transfemoral exposure and femoral artery puncture can also be associated with pseudoaneurysms, seroma formation, and wound infection. Seromas form in approximately 15% of cases but usually resolve spontaneously. Wound infection rates are low and stand at approximately 2%.[117] Inability to traverse the iliac arteries was historically the most common source of procedure failure.[118,119] This phenomenon is now rare. The routine use of stiff guidewires has minimized this problem. The external iliac arteries are usually the most tortuous, but are also the most easily corrected. The combination of tortuous and calcified common iliac arteries is more difficult, but still amenable with the use of a stiff guidewire (e.g. Amplatz) and a trackable delivery system. A trackable delivery sheath does not have to be highly flexible, merely a smooth, tapered profile.[46]

FACTORS IDENTIFYING HIGH-RISK PATIENTS FOR COMPLICATIONS OF EVAR

Female gender

Female gender is believed to be a high-risk factor for complications, due to less favorable aortic neck anatomy. Women in general have shorter and wider aortic necks, more angulations, and smaller caliber iliac arteries. These variables decrease the number of women suitable for EVAR and also make femoral access more challenging.

Large initial AAA size

Large preoperative aortic aneurysm size is another known predictor of complications from EVAR. These aneurysms are less likely to have favorable

neck anatomy by possessing wider, shorter, more angulated aortic necks.[120] There is also a positive correlation between aneurysm size and the incidence of preoperative co-morbidities.[121,122] In one EUROSTAR series, 4-year outcomes were less favorable for large and medium sized aneurysms compared with smaller aneurysms (<5.4 cm) treated with EVAR.[27,47,122] Over 4000 patients who had undergone EVAR were analyzed over 6 years. Patients were divided into three groups based on aneurysm size: group A (n = 1962), 4.0 to 5.4 cm; group B (n = 1528), 5.5 to 6.4 cm; group C (n = 902), 6.5 cm or larger. Device-related endoleaks were more frequently observed in group C compared with groups A and B (9.9% compared with 3.7% and 6.8%). Postoperatively, systemic complications were more frequently present in group C (17.4% versus 12.0% in group A, and 12.6% in group B). Thirty day mortality was approximately twice as high in group C compared with the other groups combined (4.1% vs 2.1%). Late rupture was also most frequent in group C. Follow-up results at midterm were less favorable in groups C and B compared with group A (freedom from rupture, 90%, 98%, and 98% at 4 years in groups C, B, and A, respectively). Aneurysm-related death was highest in group C (88% freedom at 4 years, compared with 95% in group B and 97% in A). The annual rate of aneurysm-related death in group C was 1% in the first 3 years, but accelerated to 8.0% in the fourth year. It is clear from this study that large aneurysms after EVAR are associated with increased rates of aneurysm-related death and rupture.

In one study by Sampram and the Cleveland Clinic group[103,123], it was observed that secondary procedures were more frequent in patients with larger aneurysms and in patients who had received larger diameter aortic stents because of proximal endoleaks at initial EVAR. The overall risk for secondary intervention was 12% at 1 year, 24% at 2 years, and 35% at 3 years. Aneurysm-related death after EVAR was 3.6% over 3 years. These data suggest a link between outcome and preoperative AAA size, with better results in patients with smaller aneurysms. Hence, an argument can be made for treating aneurysms at smaller sizes, which translates into earlier intervention. A randomized trial comparing outcome for surveillance versus early stenting for the treatment of small aneurysms is ongoing in the United States (PIVOTAL trial).

Neck angulation

Neck angulation is another risk factor for complications. Neck angulation is defined as the angle between the proximal aortic neck and the longitudinal axis of the aneurysm. Sternbergh et al studied the adverse effects of aortic neck angulation through prospective data on 148 consecutive EVAR repairs over 6 years.[37] The risk of a patient experiencing one or more adverse events was 70%, 54.5%, and 16.6% in those with severe (greater than or equal to 60°), moderate (40 to 59°), and mild (less than 40°) aortic neck angulation, respectively. In comparing patients with moderate/severe neck angulation to mild neck angulation, adverse events included death within 30 days (20% versus 0%), acute conversion to open repair (20% versus 0%), aneurysm expansion (9.1% to 20% versus 1.7%), device migration (20% to 30% versus 3.3%), and type I endoleak (23.8% versus 8.3%). Aortic neck length and diameter, age, and medical co-morbidities were not significantly different between groups. The study concluded that aortic neck angulation is an important determinant of outcome after EVAR.

Difficult access arteries

Another patient factor to consider when evaluating for EVAR is the character of the access arteries. Problems at the access sites not only compromise endograft insertion, but they also make endograft deployment at the target vessel difficult. Tortuousity and calcification of the iliac and femoral vessels can increase the risk for complications. Atherosclerotic disease can also lead to localized stenoses that pose problems for deploying the endograft via a delivery sheath. Keeping these potential complications in mind, the surgeon can usually correct tortuous and calcified vessels by using super-stiff guidewires to traverse these difficult segments. Discrete stenoses can be corrected with angioplasty.

Adjunctive techniques to negotiate tortuous vessels includes the 'push-and-pull' technique, which is done by simultaneously pulling on the

super-stiff guidewire while introducing the endograft. The tortuous vessel can also be stabilized by applying external pressure on the access vessel or aneurysm.

COMPLICATIONS OF THORACIC ENDOVASCULAR GRAFTING (EVG)

Endovascular repair of thoracic aortic disease has been applied to elective processes such as degenerative aneurysms, mycotic aneurysms, pseudoaneurysms, chronic dissections, and coarctations of the aorta. Emergency applications include ruptured thoracic aneurysms, traumatic injuries of the aorta, and acute type B aortic dissections. Thoracic endografting is a very appealing therapeutic option because of its minimally invasive nature compared to open options. It avoids the complications of open repair, such as an open thoracotomy, cross-clamping of the aorta, and left heart bypass. Perioperative mortality of EVG repair of descending aneurysms ranges from 3.5 to 12.5%.[21,124–126]

Spinal cord ischemia and paraplegia after endografting of the thoracic aorta is relatively low, with rates ranging from 0 to 6%.[21,124,127–130] The concern is obstruction of the anterior spinal arteries, which usually arise between the levels of T9 and L1.[131] These vessels may be occluded by the endograft. Mitchell et al have reported a higher incidence of paraplegia with simultaneous open abdominal aortic aneurysm repair and endovascular thoracic aneurysm repair.[132] The etiology of this increased incidence is due to the abdominal aorta being a major collateral blood source for the spinal cord, once the artery of Adamkiewicz is occluded.[131]

To predict and prevent this complication, temporary interruption of the intercostal arteries has been performed by placement of a retrievable stent graft in the descending thoracic aorta under evoked spinal cord potential monitoring.[133] If changes in amplitude or latency of evoked spinal cord potential are noted during temporary interruption, surgical repair with re-implantation of intercostal arteries may be necessary.

Endoleak in the thoracic aorta is relatively uncommon. If present, the common types are type I endoleaks, which need to be treated promptly upon discovery. Type II endoleaks are rare and are usually secondary to patent intercostal arteries.[133] Stent migration is also a concern, because of the increased forces of systemic blood flow in the thoracic aorta. It is recommended that a zone of attachment greater than or equal to 2 cm be used when performing endovascular stent grafting in the thoracic aorta. This minimum length is comparatively longer than for EVAR.[21,124,135]

When performing endografting for thoracic aortic aneurysms, it is permissible to cover the left subclavian artery with the graft in order to obtain an adequate seal. However, the potential exists for complications pertaining to retrograde endoleaks through the subclavian artery, as well as ischemia of the left upper extremity. In such cases, some have advocated transposition of the left subclavian artery to the common carotid artery.[124,127,130,132] If the right vertebral artery is patent, some groups will deploy the thoracic stent over the left subclavian artery and perform extra-anatomic reconstruction as needed.

METHODS TO DETECT/AVOID COMPLICATIONS

In order to avoid complications, the underlying theme throughout endovascular repair of the aorta is careful patient selection. Successful EVAR mandates precise measurements of aorto-iliac dimensions so that an appropriate endograft can be chosen. Relative anatomic criteria for endovascular repair are an infrarenal proximal aortic neck at least 15 mm in length, neck diameter less than 26 mm, less than 60° angulation of the proximal neck, and no significant calcifications proximal and distal to the aneurysm[136] (Table 9.3). Various schemes are used for sizing endografts (Figure 9.9).

EMERGENCY ENDOVASCULAR AORTIC ANEURYSM REPAIR

See Table 9.4.

SUMMARY

The natural history of thoracic and abdominal aortic aneurysms is enlargement and eventual rupture.

Table 9.3 Relative anatomic abdominal aortic aneurysm criteria[136]

Infrarenal aorta anatomy
- ≥15 mm of proximal neck (non-aneurysmal aorta distal to lowest renal)
- Proximal neck diameter less than 28 mm
- Less than 60° angulation of proximal neck
- No significant neck thrombus (<50%)
- No excessive calcifications of proximal neck
- Absence of indispensable inferior mesenteric artery (IMA)

Iliac artery anatomy
- Patent
- Without severe angulations
- Large caliber (to accommodate graft, 6–7 mm)

While traditional therapy has consisted of open surgical repair, newer technologies and rapid advances are allowing patients the option of undergoing endovascular stent grafting. This method of therapy commits patients to lifetime imaging surveillance because of complications inherent to stent grafting. The most commonly recognized complications include endoleaks, stent migration, and stent fracture, all of which can lead to continued aneurysm sac pressurization and potential rupture. Other injuries include hip and buttock claudication and access artery injury. Risk factors known to increase the risks of complications include female gender, large aneurysm size, tortuous aortic necks, and difficult access arteries.

While thoracic endografting has distinct advantages in avoiding complications, such as thoracotomy and left heart bypass, there remain concerns of spinal cord ischemia resulting in paraplegia, as well as compromised circulation to upper extremities from stenting over the left subclavian artery. As with abdominal aortic aneurysm repairs, endovascular stent grafting of the thoracic aorta has similar issues with endoleaks and device migration.

D1 Suprarenal aortic diameter

D2 Infrarenal aortic neck diameter

(a, proximal; b, mid; c, distal)

D3 Maximal aneurysm diameter

D4 Terminal aortic transverse diameter

D5 Common iliac artery (CIA) diameters

(a, right; b, left)

Length from lower renal artery to

H1 aneurysm neck

H2 distal aneurysm

H3 aortic bifurcation

H4 CIA bifurcation (a, right; b, left)

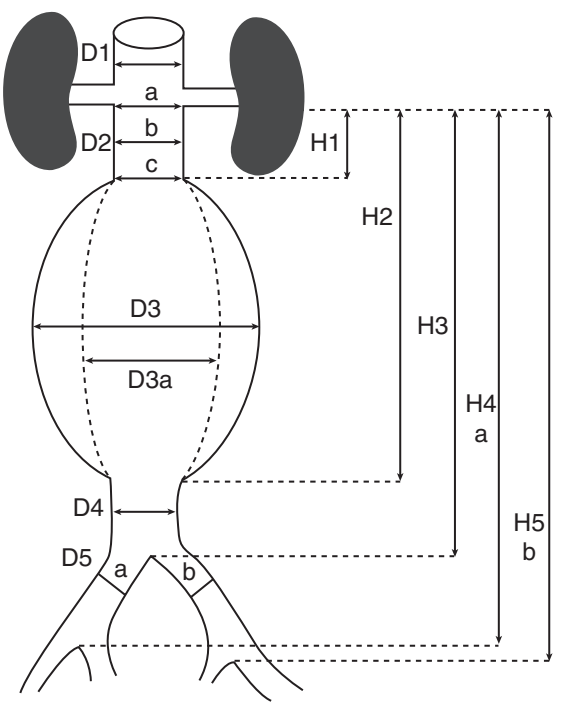

Figure 9.9 Method for measuring aortic dimensions. Figure adapted from Mohan et al.[82]

Table 9.4 Equipment necessary for emergency endovascular aortic aneurysm repair

C-arm digital fluoroscope with subtraction capabilities and contrast injector (portable or fixed system)	**Guidewires** 0.035-inch Glidewire (180, 260 cm*) Bentson Lunderquist extra stiff Amplatz super stiff
Catheters Kumpe RIM Cobra Marker pigtail Sos Omni Flush 125 cm multi-purpose	**Balloons** Cook Coda balloon up to 40 mm BSC equalizer 40 mm* Cordis Maxi 15, 20, 25 mm PTA balloon 12 mm diameter
Sheath Cook 5, 7, 9, 12, 14*, 18, 20, 23 Fr (10–15 cm long)	**Stents** Balloon-expandable (Palmaz) Self-expanding (SMART) AAA Stent grafts (Cook, Gore, Medtronic)

*Denotes for brachial approach.

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10

Complications in renal and mesenteric vascular interventions

Martin Schillinger and Thomas Zeller

Introduction to the frequency and type of complications • Factors identifying high-risk patients for complications • Complications of specific interventional steps and complications of specific interventional tools • Methods to detect potential complications – which diagnostic steps are needed routinely to rule out or identify complications • Endovascular, surgical and/or medical techniques to resolve complications • Methods to avoid complications • Summary • Check list for emergency equipment for interventions

INTRODUCTION TO THE FREQUENCY AND TYPE OF COMPLICATIONS

This chapter covers complications related to endovascular treatment of celiac, superior mesenteric, renal, and occasionally inferior mesenteric arteries. Systematic data on complications mainly are available for renal artery stenting, only very few reports cover complications of mesenteric artery interventions. The principle mechanisms of complications for renal and mesenteric arteries are very similar, thus this chapter mainly covers the literature on renal arteries.

The occurrence of any complication described in the literature on *renal interventions* is reported to be between 3 and 36%.[1–15] Particularly in historical series using the over-the-wire (OTW) approach[7–9] without guiding catheters or long sheaths, complication rates above 10% were frequently observed: the rate of minor complications was at maximum 26%,[7,10] the rate of major complications was reported to be between 1 and 14%,[4–7,11–14] and a 30-day mortality rate of 1% due to renal artery perforation, cholesterol embolization, acute renal failure, and fatal bleeding at the access site was observed.[15] These figures completely changed with the introduction of coronary technologies. Complication rates below 3%[16,17] seem realistic when low profile rapid exchange systems and renal guiding catheters or sheaths are used.

Frequencies of complications during treatment of *celiac or mesenteric arteries* are available only from small case series. The extent of ischemia of the related target organs mainly determines the impact of complications in these vessel areas. Distal embolization from the celiac trunk and the superior mesenteric artery or acute occlusions of these vessels may result in ischemia of the stomach, small and large intestinal infarction, hepatic ischemia, ischemic pancreatitis, or ischemic colitis. While this may occur infrequently for chronic disease, in acute settings there is a greater chance of bowel infarction and exploratory laparotomy may be indicated as a concurrent procedure. For mesenteric procedures, bowel infarctions were reported in up to 11% of the cases, with a periprocedure mortality rate of up to 4% and a frequency of renal failure of also 4%.[18,19] Acute thrombosis was seen in 3% and additionally compromised arterial perfusion due to severe spasm has been reported in numerous cases.

Specific complications of renal and mesenteric artery stenting include local complications at the target vessel segment like *stent misplacement*, arterial *dissection* or *rupture*, *renal artery thrombosis*, and *perforation* of the renal parenchyma, and *renal infarction* as a potential consequence of all these complications, as well as systemic complications like *cholesterol emboli,* which refers to a worst case scenario after the intervention. Some patients suffer multiple and repetitive emboli, intra- as well as extrarenal, until days after the procedure. Finally, interventions can be complicated by *renal failure*, which can be due to local complications, embolization, or contrast agent induced, and *secondary nephrectomy* – a rather rare complication (below 1%) even in times when low profile systems were not available.[15]

Stent misplacement

There are no data indicating the frequencies of stent misplacement. From personal experience the frequency certainly is below 5%. Ideally an ostial renal stent extends 1 to 2 mm into the aorta to firmly cover the ostium and to reduce the risk of recoil and restenosis at the renal orifice, but still enable repeat interventions in case of restenosis. Precise placement of the stent is crucial. Three factors may influence the precision of stent placement. First, precise stenting can be best achieved during apnea of the patient during stent inflation. Second, in patients with tight and focal ostial lesions, predilation reduces the risk of stent misplacement. Third, adequate projection of the renal artery and the stenosis is crucial.

Figure 10.1 demonstrates a case of stent misplacement in a patient with inadequate angiographic projection during renal artery stenting. The initial result looks perfect in the posterior-anterior view, in fact the stent was misplaced and the ostium was not covered. The patient came back with a high-grade restenosis and had to undergo repeat angioplasty. The 25° LAO view indicates that the stent was initially misplaced and did not cover the ostium (Figure 10.1). In contrast, Figure 10.2 shows an example of stent misplacement with the stent protruding 5 mm into the lumen of the abdominal aorta. Although the initial result is acceptable, repeat interventions in this patient will be difficult: a wire may easily pass through the struts of the stent rather than through the lumen, furthermore, the aortic edge of the stent may be damaged or dislocated[20] during later interventions in the renal or any other proximal territory.

Dissection

Dissection of the renal artery may occur during virtually all phases of the intervention, particularly during wiring and dilation of the artery. Reported frequencies range from around 0 to 8%.[15] Diagnostic or guiding catheters may cause dissection, particularly when advanced through the stenosis (Figure 10.3); wiring the artery can initiate a dissection, stenting and postdilation may cause miniruptures and subsequent vessel dissection. Leaving a dissection untreated is associated with a high risk of early vessel thrombosis. Figure 10.3 shows a case with a large dissection, which could be resolved by bare stent implantation. Besides dissection of the renal artery, dissection of the aorta may occur both due to manipulation with the guide or following stent implantation with an incidence of 0 to 2.2%.[15] These dissections can be left untreated as long as the origin of the dissection is covered by the renal stent and as long as there is no retroperitoneal bleeding or progressive enlargement of the dissection. Follow-up by serial computed tomography investigations is mandatory to ascertain healing of the leakage.

Rupture

Fortunately, this worst potential complication of renal and mesenteric artery stenting very rarely occurs (below 1%).[15] Clinical signs of rupture are back, flank, or inguinal pain, tachycardia, and hypotension. Unexplained pain after balloon inflation or stenting always has to be followed by a thorough interrogation for rupture and bleeding. Ideally, the rupture should be recognized before the wire is removed, otherwise reentry can be very difficult. The most devastating complication which can hardly be resolved by endovascular techniques is a complete rupture of the renal artery from the origin from the aorta. The risk for this complication seems to be higher in patients with circular heavy calcification of

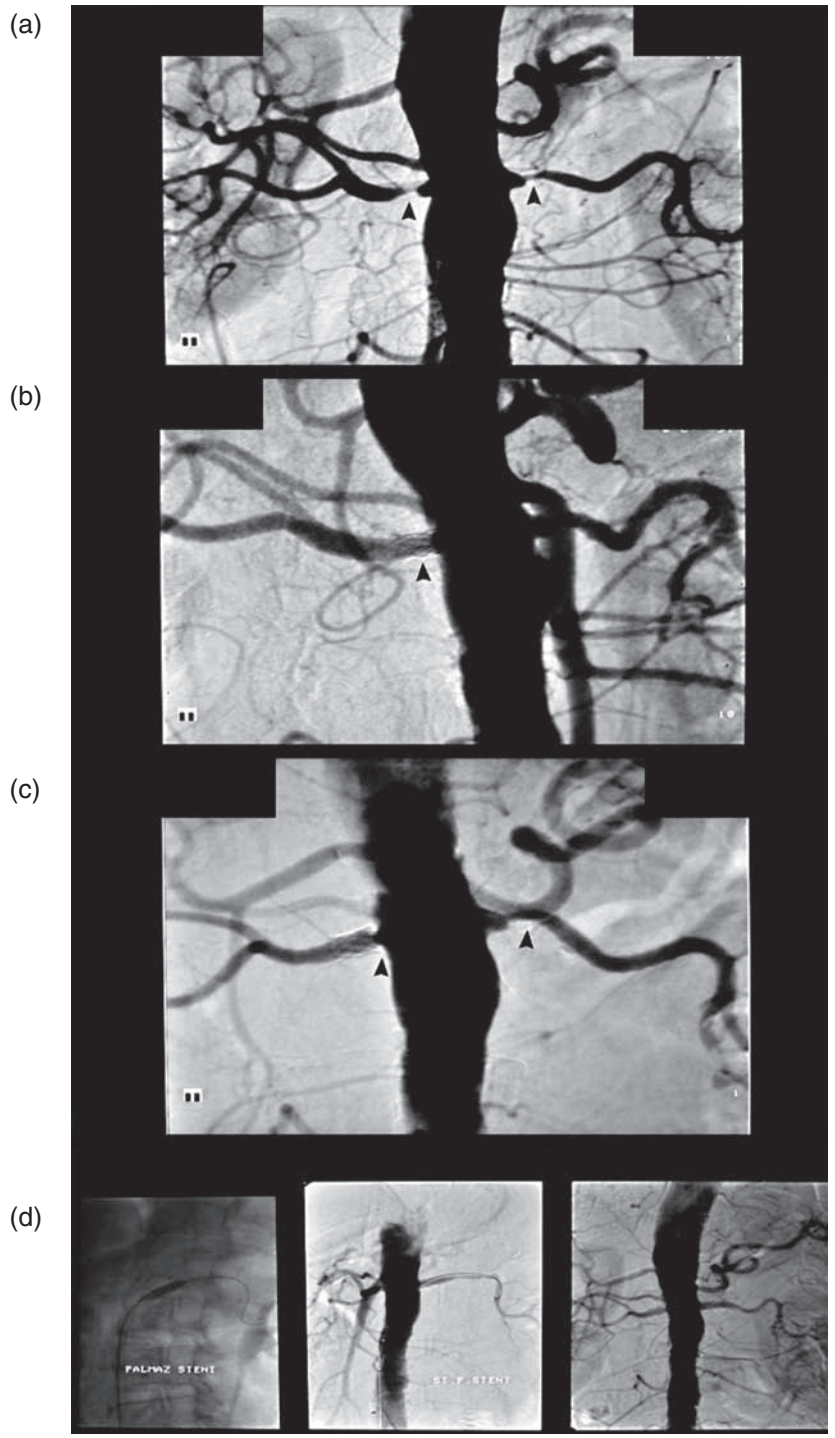

Figure 10.1 Renal artery stenting in a case of bilateral ostial renal artery stenosis demonstrating the importance of covering the renal ostium – restenosis after 3 months due to suboptimal stent placement. (a) High grade bilateral renal artery stenosis. (b) Stent implantation in the right renal artery with apparently optimal result. However, the suboptimal placement of the stent – not completely covering the ostium of the renal artery – cannot be seen in this projection. (c) Moderate restenosis after 3 months at the proximal edges of the stent. (d) Stent implantation in the left renal artery with excellent technical result.

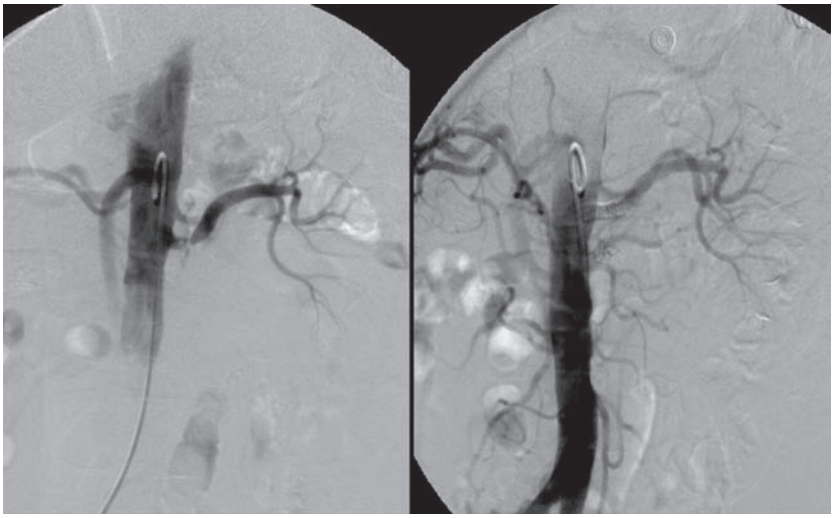

Figure 10.2 Misplacement of a renal stent with the stent extending too much into the aorta. Clinically, no complications were observed in this patient.

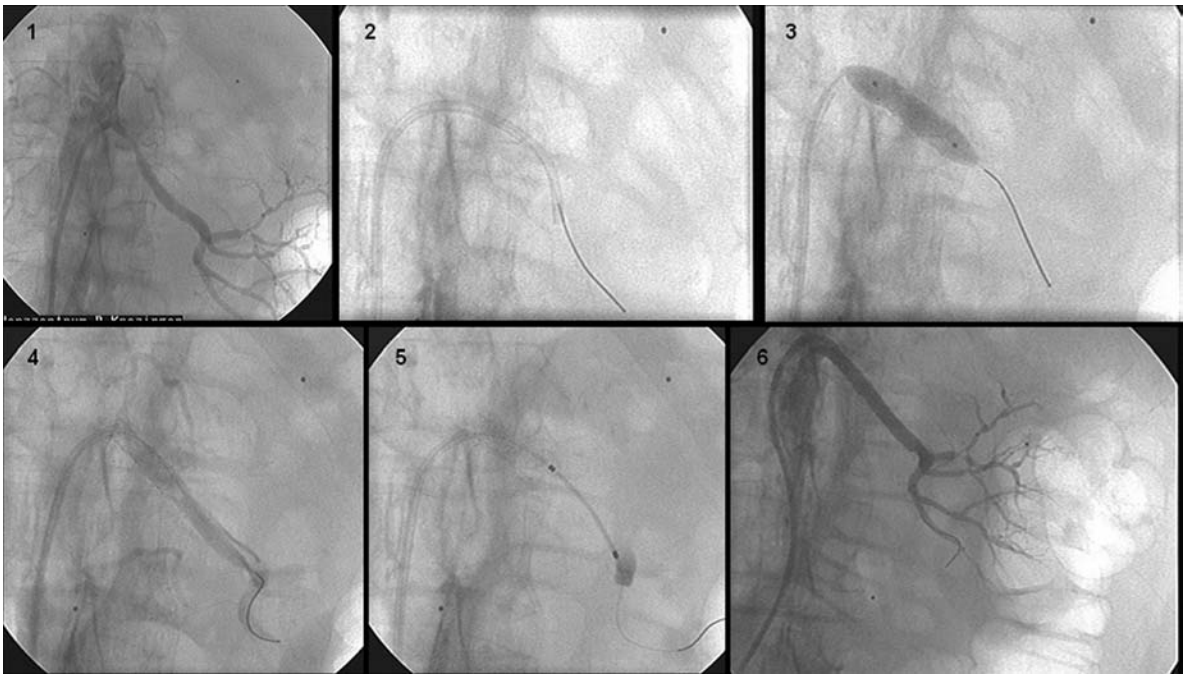

Figure 10.3 Dissection of a renal artery after placement of a guiding catheter through the stenosis. The dissection could be resolved by stenting with a balloon-expandable bare metal stent.

the renal ostium, and when high pressure dilation is needed to dilate or expand the stent. In this case, the rupture site has to be immediately sealed with a balloon and further with a covered stent graft, otherwise most patients will need an emergency operation. When ruptures cannot be handled by endovascular treatment, the occlusion balloon has to be kept in place and the patient transferred to the operating room. The 'warm ischemia' time has to be reduced as much as possible to avoid renal infarction and nephrectomy. Figure 10.4 shows an example of a complete rupture of a renal artery after balloon dilation. The orifice of the artery was immediately sealed with a large balloon in the aorta. A covered stent then could not be passed to the renal artery, therefore the patient was transferred to the operating room. Besides rupture at the renal ostium, the artery may also rupture more distally, particularly in non-compliant, calcified artery. Again, immediate balloon occlusion and implantation of a stent graft is the treatment of choice.

Perforation

Manipulation with the guidewire in the subsegmental arteries is the most frequent cause of perforations, while perforation during passage of the stenosis occurs relatively seldom. This complication is more frequent during recanalization of chronic total occlusions. The choice of the wire as well as a stable position of the tip of the wire during the entire intervention is crucial to reduce the risk for this complication. Figure 10.5 shows a case with a perforation of the renal parenchyma during recanalization of a chronic total occlusion. The bleeding could be stopped by antagonizing heparin with protamine and spontaneous tamponade. As a consequence of perforation, deleterious bleeding may occur and secondary

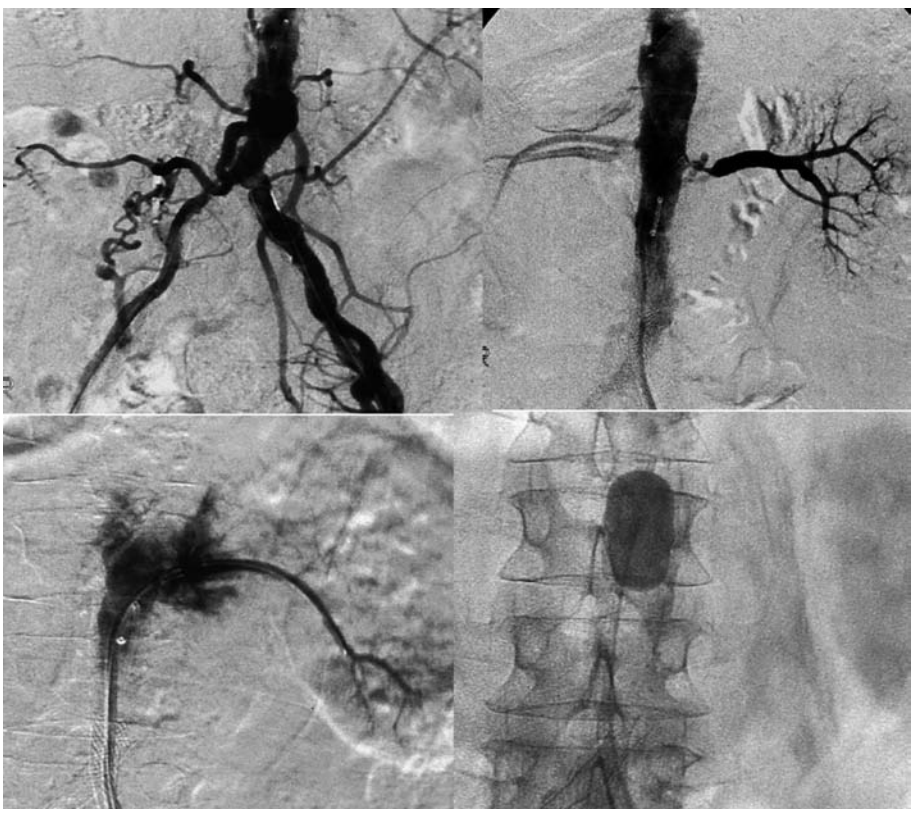

Figure 10.4 Rupture of the renal artery during balloon angioplasty of a left-sided ostial renal artery, stenosis, and successful sealing of the rupture site using a large compliant balloon. (Courtesy of Dr P Waldenberger, Innsbruck, Austria.)

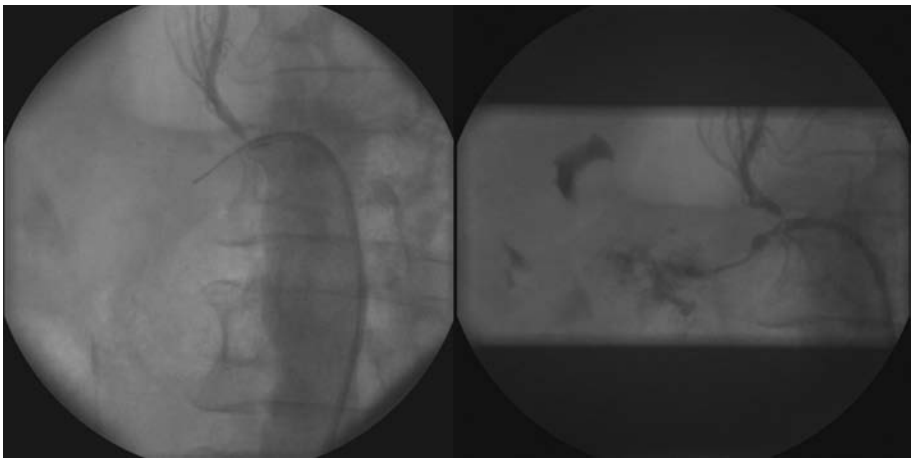

Figure 10.5 Perforation during recanalization of a chronic total renal artery occlusion. The bleeding could be stopped by antagonizing heparin with protamine and spontaneous tamponade.

(partial) nephrectomy is a feared consequence. Figure 10.6 shows a case when perforation and bleeding resulted in secondary nephrectomy.

Thrombosis

Renal artery occlusion as a complication during the intervention is reported in 1 to 2.5% of the procedures in the renal trunk, segmental artery occlusion in 1 to 2%.[15] However, most of these acute occlusions can be successfully recanalized during the procedure and the rate of renal infarction due to acute procedure-induced thrombosis is expected to be below 1%. Stent thrombosis very rarely occurs with modern stents, adequate (dual) antiplatelet therapy including aspirin and a thienopyridine, and a good final result after stenting (residual stenosis below 30%, no dissection). However, when dissections distal to the stent remain unrecognized, early stent thrombosis may occur despite adequate antiplatelet medication. Good quality final angiograms are therefore important before removing the wire and the guide.

Embolization

Microemboli to the renal artery presumably occur in most interventions and may be the cause for renal deterioration in a considerable number of patients; unfortunately, data on the frequency and the true impact of this complication are not available. Macroembolization was reported in up to 8% in early series; more recent data indicate a macroembolization rate of around 1%.[15] Furthermore, besides the use of low profile catheter material and atraumatic techniques, there is no reliable technique to avoid microembolization. Current protection devices seem inadequate for most renal or mesenteric procedures.

Cholesterol embolization is a worrying syndrome and occurs especially in a diffuse atheromatous or aneurysmatic aorta. The syndrome may become evident days after the procedure with an incidence of up to 3%. Signs of peripheral embolization (Figure 10.7) as well as systemic inflammation and renal deterioration are characteristic for this potentially life-threatening condition.

Spasm

Renal artery spasm can be induced by the wire, guiding catheter, balloon, or stent. Spasm less frequently occurs in calcified artery and mostly can be resolved by local administration of 0.1 mg diluted nitroglycerin or by papaverine in case of mesenteric interventions. The most important differential diagnosis is perforation and dissection – which per se might induce severe spasms and need mechanical stabilization by stent implantation.

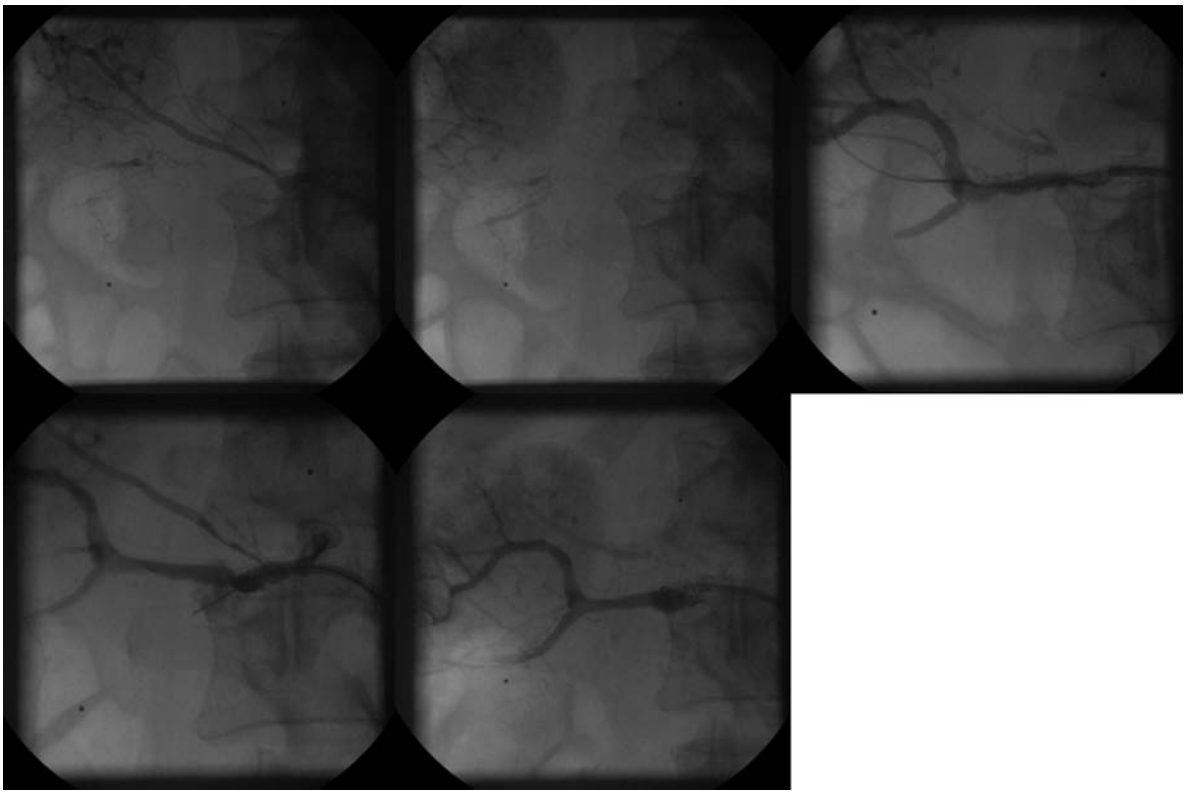

Figure 10.6 Renal main stem perforation during recanalization of a segmental artery occlusion which resulted in secondary nephrectomy.

Renal failure

Deterioration of renal function after renal artery interventions is reported in approximately 15% of the patients.[21] Several risk factors have been acknowledged and there exist some effective strategies to minimize the risk for this complication. In contrast to other percutaneous interventions – when renal dysfunction is a contraindication for an intervention – renal dysfunction can be a good indication to treat renal artery stenosis. Nevertheless, the patient and physician have to be aware that, particularly in cases with pre-existent renal impairment, there is much to win but at least as much to lose following a percutaneous renal treatment.

According to the Society of Interventional Radiology, the overall threshold for major complications of percutaneous renal revascularization is 10%,[15] realistically this rate can be reduced to below 3% in skilled hands. Thresholds[15] for 30-day mortality (1%), secondary nephrectomy (1%), surgical salvage operation (2%), symptomatic embolization (3%), main renal artery occlusion (2%), branch renal artery occlusion (2%), complicated access site hematoma (5%), and acute renal failure (2%) also seem unacceptably high and certainly can be reduced by adequate training and the use of proper materials.

FACTORS IDENTIFYING HIGH-RISK PATIENTS FOR COMPLICATIONS

Two major determinants of complications have to be considered. First, patients' *comorbidities* including age, pre-existent renal failure, congestive heart failure and diabetes mellitus. Second, anatomical factors of the renal arteries and the access route. *Unfavourable anatomies* include tortuous iliac arteries, heavy calcification and kinking of the aorta, steep angle of the renal artery

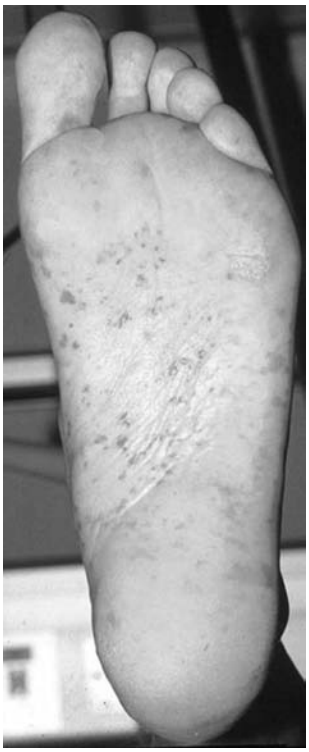

Figure 10.7 Sign of peripheral embolization in a patient after renal artery stenting.

origin, short trunk of the renal artery – i.e. early bifurcation to segmental arteries, heavily calcified stenosis, or fresh thrombotic lesions, and finally extended soft, mainly thrombus containing plaques of the aorta.

Comorbidities

With increasing *age*, the degree of calcification usually rises and the likelihood for arterial kinking and tortuosity increases. Furthermore, renal functional reserve naturally decreases with increasing age, making patients more vulnerable for contrast-induced complications. Increased age, per se, of course is not a contraindication for a renal or mesenteric intervention, but the interventionist has to be aware that some specific measures like preprocedure hydration and MR angiography of the access route should be considered mandatory in these patients.

Pre-existent renal failure frequently is the indication to perform renal artery stenting. Particularly in these patients, the benefit of the intervention can be striking; unfortunately, the risk for renal failure following an intervention also is increased. Again, preprocedure care, including adequate hydration, administration of acetylcysteine (600 mg bidaily), and limiting the amount of contrast agent, is a cornerstone in the management of these patients. The use of alternative contrast agents like carbon dioxide or gadolinium alone or in combination with iodinated contrast agents may reduce the risk of deterioration of renal dysfunction.[22,23]

Congestive heart failure (CHF) is a frequently neglected risk factor for renal failure after percutaneous interventions. The main impact of CHF on renal function is based on chronic renal hypoperfusion due to low cardiac output on the one hand as well as renal vasoconstriction following enhanced sympathetic activity. Patients with CHF require monitored fluid management periprocedure which has to balance hydration in relation to urine volume and the risk of pulmonary congestion.

Diabetes mellitus increases the risk for complications due to its impact on microvascular and macrovascular disease. Microvascular renal disease causes impaired renal function and elevated renovascular resistance, which is considered a risk factor for non-response with respect to blood pressure improvement after renal interventions.[24] Macrovascular diabetic disease is characterized by a tendency for extensive calcification of the access route, aorta, and renal arteries, which increases the risk for embolic complications.

Anatomic factors

Tortuous iliac arteries can complicate the access and even if access through these arteries can be achieved, tortuosity reduces the steerability of the catheter material at the site of the target vessel. Preprocedure imaging with magnetic resonance imaging angiography helps to identify patients with complicated access routes and in these patients alternative routes like transradial or transbrachial access can be an adequate choice. The *morphology of the aorta* is a key determinant for potential problems during the intervention.

Heavy calcification, multiple (ulcerated) plaques, and kinking of the aorta can cause complications during positioning of the guiding catheter or sheath even before access to the target vessel has been gained. Again preprocedure imaging and planning of the intervention is crucial in this context. Furthermore, specific atraumatic techniques for placement of the guiding catheter or sheath should be applied (which will be described below). Usually, right renal arteries will be best accessed from the right transfemoral approach and left renal arteries from the left groin. The easiest access route for the celiac trunk and superior mesenteric artery is from a transbrachial or transradial approach. The *angle of the renal artery* originating from the aorta usually is between 60 and 90°; in patients with very steep angles, transfemoral access can be difficult. However, in these patients, coming from above frequently is an easy and safe solution and avoids the problem of unstable catheter back-up.

A short trunk of the renal artery due to an early bifurcation to segmental arteries as well as *bifurcated lesions* (Figure 10.8) can complicate renal procedures. The use of multiple wires and the kissing balloon technique demands high interventional skills, but enables safe treatment of bifurcated lesions.

Unfavorable *lesion morphology* includes heavily calcified stenosis or fresh thrombotic lesions. Calcification can be a particular problem when primary stenting is anticipated. First, placement of the stent may be difficult – even low profile rapid exchange stents can get lost in patients with very tight and rigid stenosis when predilation is not done adequately. Second, some lesions can be resistant even to high pressure postdilation, causing a significant residual stenosis in the stented segment. In these patients the risk for stent thrombosis and restenosis is increased, and ruptures have been reported when postdilation of the artery was done with very high pressures.

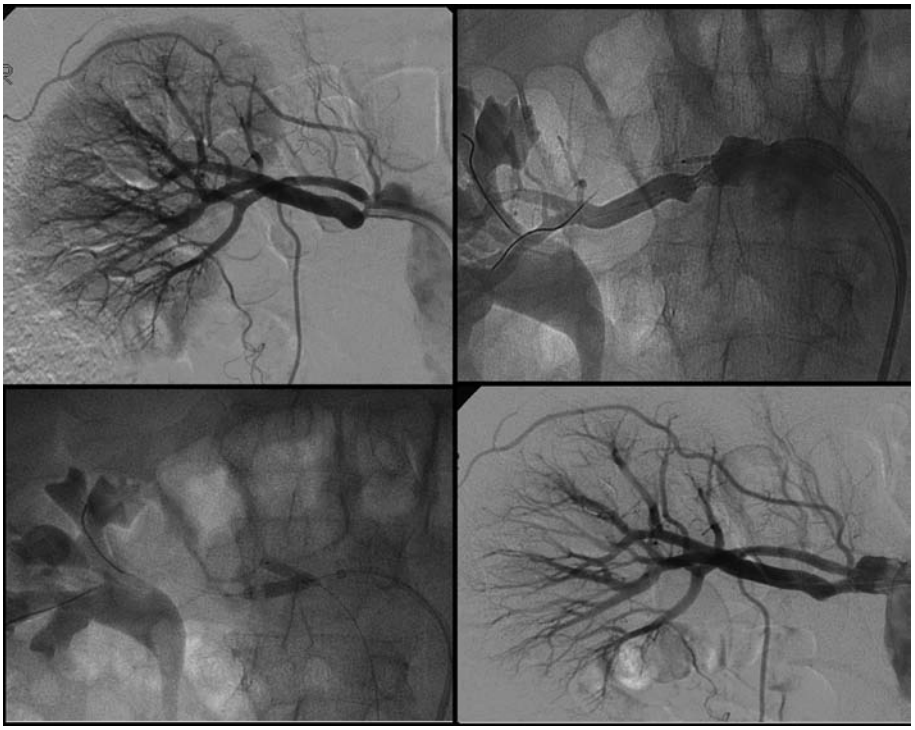

Figure 10.8 Double wire and kissing stent technique for treatment of a renal bifurcated lesion. (Courtesy of Dr P Waldenberger, Innsbruck, Austria.)

In these patients lesion preparation by predilation – eventually using cutting balloon angioplasty – can be helpful to avoid these complications.

COMPLICATIONS OF SPECIFIC INTERVENTIONAL STEPS AND TOOLS

Placement of the guiding catheter or long sheath

Engaging the ostium of the renal artery has to be done as atraumatically as possible. Particularly, plaque disruption of the aorta during the access to the renal artery frequently may cause *embolization*. Most frequently, these are microembolic showers, both to the renal and peripheral arteries. In this context, *cholesterol embolization* can be a worst case scenario. It has been suggested that plaque rupture and delayed healing of the vulnerable plaque at the renal artery or in the abdominal aorta causes these severe embolic complications. Treatment options for this complication are unclear, and different approaches have been proposed: aggressive anticoagulation on the one hand, to inhibit further local thrombotic applications and support emboli resolution, as opposed to discontinuing any antithrombotic drugs on the other hand, to allow healing of the vulnerable plaque. Fatal courses of cholesterol emboli are relatively frequent, and as yet all recommendations to prevent or treat this symptom are not evidence-based.

Manipulation with the guiding catheter or sheath may also initiate a *dissection* of the renal artery, celiac or mesenteric artery, or the aorta. This is a rather infrequent complication as long as dedicated materials with soft tips are used and the tip of the guiding catheter or sheath is kept out of the orifice of the renal artery. In this context, we recommend not inserting the tip of the guiding catheter or sheath through the stenosis.

Wire passage

Potential complications during this interventional phase are *dissection* of the plaque, *plaque shift* and *acute vessel thrombosis*, and *perforation* of the renal parenchyma. Non-hydrophilic wires with malleable soft tips (usually 0.014 inch) certainly reduce the risk for these complications.

Predilatation

The risk for complications during predilatation is relatively small; usually undersized balloons are used for plaque preparation. Potential complications mainly include peripheral *embolization*, which remains asymptomatic in most patients.

Stenting

Implantation of the stent according to the nominal diameter of the artery or with minimal oversizing bears several possible risks. *Rupture* of the artery certainly is a rare but worst scenario. Other complications are *dissection* at the distal edge of the stent, *acute stent thrombosis*, and *stent misplacement*. The risk for rupture and dissection increases with an increased stent-to-artery ratio; oversizing therefore should be limited to 10% of the reference vessel lumen. Acute stent thrombosis can be more or less completely avoided with adequate premedication with dual antiplatelet inhibitors (clopidogrel or ticlopidine plus ASA) and low dose peri-intervention heparin (usually 2000 to 5000 IU heparin) or bivalirudin.

Postdilatation

Since the recommended stents for renal arteries are balloon expanding, postdilatation will not be needed routinely. Aggressive postdilatation again bears the risk of *rupture* and *dissection*, particularly when the edges of the balloon are not kept strictly within the margins of the stent. When choosing the size of the postdilatation balloon, the interventionist has to be particularly careful in patients with post-stenotic dilatations of the renal artery distal to a high-grade stenosis. In these patients, the stent and balloon have to fit to the size of the renal artery prior to the post-stenotic dilatation to reduce the risk of oversizing and severe vessel injury.

METHODS TO DETECT POTENTIAL COMPLICATIONS – WHICH DIAGNOSTIC STEPS ARE NEEDED ROUTINELY TO RULE OUT OR IDENTIFY COMPLICATIONS

Angiography

It is still mandatory to be aware of the necessity to minimize the amount of contrast agent and for

adequate pre- and postintervention angiograms of the entire renal artery and the kidney. The main issues which have to be ascertained in the final angiogram are a good local result, exclusion of dissection, perforation, and bleeding. The latter in particular has to be excluded with certainty, as unrecognized and untreated bleeding may endanger the patient's organ and life.

Ultrasound

This has a limited role in excluding complications at the renal artery, but can be helpful as a rapidly available technique to visualize renal infarct or parenchymous bleeding. Duplex ultrasound can be helpful in excluding renal stent thrombosis. Unfortunately, renal arteries cannot be adequately visualized by ultrasound in approximately 20% of the patients.

Computed tomography

This is the method of choice to exclude bleeding and infarcts. The main shortcoming of CT is the additional amount of contrast agent needed to exclude bleeding complications.

ENDOVASCULAR, SURGICAL AND/OR MEDICAL TECHNIQUES TO RESOLVE COMPLICATIONS

Endovascular techniques

Most complications of renal and mesenteric artery interventions can be resolved by endovascular techniques.

Balloon inflation

Balloons are effective for sealing ruptures or perforations in all cases when a wire can be passed by the site of the bleeding. The balloon should be inflated to low pressures only in a 1:1 balloon-to-artery ratio. It has to be checked angiographically that the balloon adequately occludes the site of perforation. Balloon inflation in patients with rupture always has to be combined with reversal of heparin using protamine. An initial inflation time of 3 to 5 minutes usually helps to stabilize the patient. In patients with massive bleeding and when the bleeding site cannot be passed with a balloon, sealing of the ostium of the artery or even the aorta can be effective and life-saving as a bridge to an emergency operation (Figure 10.4). In contrast to other peripheral vessels, dissections are usually treated by stent implantation rather than by prolonged balloon angioplasty only.

Bare stents

These are the methods of choice to resolve dissections (Figure 10.9) or residual stenosis after balloon angioplasty in patients with fibromuscular dysplasia or non-ostial stenosis, when balloon angioplasty alone was attempted. However, if dissection and perforation occur during the initial wire passage, endovascular management becomes complex (Figure 10.10). The most critical point is safe re-entry with the wire through the true lumen. As soon as this step has been

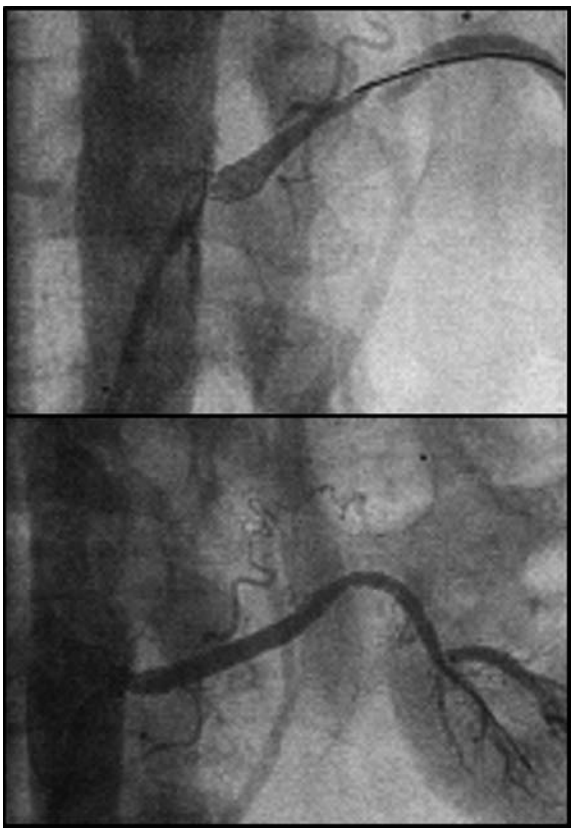

Figure 10.9 Wire-induced dissection of the renal artery trunk which could be resolved by implantation of a balloon-expandable bare metal stent.

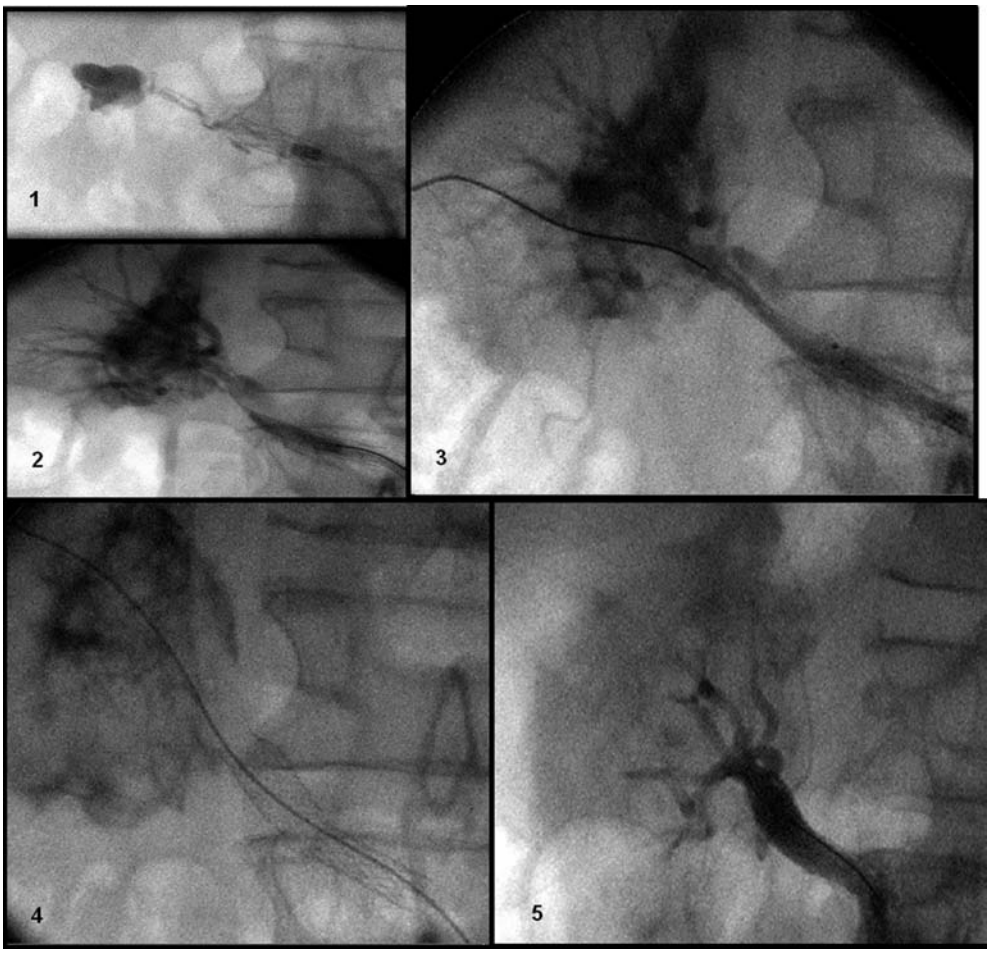

Figure 10.10 Perforation and bleeding during wire passage for recanalization of an in-stent occlusion of a right renal artery (1, 2). Finally, the wire can be re-advanced through the true lumen (3) and a self-expanding stent is implanted to re-open the artery (4, 5).

completed, bare stents (self-expanding or balloon-expandable) can be used to ensure a sufficient result (Figure 10.10).

Covered stents

Recently, balloon-expandable and self-expanding covered stent grafts in sizes and profiles adequate for renal and mesenteric arteries became available. These devices usually are more rigid than bare metal stents. However, covered stents are very effective in treating complications like rupture, bleeding, or aneurysms. Figure 10.11 shows an example of the use of a covered self-expanding stent graft in a patient with an aneurysm of the right renal artery; it can be used in similar ways to cover perforations and bleeding sites.

Embolization

In cases with perforation of the renal parenchyma with the tip of the wire, antagonizing anticoagulation and immediate embolization of the perforated segmental artery with coils can save the patient's kidney. Adequately sized coils for vessels from 2 to 6 mm have to be available in the cath lab.

Aspiration and thrombolysis

Local thrombolysis is very effective for the treatment of acute renal or mesenteric artery

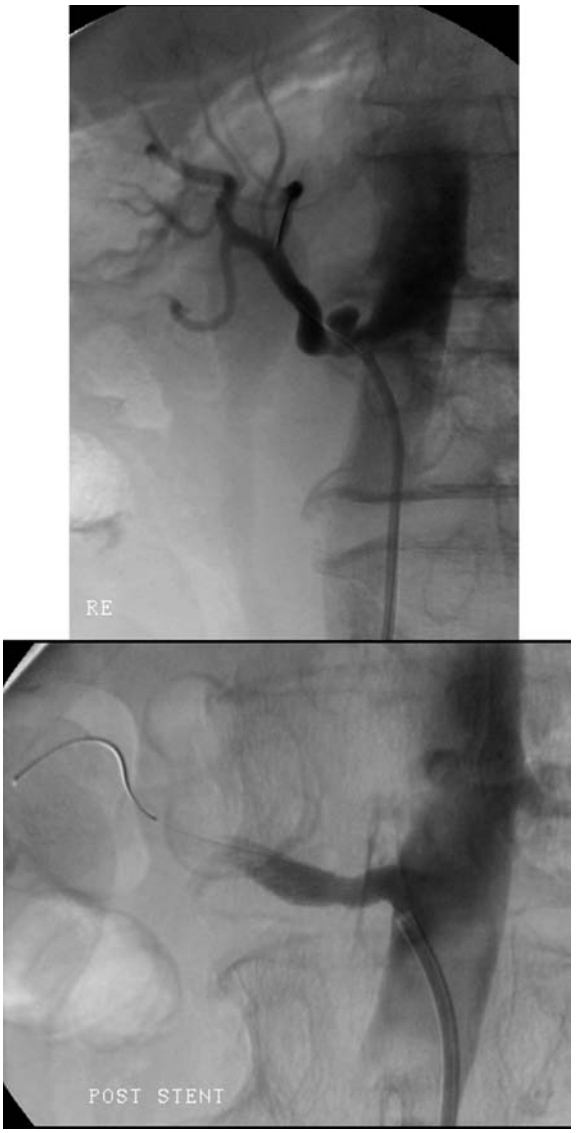

Figure 10.11 Example of the use of a covered stent graft in a patient with a renal artery aneurysm. These devices can also be applied to seal perforations or ruptures of the artery.

thrombosis including stent thrombosis. Before thrombolysis is initiated, aspiration thrombectomy can be attempted, using coronary aspiration catheters (like the Export or Pronto device). Urokinase as well as rt-PA can be used locally via perfusion catheters.

Surgical techniques

Secondary surgical procedures are reported in 1 to 2.5% of cases in larger series.[15] Uncontrolled bleeding usually necessitates *nephrectomy*. The rate of complications of elective nephrectomy is low; emergency nephrectomy carries an operative risk for major complications of 15 to 30%. In patients with complete rupture of the artery, emergency *bypass surgery* can resolve the problem, again at a risk for major complications ranging between 10 and 25%.

Medical approaches

Besides the use of *thrombolysis*, the interventionist has to be familiar with *antagonizing anticoagulation* – e.g. heparin by administration of protamine. Figure 10.12 shows an example of a severe bleeding after perforation with the guidewire, which could be handled conservatively by antagonizing anticoagulation. Dosage of protamine is usually recommended in a 1:1 ratio to heparin. In patients with complex bleeding disorders, fresh frozen plasma and prothrombin complex concentrates may be necessary.

METHODS TO AVOID COMPLICATIONS

Preprocedure work-up

Before starting the procedure, the interventionist has to know the patient's *medical history*, medication and comorbidities, the degree of stenosis, anatomy of the aorta, and level of the renal ostium. In skilled hands, *duplex ultrasound* is the most adequate non-invasive method to assess the degree of stenosis and hemodynamic significance of a renal artery. Unfortunately, duplex ultrasound will not give adequate information on the access route in many patients. *MR angiography* (MRA) seems most adequate to assess these anatomic conditions, although the degree of stenosis is frequently overestimated by MRA. We recommend using MRA in all patients with risk factors for extensive atherosclerosis like elderly, diabetic patients, patients with known coronary or peripheral artery disease, and patients with pre-existing renal dysfunction, to minimize the amount of contrast agent. However, recent data indicate that particularly in patients with advanced renal insufficiency the use of the MR-contrast agent Gadolinium may lead to severe systemic complications called *nephrogenic systemic fibrosis* and therefore has to be limited whenever possible.

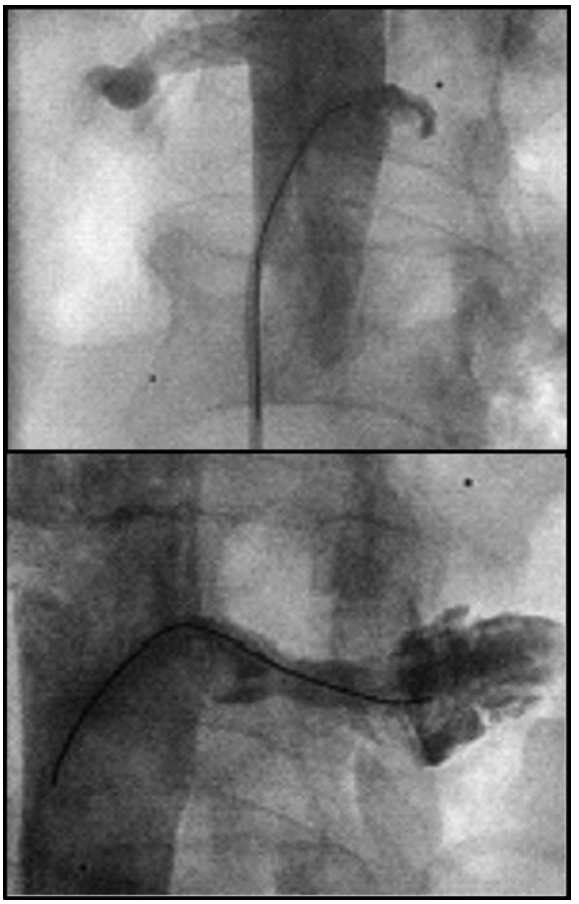

Figure 10.12 Bleeding due to guidewire perforation which could be managed conservatively by antagonizing heparin with protamine.

Medical pretreatment

Intravenous *hydration* of the patient with intravenous saline solution starting the day before the intervention should be anticipated in all patients with increased risk for renal failure including the elderly, diabetics, patients with CHF, and patients with pre-existent renal dysfunction. Furthermore, data support the use of *acetyl cysteine*, 600 mg bidaily, starting the day before the intervention and continuing until one day after the intervention. Finally, dual antiplatelet therapy has to be given; in patients without pretreatment of *clopidogrel or ticlopidine* we recommend 300 mg clopidogrel (1000 mg ticlopidine) as a loading dose.

Choice of contrast agent

Iodinated contrast medium can result in nephropathy. *Iso-osmolar contrast agents* like iodixanol have been demonstrated to exhibit an improved renal safety profile compared to low-osmolar contrast agent.[25] Therefore, the uniform use of iso-osmolar contrast agents in patients undergoing renal interventions is recommended.

Projection

Precise placement of the stent is crucial, for this purpose the stenosis has to be adequately visualized during angiography. MRA can be helpful to determine the best angiographic angle for angiography. In patients without MRA, we recommend a *20 to 25° LAO projection* as a standard view for renal interventions.

Low profile rapid exchange systems

Low profile rapid exchange (RX) or 'monorail' systems are today's standard for coronary interventions, and RX therefore was formerly referred to as 'coronary technique', implicating the use of guiding catheters and low profile devices. Technologic improvements in renal artery interventions have substantially reduced the complication rate in the past 5 years,[6] and the introduction of RX systems certainly contributed to this development. A significant reduction in fluoroscopy and procedure time was found when RX catheters were used for renal stenting, with identical success and complication rates compared to the conventional over-the-wire coronary angioplasty systems.[1] Besides the advantages for the interventionist of comfortably handling shorter wires, the introduction of RX devices also enabled a decrease in the diameter of wires and size of catheters and stents. Data suggest that the use of RX systems also translates into an improved safety of the procedure.[16]

Choice of wire

Passage through the stenosis can be done either with a non-hydrophilic 0.035-inch wire (Bentson) using an atraumatic technique described by Dr Sos, or directly with non-hydrophilic 0.014-inch wires. During the intervention, *non-hydrophilic*

0.014-inch wires with a stiff body and flexible and soft tips should be used throughout. The tip of the wire has to be visualized during the entire procedure and should be kept in the segmental arteries without entering the subsegmental space. The use of hydrophilic glide wire should not be considered for renal and mesenteric interventions.

Engaging the renal artery

An atraumatic technique to place the guiding catheter or sheath and enter the renal artery is the key for success in renal and mesenteric intervention. The technique displayed in Figure 10.13 was described by Dr Sos and is probably one of the easiest and fastest ways to get safe access. Using a small shepherd hook shaped catheter (Sos-omni) and a 0.035-inch non-hydrophilic guidewire (Bentson) the renal artery is approached from below. The guidewire is retracted in the diagnostic catheter until approximately 1 cm of the tip of the wire is extending out of the diagnostic catheter. The catheter and the guidewire are then advanced cranially until the tip of the guidewire jumps laterally into the renal ostium. The catheter is then slightly retracted and the guidewire advanced through the stenosis. In the coaxial technique, a guiding catheter or sheath can now be safely advanced to the renal ostium, the 0.035-inch wire is exchanged for a 0.014-inch renal wire and the diagnostic catheter can be removed.

If the traditional technique of direct cannulation of the renal artery ostium with the guiding catheter is used, to avoid renal embolism prior to selective renal angiography, the guiding catheter should be cleaned from debris by aspiration of blood through the guiding catheter ('proximal protection'). This technique cleans the tip of the guiding catheter from debris collected during the engagement of the renal artery and therefore reduces the risk of renal embolism.

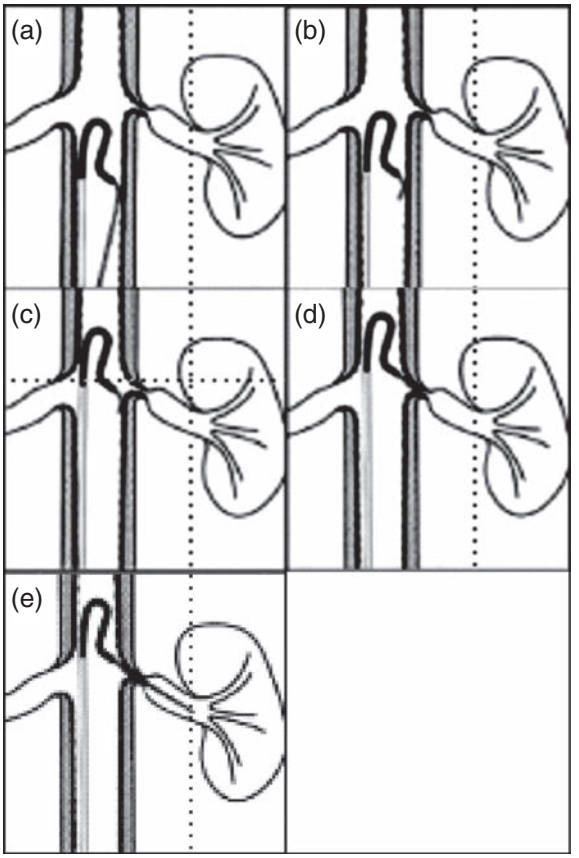

Figure 10.13 Atraumatic approach for treatment of renal or mesenteric artery stenosis. (a) Using a small shepherd hook shaped catheter (Sos-omni) and a 0.035 non-hydrophilic guidewire (Bentson) the renal artery is approached from below. (b) The guide wire is retracted until approximately 1 cm of the tip is extending out of the diagnostic catheter. (c) The catheter and the guidewire are advanced cranially until (d) the tip of the guidewire jumps into the renal ostium. (e) The catheter is slightly retracted and the guidewire advanced through the stenosis. In the coaxial technique, a guiding catheter can now be safely advanced to the renal ostium.

Pressure gradients

With adequate preprocedure work-up, measurement of pressure gradients usually is not necessary, particularly if high-grade stenosis is treated. For pressure measurement, pressure wires rather than 4 Fr diagnostic catheters should be used to reduce the risk for trauma, plaque disruption, and acute occlusion of the artery during this diagnostic work-up.

Predilation

When low profile catheter systems are used, predilation is not mandatory any more. However, in short and ostial stenosis, when calcification is suspected, and in all cases when the interventionist is in any doubt about easy passage of the stent, predilation should be considered. There is

hardly any complication which may arise due to predilation with undersized balloons, but this additional step may significantly facilitate stent deployment, reduce the risk for 'jumping' of the stent, and thus increase the safety of the procedure. In patients with very rigid stenosis, *cutting balloon angioplasty* can help to prepare the plaque and avoid high pressures during stent implantation and postdilation.

Stenting

Precise sizing and placement of the stent are crucial. It is known from several studies that the risk for restenosis correlates with the diameter of the stent – larger stents have a lower risk for restenosis. However, oversizing increases the risk for dissection and rupture and should not be done to more than 10%. Stent length is also associated with restenosis – as long as bare-metal stents are used. Nevertheless, the length has to be adequate to cover the entire plaque and avoid distal plaque shift. Stent deployment is best done under the patient's apnea after expiration. The degree of residual stenosis has to be minimized to reduce the risks for stent thrombosis and restenosis.

Postdilatation

Postdilatation of balloon-expanding stents is not mandatory, but should be considered in patients with a suboptimal result (> 10% residual stenosis). The risk of rupture and bleeding increases with pressure, particularly after high-pressure postdilatation a control angiogram should be taken, before the balloon is removed, especially if the patient is complaining of an acute onset of back pain; in case of bleeding the balloon can be rapidly re-inflated to seal the leakage.

Protection devices

Currently, no protection device adequately designed for renal or mesenteric arteries is available and the number of patients with an anatomy suitable for carotid protection devices is low. Furthermore, carotid protection devices may introduce the risk for additional complications – in particular removal of the filter devices after stenting sometimes can be challenging, when the retrieval catheter cannot be advanced through the stent. Therefore, current protection devices cannot be recommended for routine applications in the renal and mesenteric arteries.

Final angiography

We recommend to always perform two final angiographic runs: one before the wire is removed to exclude dissection, perforation, and bleeding, and a second run after removal of the wire to document the final result. In particular, the first run with the wire still in place is crucial, as re-entering the wire through a dissection or ruptured artery can be very difficult. Angiography always has to be done during the procedure in case of unexplained back or flank pain to rule out severe complications.

Knowing where to stop

Finally, stopping an intervention before the occurrence of a complication is always preferable to the treatment of a potentially avoidable complication. Time is usually a good indicator of how things are going during an intervention. The standard time for a renal or mesenteric ostial angioplasty is between 15 and 35 minutes from puncture to closure – if these times are vastly exceeded, stopping the procedure seems an adequate option.

SUMMARY

Renal and mesenteric artery interventions can be one of the safest and fastest peripheral interventions. Adequate indication, thorough preprocedure work-up, choice of medication and materials, and atraumatic technique are the key issues for success.

CHECK LIST FOR EMERGENCY EQUIPMENT FOR INTERVENTIONS

- covered stent grafts 4 to 7 mm in diameter and 10 to 20 mm in length (balloon-expandable or self-expanding)

- large diameter balloons to seal the aorta
- vascular coils suitable for vessels of 2 to 6 mm
- 0.014-inch guidewire compatible aspiration catheters
- thrombolytics
- protamine.

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11

Complications of aorto-iliac intervention

Deepa Gopalan and Peter Gaines

Introduction to the frequency and type of complications • Factors identifying high-risk patients • Complications of specific interventional steps and tools • Methods to detect complications • Endovascular, surgical, and medical techniques to resolve complications • Check list for emergency equipment

INTRODUCTION TO THE FREQUENCY AND TYPE OF COMPLICATIONS

Aorto-iliac intervention is a commonly performed endovascular procedure and yet the data to indicate the prevalence of complications are few. The problem is compounded by a lack of uniformity in the definition of a complication of endovascular intervention. Perhaps the best contemporary data come from the second BIAS II report, which prospectively looked at outcomes in 2152 patients from 46 hospitals in the United Kingdom.[1] That report detailed an overall periprocedural complication rate of 5.7%. Complications were more likely to occur in patients with critical limb ischemia (CLI) compared to claudication (18% vs 2.5%), but interestingly there was no significant difference between those patients treated with angioplasty or stents. Such information will be undoubtedly skewed by patient selection. More complex lesions are likely to have been treated by stent placement including their primary use in iliac occlusions rather than simple stenoses. In addition, there was a low rate (0%) of complications in patients treated as a day case, again reflecting good patient selection and an undoubted bias towards claudicants rather than patients with CLI.

The meta-analysis of aorto-iliac intervention performed by Bosch et al detailed a systemic complication rate of 1%, a local (access and treatment site and embolization) complication rate of 9%, a complication rate requiring intervention of 5.2%, and a mortality rate of 0.3%.[2]

The Dutch iliac stent trial had prospective assessment and recorded an overall complication rate of 5.7% in a group of patients who were predominantly claudicants.[3]

Periprocedural complications can be assessed as occurring (a) at the access site, (b) at the treatment site, and (c) systemic, away from the treated area. Access-related issues have been described in an earlier chapter.

Target site complications

Acute closure

The frequency of occlusion at the angioplasty site varies between 1 and 7% and does not seem to be related to the severity or location of the lesion.[4] When management of a stenosis results in acute closure at the time of treatment the mechanism is usually dissection. When closure follows balloon dilatation of an occlusion then

vessel recoil may be responsible. Acute thrombosis typically follows a primary mechanism that limits flow (Figure 11.1). Spasm of sufficient intensity to close a diseased iliac artery must be extremely rare.

Delayed closure

Closure of the treatment site within a few days either follows a technically imperfect primary treatment (a high-grade residual stenosis/dissection or misplacement of a stent) or results from poor run-off below the treated segment.

Rupture

Arterial rupture during balloon angioplasty is a potentially life-threatening complication but, fortunately, it occurs in only about 0.5% of cases.[5,6] In the BIAS II data set the rupture rate was 1.2% and entirely limited to stent placement. This is likely to be because stents will have been placed to manage complex disease such as iliac occlusions.

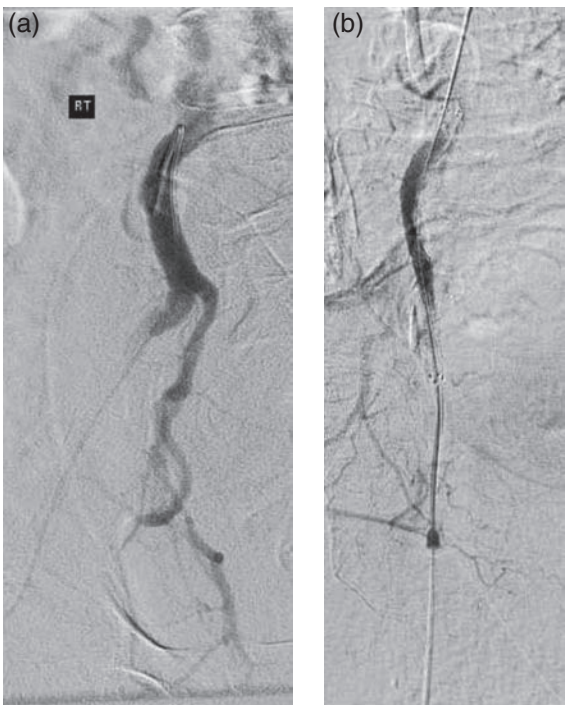

Figure 11.1 (a) Acute iliac occlusion during an attempted puncture reversal on a restless patient. (b) Immediate stenting failed to re-establish flow and the patient subsequently underwent surgery.

Stent infection

Since the publication of the first suspected infection associated with an endovascular stent by Chalmers et al,[7] the growing number of infections involving stent grafts represents an emerging problem. However, it still remains a very rare complication of simple stents placed in the iliac vessels. An international enquiry by Fiorani et al estimated the frequency of endograft infection to be about 0.4%.[8] This estimate is, however, in excess of our own experience. This report suggested that the development of endoprosthetic infection may be influenced by secondary adjunctive procedures, immunosuppression, treatment of false aneurysms, and infected central lines.

Embolization

Inadvertent embolization distal to the target vessel occurs in about 1–5% of procedures and is most frequent when there is attempted recanalization of occluded segments[9] (Figure 11.2). Within BIAS II this occurred as a complication of 1% of cases.[1]

Cholesterol embolization

Prolonged catheter manipulation in a diseased aorta can cause cholesterol plaques to gain entry into peripheral or visceral circulation. It is associated with a mortality rate of about 80% with poorly described and inadequate treatment options.[10] Its development is heralded by leg pain with livedo reticularis despite palpable pulses. Outcome is poor despite any active intervention often resulting in confusion, renal failure, and death.[11]

FACTORS IDENTIFYING HIGH-RISK PATIENTS

- Whilst there is considerable discussion amongst interventionalists about which factors result in high risk for endovascular intervention, there is little in the way of an evidence base.

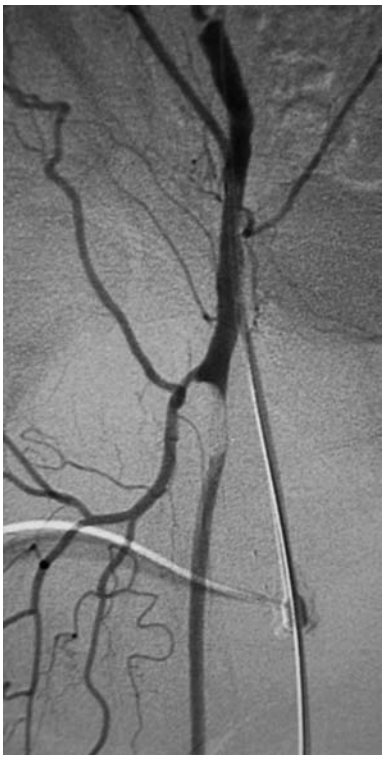

Figure 11.2 Distal embolus seen as filling defect at femoral artery bifurcation.

- Calcified lesions and tortuous anatomy make the procedure more technically demanding and possibly therefore more liable to complications due to overly zealous attempts by the interventionists.
- All plaques are ulcerated and therefore this is a poor discriminator.
- Occlusions rather than stenoses have long been identified as resulting in a high risk of distal embolization, particularly when the lesion is long (e.g. longer than 6 cm) and managed by angioplasty rather than stenting.
- Rupture is much more common following treatment of occlusions rather than stenosis.[1] This is possibly because frequently recanalization involves entering the 'subintimal' plane that has a thinner outer aspect compared to intraluminal recanalization. External iliac occlusions are at higher risk of rupture due to the poor adventitial support compared to the common iliac artery. Patients taking steroids may be at particularly high risk.[12]
- Diabetic patients are at increased risk of complications because of poor renal function, extensive disease, and poor distal run-off.
- Plaque prolapse is a difficult subject. It was once considered mandatory to treat ostial common iliac artery disease with kissing balloons or stents. This is unnecessary as the risk of plaque prolapsing across into the contralateral iliac artery is low and can be appropriately managed on the rare occasion that it is identified on the completion angiogram.[13] Occasionally plaque does protrude into the internal iliac artery, which is why in some institutions patients are warned against the risk of impotence.

COMPLICATIONS OF SPECIFIC INTERVENTIONAL STEPS AND TOOLS

Stenosis

Once access has been achieved from the ipsilateral groin the lesion is crossed with a guidewire. Hydrophilic wires in general are associated with a higher number of complications because they have less tactile feed-back, are more likely to lift plaque, pass subintimally, and cause inadvertent dissection. It is our practice therefore to initially use a straight wire directed by a curved (e.g. cobra) catheter. If this fails then we will use a hydrophilic wire.

We treat lesions with a non-compliant balloon whose size is matched to the diameter of the normal vessel. Oversizing the balloon runs the risk of arterial rupture. The experienced interventionist will usually 'eye-ball' the angiogram and estimate balloon size. If the interventionist is not experienced they should either ask, assess size from another imaging modality (e.g. graduated catheter angiogram, duplex, CT, etc.). Balloons should be inflated with a manometer since they all have a recommended burst pressure, and failure to recognize this makes the interventionist responsible for any complication following a burst balloon. Balloons tend to burst longitudinally and therefore without sequelae. Occasionally the balloon will burst circumferentially. This makes removal out of the sheath more difficult. In this situation it may be

necessary to increase the size of the sheath or even use a guide catheter to close the balloon if it cannot be brought to the groin from the site of rupture. Finally, surgery may be required.

Iliac stenoses are usually managed by angioplasty rather than stent placement. If a stent is chosen then consideration should be given to the type. Balloon-mounted stents are capable of precise placement and therefore we use them for disease that impinges on the aortic bifurcation so that we do not overhang the opposite common iliac artery. In addition, they can be quite short so that a focal lesion can be treated without covering the internal iliac artery. Self-expanding stents are more difficult to place precisely, but come as longer units and are flexible. For these reasons we tend to use them when managing tortuous, long segments.

Aortic stenoses are usually treated with kissing balloons since the long-term results are good, the stenosis often impinges upon the iliac vessels, and the long-term patency of kissing stents is in doubt. In addition, a single large balloon will extend down the iliac artery causing rupture unless the stenosis is a long distance from the aortic bifurcation. Stent placement is difficult in this area. Most self-expanding stents are not big enough for the aorta and some do not have the required radial force (e.g. Wallstent). Most balloon expandable stents are not large enough. Those that are (e.g. Palmaz Extra Large) require a single large balloon and are therefore impossible to place accurately when the stenosis is close to the aortic bifurcation. Stents in the aorto-iliac segment have their own complications:

1. The stent may not be placed across the stenosis. If this occurs then a second stent should be placed. There is usually little need to move the first stent.
2. If the stent covers the contralateral common iliac artery there are two solutions. Our preference is to simply place the patient on dual antiplatelet treatment to try to restrict platelet deposition on the exposed metal. Alternatively an attempt can be made to place a second stent in the contralateral iliac artery to hold the offending first stent off the orifice.
3. Most balloon-expandable stents do not move off the delivery balloon until after deployment. Should the stent move forwards then it may not be possible to pass a 5 Fr balloon back into the stent. This can be remedied by exchanging the 035" wire for a 018" or 016", passing a 3 Fr balloon catheter into the stent and dilating. If further dilatation is required this can then be done using a 5 Fr system.
4. If the partly expanded stent moves back off the balloon this is a more difficult situation. It may be possible to bring the balloon back into the stent and continue dilatation. If it is not we have either retrieved the balloon from the contralateral femoral artery using a snare and cutting the hub off the balloon, or passed a second 018" wire through the stent from the ipsilateral side and increased the diameter of the stent with a 3 Fr balloon.
5. Occasionally a self-expanding stent may restrict the retrieval of the delivery nose cone. Persistent jiggling may overcome this. If not, the outer delivery catheter can often be advanced up to the nose cone. Finally, the stent can be dilated by a second access followed by nose cone retrieval.

Occlusion

Occlusions have their own procedural complications in addition to those described for stenoses. Approximately 40% of occlusions are crossed from the ipsilateral side. Commonly the wire continues to pass subintimally in the aortic wall, but this is invariably without consequence. If ipsilateral recanalization fails then the wire loop (through-and-through) technique is required.[14] This technique requires that a wire is passed antegradely across the occlusion, usually from the contralateral groin. This wire often re-enters the channel formed by the first wire and the wire is then brought out through the ipsilateral groin and the occlusion treated from the ipsilateral side. However, occasionally this second channel remains independent and continues into the common femoral artery. We have elected in this situation to treat the iliac disease from the contralateral side and leave the re-entry site in the common femoral artery alone.

Distal embolization is more common if the occlusion is predilated. We therefore stent all lesions primarily, followed by postdilatation.

Occasionally left brachial artery access helps overcome technical difficulties related to aorto-iliac anatomy. Catheterization of the right brachial artery is undesirable because of the potential embolic complications up the carotid artery. Brachial artery occlusion after percutaneous placement of a 7 Fr sheath has been reported to occur in 1.3% of cases.[15] Limiting sheath size to 5–6 Fr may mitigate this problem. Absent or weak pulsations, brachial pressure differential, or other features suggestive of possible proximal arterial stenosis or occlusion contraindicate brachial artery catheterization. 'Blind' retrograde advancement of guidewire and catheter can also lead to arrhythmia or ventricular perforation from intracardiac entry and, therefore, continuous fluoroscopic visualization and guidance are mandatory. Caution should be exercised when applying tension on a brachial-femoral guidewire. A catheter should always be placed over the wire to protect the arch and proximal subclavian artery from the cheese-cutting effect of a tensed, rigid wire going across the aorto-subclavian junction.

METHODS TO DETECT COMPLICATIONS

The diagnosis of complications at the time of intervention requires a combination of clinical assessment and appropriate imaging.

Procedural complications

Clinically, most dissections are uneventful and do not require intervention. Occasionally the patient will complain of pelvic pain or the ipsilateral limb may become acutely ischemic. The diagnosis of dissection is usually made by a subsequent angiogram, although intravascular ultrasound (IVUS) can be helpful in difficult cases.

Rupture results in acute blood volume loss. Typically the patient experiences pain that persists after deflation of the balloon associated with hypotension. The pulse rate normally increases but occasionally the clinical picture may mimic a vagal episode with initial bradycardia. It is commonly noted that the retroperitoneal blood displaces the contrast-filled bladder to the contralateral side, and this can be clearly witnessed on fluoroscopy. The diagnosis can be confirmed by a quick angiogram following brisk resuscitation. Delayed rupture occasionally occurs. The clinical features are again those of acute blood loss and the diagnosis is best confirmed by emergency CT scan.

The diagnosis of embolization is made either by routine completion angiography or because the patient experiences ischemic pain on the table. Common impaction sites are where arterial lumen narrows abruptly, e.g. areas of pre-existing atherosclerosis, and branching sites such as the common femoral bifurcation and popliteal trifurcation.

Delayed complications

Following apparently uncomplicated intervention, patients are observed by nursing personnel. The period of bed rest depends on the sheath size, use of closure device, and status of access site. The patient's clinical condition is monitored for evidence of bleeding, including access-site hematoma, neurologic changes, and hypotension by following standard instructions.

Delayed closure at the treatment site may not necessarily result in an ischemic leg. If clinical examination confirms a weak or absent femoral pulse, and a decision has been made to intervene, then non-invasive imaging (usually US) will confirm the diagnosis.

The clinical manifestation of stent infection comprises localized pain, swelling, and erythema of the affected limb accompanied by relatively non-specific systemic symptoms like fever, generalized malaise, and abdominal or lumbar pain. Patients with aorto-enteric fistulas develop gastrointestinal bleeding. Blood culture and periprosthetic drainage fluid may reveal the offending organism, staphylococcus species being the most commonly implicated microbiological agent. CT is the imaging modality of choice and facilitates the aspiration of infected fluid for culture to confirm the diagnosis and to guide treatment. The role of MRI has yet to be clarified since, whilst it can distinguish hematoma from perigraft fluid and inflammatory changes in the postoperative cases, images may well be too badly

degraded by the presence of metallic stents.[16] Radionuclide studies such as technetium or indium labelled leucocyte scanning are highly sensitive but relatively non-specific, and are therefore usually reserved for those instances in which imaging studies do not confirm or exclude the diagnosis of infection.[17]

ENDOVASCULAR, SURGICAL, AND MEDICAL TECHNIQUES TO RESOLVE COMPLICATIONS

Some basic rules should be applied to limit the development of complications:

1. Interventionists should be trained appropriately, have sufficient work load to maintain competence, and continue with postgraduate education to justify their practice. Practitioners should be aware of their own and their unit's limitations.
2. Heparin immediately after arterial access will limit thrombosis on the catheters, wires, devices, and treatment site.
3. Balloons should be sized appropriately to avoid rupture.
4. Stents should be sized appropriately to avoid misplacement.
5. To limit embolization, iliac occlusions should be stented without predilatation.
6. The guidewire should not be removed across the lesion until a decision has been made to stop the procedure.
7. Pain during dilatation indicates that further stretching may result in rupture.

It is our practice to treat the specific complications in the following way.

Acute closure

- As indicated previously, the majority of acute closures of the treatment site are due to either recoil or dissection.
- The patient should be sufficiently anticoagulated so that fresh thrombus does not form at the closure site.
- Vessel recoil is simply managed by the placement of a stent in the usual manner.
- A small dissection flap is part of the angioplasty process and when there is no impediment to flow does not require treatment. A retrograde dissection formed by guidewire manipulation often does not impede flow and is not significant.
- Antegrade dissection is more harmful when blood flow keeps the false lumen open, resulting in a hemodynamic problem.
- If the dissection in the iliac vessels is flow limiting, it is best treated by a bolus of heparin to limit thrombus formation (e.g. 5000 IU) and immediate stent placement (Figure 11.3). Dissection may extend beyond the treatment site such that careful angiography is required to define the extent prior to stent placement.
- Basic good interventional technique requires that the interventionist maintains a guidewire across the treatment site until a decision to stop has been reached. By doing so there is always access to pursue further intervention or treat complications. If the guidewire has been removed before the dissection is discovered it can be very difficult to recross the dissection site because the wire often persistently tracks back into the false lumen. On this occasion the dissection may be best traversed from the contralateral limb. If the dissection involves the common femoral artery alone or in combination with iliac artery dissection then surgery may be required to completely resolve the problem.

Delayed closure

The degree of resulting ischemia will determine the nature and haste of intervention. If the patient has a white acutely ischemic limb then there is little time for thrombolysis and immediate surgical intervention is required. If the limb is acutely ischemic, but not white, and examination would indicate that immediate intervention is not required then immediate heparinization to limit clot formation with urgent endovascular intervention is reasonable. If the ipsilateral common femoral artery was patent on ultrasound then this should be used for access. Angiography will confirm an acutely occluded iliac segment and any fresh thrombus can be removed by aspiration, thrombolysis, mechanical thrombectomy, or balloon embolectomy. Once the offending lesion has been revealed this needs

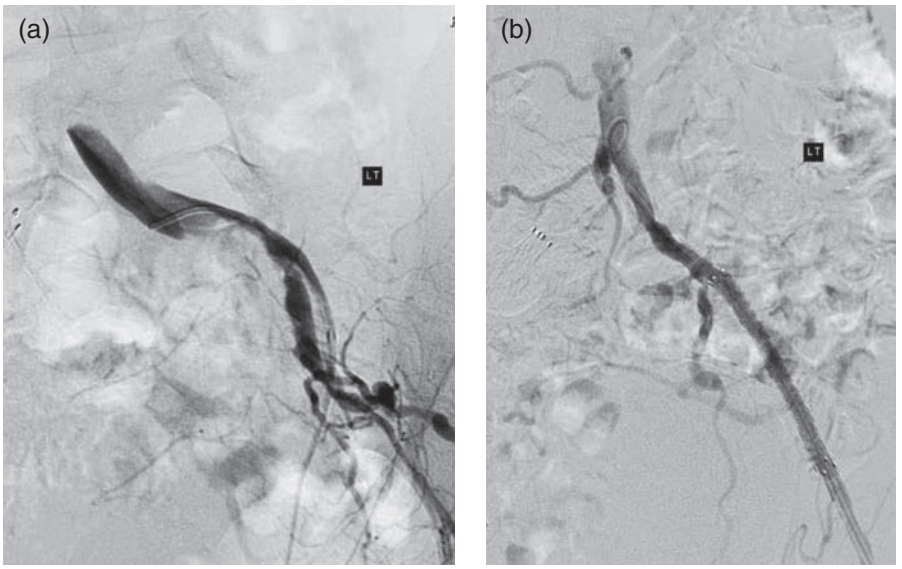

Figure 11.3 (a) Extensive dissection of the left iliac artery during a difficult femoral puncture. (b) Flow-limiting dissection has been successfully treated by insertion of a stent in the left external iliac artery.

appropriate intervention with either further balloon dilatation or stent placement. Some recent evidence would suggest that fresh occlusions may be treated by direct stent placement without the need to initially remove the thrombus.[18] If the ipsilateral common femoral artery is occluded on ultrasound thrombosis is likely to be extensive and further imaging should be obtained, either by angiography from the contralateral side or Computerised Tomographic Angiography (CTA)/Magnetic Resonance Angiography (MRA). The extent of thrombosis will then determine whether endovascular or conventional surgical revascularization is required.

If the patient is asymptomatic or a claudicant it may be unreasonable to immediately intervene given the risks of thrombolysis or embolization when dealing with fresh thrombus. In this situation we delay any further intervention for several months. This allows the thrombus to mature and then a clinical decision can be taken as to whether intervention is required.

Arterial rupture

This is a clinical emergency. Once the clinical diagnosis has been made the patient should have: (a) rapid blood volume replacement (crystalloid followed by colloid), (b) tamponade of the rupture by gently inflating a balloon across or proximal to the tear, (c) reversal of anticoagulation, (d) analgesia. Once the clinical picture is stabilized then a covered stent should be placed across the rupture site[19,20] (Figure 11.4). Our preference is for a self-expanding stent graft since it makes little sense to further increase the size of the hole by forcefully deploying a balloon-mounted stent.

Distal embolization

The decision as to whether to intervene depends upon the mode of presentation. If, for example, the embolization was found to affect a single tibial vessel leaving two patent crural arteries without any clinical features of acute ischemia it could reasonably be argued that no active intervention is required and the patient should simply be given 24 hours' anticoagulation to limit extension of the thrombus. If, however, the embolus resulted in acute ischemia then active intervention is required following immediate anticoagulation. The nature of intervention will depend upon the site of the embolus and local expertise. A common femoral embolus is easily removed surgically. We would treat more distal embolization by percutaneous aspiration thromboembolectomy,

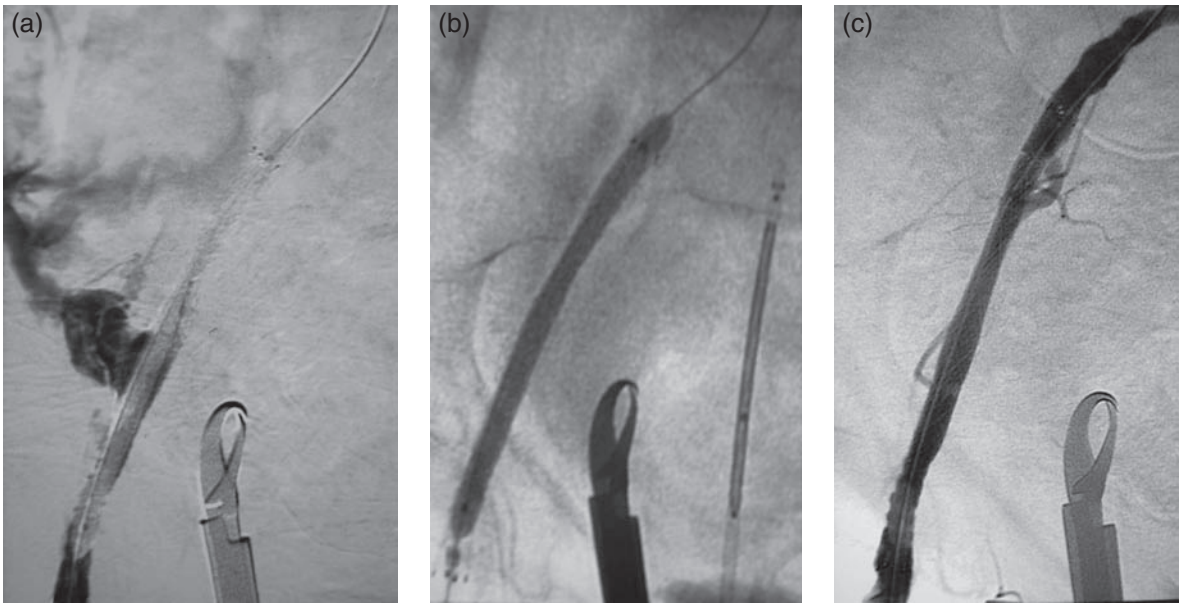

Figure 11.4 (a) Extravasation of contrast medium secondary to iliac rupture noticed immediately following placement of iliac stent. (b) Balloon tamponade whilst getting ready for placement of a covered stent. (c) Successful treatment of the rupture with a covered stent.

which has a 90% success rate.[21] Initially the puncture needs to be reversed into an antegrade position. Alternatively a separate puncture can be made, but this provides two large holes to subsequently bleed from. A large bolus of heparin is then given (5000–7500 IU) to restrict further thrombosis. A wide-bore single endhole catheter (typically a 7–9 Fr guide catheter) is then placed ipsilaterally and the embolus is removed by suction. A removable valve is useful in preventing the embolus from getting dislodged as it passes through the valve. If aspiration fails then we refer patients for surgical embolectomy because it is unlikely that thrombolysis will remove emboli consisting of plaque.

Stent infection

Until there are data to the contrary, it seems sensible that an artery infected by a foreign body requires removal. It is therefore our policy that patients receive antibiotics followed by appropriate surgery. The infrequency of this complication and the problems associated with the overuse of antibiotics in hospital practice mean that we do not routinely give antibiotic cover for simple iliac stent procedures.

CHECK LIST FOR EMERGENCY EQUIPMENT

Any responsible catheter laboratory performing intervention will have a range of balloons and stents to manage many of the complications detailed. In addition, there should be the equipment available that will salvage an acute limb or life-threatening complication. Such basics should include:

- resuscitation trolley with staff capable of using it
- covered stents Wallgraft™ (Boston Scientific) or Fluency™ (CR Bard, Inc, Murray Hill, NJ)
- thrombolytic agents and mechanical thrombectomy devices
- aspiration thromboembolectomy catheters (we recommend Cordis bright-tip 7–9 Fr guide catheters and removable hemostatic valves).

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Femoropopliteal segment

Richard R Heuser

Introduction to the frequency and type of complications • Factors identifying patients at high risk for complications • Complications of specific interventional steps and tools • Diagnostic methods to detect potential complications • Endovascular, surgical, and medical techniques to resolve complications • Methods to avoid complications • Summary • Check list for emergency equipment

INTRODUCTION TO THE FREQUENCY AND TYPE OF COMPLICATIONS

Peripheral arterial disease of the lower extremities affects approximately 8 million people in the United States, causing significant morbidity, such as claudication and pain during ambulation and, ultimately, insufficient perfusion of the distal extremities that may yield ischemic ulceration and gangrene. It is a marker for systemic arteriosclerosis, and mortality in patients with claudication is significantly higher than in controls.[1]

The superficial femoral artery (SFA) is the longest artery in the body and its geometry and elasticity are noticeably affected by the surrounding musculature and its mobility and location between two joints. Significant changes in arterial blood flow characteristics are seen in patients with peripheral arterial disease with respect to the span between the peak positive and negative blood flow velocity in the femoral artery[2] and, overall, the SFA's structural and functional properties predispose it to arteriosclerosis, calcification, and ulceration, and the development of fibrous plaques and local thrombus.[3]

Initial management of patients with peripheral arterial disease includes relief of symptoms and reduction in cardiovascular risk factors and may involve antiplatelet therapy, exercise, smoking cessation, and treatment of diabetes, hyperlipidemia, and hypertension. When medical interventions fail to ameliorate symptoms, endovascular therapy is often considered a first line of defense. Indeed, minimally invasive therapies have become established techniques for treating vascular disease; initially with the widespread application of balloon angioplasty,[4] and followed by the introduction of peripheral stents[5] and atherectomy techniques.[6]

Standard angioplasty techniques have been in use for decades, but they are generally more appropriate in the iliac vessels – where there is good distal run-off, and lesions are usually stenotic rather than occlusive. The difficulty in negotiating femoropopliteal lesions and the potential for embolic consequences has kept many away from more distal territory. Balloon angioplasty is a controlled injury to the vessel wall, causing rupture and dissection of plaque, partial dissection of the intima and media, and overstretching of the vessel wall. The intrinsic coagulation pathway is activated, and platelet adhesion and thrombus formation are encouraged; if fibroblasts continue to form intercellular matrices, intimal hyperplasia continues unabated.[7]

The femoropopliteal segment is fairly straight and in general side branches are not relevant except for the deep femoral artery. The deep femoral artery's importance in maintaining viable circulation to the leg cannot be underestimated. Compromise of the deep femoral artery can result

in a true medical emergency in patients presenting with severe symptoms of critical limb ischemia. This problem can be obviated by either the use of atherectomy devices or a kissing balloon technique at the site of the common femoral and deep femoral junction. Embolization also occurs in this patient population, but it is underrecognized and by the time it is recognized either large particles have already been expelled or there is the blue toe syndrome. Some investigators working in this region have suggested using embolic protection devices, but this has not been widely embraced clinically.

Endovascular stents were introduced to prevent residual stenosis, elastic recoil, and flow-limiting arterial dissection following balloon angioplasty. Initial reports of stenting for occlusive atherosclerotic disease in the femoropopliteal segment were encouraging, with primary and secondary patency rates of ~90% at 18 months.[8] Unfortunately, intimal hyperplasia and in-stent restenosis have since proven to be significant problems affecting long-term patency.[9] One of the problems in stenting in the superficial femoral and popliteal region is that with movement in the leg, there is external compression of the stent which can result in fracture, restenosis, or in some cases late thrombosis. While the TransAtlantic Inter-Society Consensus (TASC) recommendations for femoropopliteal stent placement do not indicate it should be a primary approach to the interventional treatment of intermittent claudication,[10] percutaneous stent placement into femoropopliteal arteries has become a widely accepted therapeutic strategy when angioplasty fails due to residual stenosis or dissection.

FACTORS IDENTIFYING PATIENTS AT HIGH RISK FOR COMPLICATIONS

In general, it appears the risk factors for development of peripheral arterial disease mirror those that affect the success of treatment. In a recent study, male gender, diabetes mellitus, and chronic renal failure were significant independent risk factors for distal (rather than proximal) lower extremity arterial vascular disease, with hypertension nearing statistical significance ($p = 0.06$).[11] Accordingly, patients with diabetes have a higher rate of in-stent restenosis following endovascular procedures,[12] and diastolic hypertension and the percent stenosis may predict immediate angioplasty failure.[13] In another more recent study, however, hypercholesterolemia was less prevalent in patients with lesions below the knee and there was no distinct association with arterial hypertension.[14] While cigarette smoking has long been associated with risk for peripheral arteriosclerosis[15,16] and with vessel occlusion after deliberate extraluminal recanalization,[17] one study indicated that smoking 10 or more cigarettes daily was associated with a reduced rate of intermediate-term restenosis after lower-limb endovascular interventions.[18] Presenting symptoms – whether the patient had simple claudication or critical ischemia – also predict the success of intervention, with poorer outcomes in severely ischemic patients.

Immediate causes of interventional failure include intimal dissection, elastic recoil of the vessel wall, and arterial rupture. Predictors of early clinical failure are advanced age, SFA occlusion, and the presence of residual stenosis, dissection, or occlusion. Many factors adversely affect mid- to long-term patency, including type of lesion, and length of lesion.[19–22] In general, stenoses are associated with better patency than occlusions; thrombosis of total occlusions is not uncommon and usually occurs within hours of the procedure. As a rule, focal stenoses are easier to treat than long-segment lesions. In addition, treatment of concentric lesions is often more successful than that of eccentric lesions. Overall, poor distal runoff correlates with worse outcomes. The absence of calcification, dissection, or plaque rupture as judged by intravascular ultrasound, and a residual stenosis of less than 30%, is associated with improved outcomes.[23] Restenosis due to intimal hyperplasia and progression of atherosclerosis are the most common causes of late failures.

COMPLICATIONS OF SPECIFIC INTERVENTIONAL STEPS AND TOOLS

Endovascular procedures have many advantages over open surgery – they can be performed under local anesthesia, are generally well tolerated by the patient, and are usually associated with fewer complications and shorter hospitalization and recovery periods than surgery – but the risks of

minimally invasive procedures include embolization, dissection, thrombosis, perforation, bleeding, atherosclerotic stenosis and occlusion, and aneurysm and arteriovenous fistula development.

Imaging

While advances in preoperative imaging modalities such as magnetic resonance imaging (MRA) and duplex ultrasound arterial mapping are impressive, their superiority over contrast angiography has not been clearly demonstrated. In particular, the use of MRA in the infrapopliteal segment resulted in both false negatives and false positives, and duplex exams were inadequate when low flow or severe arterial calcifications were identified.[24] As such, angiography is used to define the disease distribution. Most angiography is performed with iodinated contrast agents, and low-osmolar agents are often used in peripheral arterial studies to minimize discomfort. These agents carry a low risk of allergic reaction and volume overload; however, renal toxicity varies according to patient characteristics, and those with renal insufficiency may require alternative contrast.

Puncture site

Catheter-based angiography of the arterial system is generally performed via the common femoral artery. Interventionists involved with treating superficial femoral, deep femoral, or popliteal disease, or below, should be widely familiar with the antegrade approach. The antegrade approach can be difficult in obese patients and also can be difficult with an inexperienced operator. Complications that can occur with antegrade passage can be dissection, retroperitoneal hematoma, as well as a possibility of an AV fistula or pseudoaneurysm following the procedure. The contralateral approach is also an excellent and safe approach in treating patients with SFA or popliteal disease; however, this can be difficult when a patient has a very tortuous aorto-iliac junction or if the patient is status postendoluminal grafting. The radial approach in patients with femoral and popliteal disease is difficult, not because of technique but because of the lack of availability of long catheters, stents, etc.

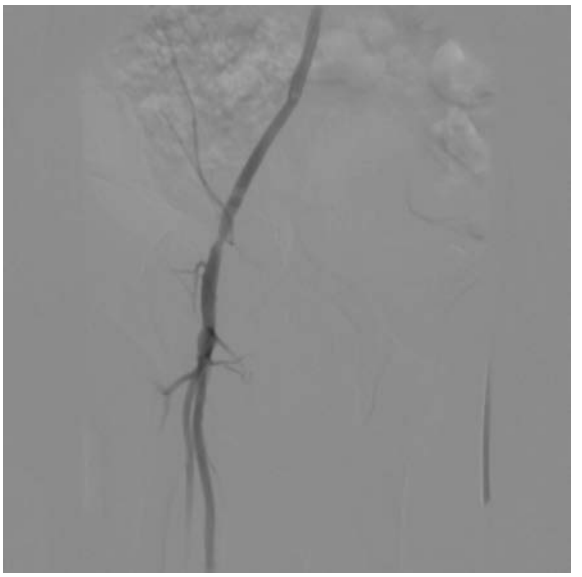

Figure 12.1 This arteriogram of the right iliac and femoral artery depicts the stenosis in the right common femoral artery at the site of previous closure.

Experience with the popliteal puncture technique is essential when performing interventions in this segment. Our experience with the popliteal approach is to direct the needle by a contralateral small catheter injection with roadmapping techniques. This technique makes it possible for us to have less likelihood of hematoma, dissection, etc. as we place the sheath. The risks of the technique include serious puncture site complications and, since the deep or superficial femoral artery lacks this bony support, hemostasis may be difficult to achieve during arterial compression after catheter removal if the puncture site is distal to the common femoral artery (Figure 12.1). Figure 12.2 shows the same vessel after treatment with an atherectomy device (SilverHawk™, Foxhollow Technologies, Redwood City, CA); the patient's ankle brachial indices (ABIs) improved from 0.68 to 1.02.

Wire passage

Passage of wires into the infrapopliteal region may initiate spasm and subsequent thrombosis in these small, sensitive vessels. Multiple lesions should be approached in a distal-to-proximal fashion.

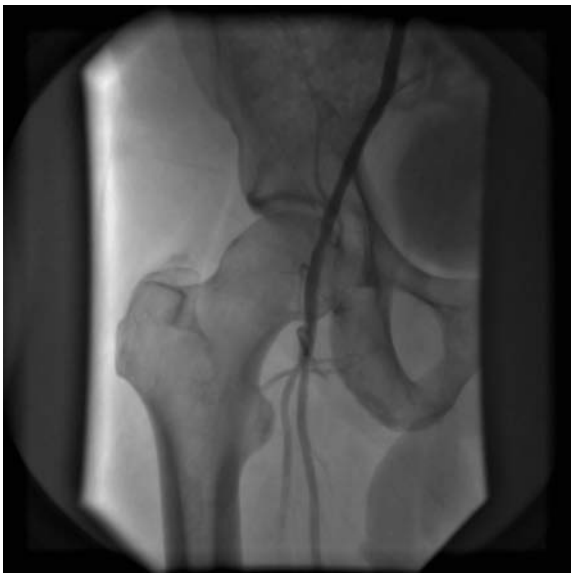

Figure 12.2 This is the same vessel as in Figure 12.1 after treatment with the SilverHawk™ (Foxhollow) atherectomy device. Note the improvement in the stenosis; the patient's ABIs went from 0.68 to 1.02.

Ballooning/stenting

We still minimize stent usage in the infrapopliteal region. Overinflation may be associated with rupture of the balloon catheter, while the use of oversized balloons relative to the reference segment may also cause injury to the vessel wall. *Abrupt closure is commonly caused by dissection from balloon angioplasty with superimposed thrombosis. It occurred in 2–4% of cases with balloon angioplasty in the prestent era.* Clinical features associated with increased risk of abrupt closure include diabetes mellitus, female gender, inadequate antiplatelet therapy, and advanced age. Long lesions, total occlusions, and the presence of multivessel disease may also increase the risk of abrupt closure. Signs and symptoms include pain, pallor, pulselessness, paresthesias, and coldness of the extremity, and are similar to those seen with stent thrombosis.

Appropriate stent sizing is imperative to the success of the procedures. When a stent is too small, migration of the device can occur from the proximal segment of the SFA into the common femoral artery. Distal embolization is another complication that may be stent-related or produced by the balloon angioplasty procedure. In some cases, distal embolization may be treated by thrombectomy alone; however, thrombolytic management may also be appropriate. Contraindications to thrombolysis include recent neurologic, thoracic, or abdominal surgery, recent stroke, evidence of active gastrointestinal or genitourinary bleeding, central nervous system metastatic disease, and bleeding diathesis.

The superficial course of the artery and crossing of flexion points exposes the superficial femoral and popliteal arteries to relevant biomechanical forces, including compression, torsion, and elongation, which may result in stent fracture. Multiple stent deployment and stent overlap carry a higher risk of fracture and should be avoided. The problem was minimized with the advent of self-expanding nitinol stents. Finally, the impact of fracture on long-term patency of the stent has varied among studies, and is not very well defined yet.

Other devices

Atherectomy/debulking

Atherectomy and debulking techniques may improve outcome, but the risks of dissection, embolic debris, and distal embolization are notable.[25,26] Likewise, mechanical thrombectomy devices may introduce similar complications due to embolic debris.[27]

Cryoplasty

Cryoplasty has been used to administer a cold-induced injury to inhibit restenosis. Complications during such procedures are uncommon, but patients who undergo successful cryoplasty should still be monitored carefully following the procedure. Signs of complications may include severe leg pain, pallor, and absent pulses in the popliteal artery and dorsalis pedis. An angiogram can demonstrate problems such as abrupt closure of the SFA, spasm, dissection, or embolism.

Laser

Early laser interventions were plagued by complications resulting from thermal damage to surrounding tissue. Today, the use of 'cool' tip lasers has limited such problems. However, procedural complications still include acute re-occlusion, perforation, and embolization.[28]

DIAGNOSTIC METHODS TO DETECT POTENTIAL COMPLICATIONS

Physical exam

The physical exam should include evaluation of femoral-popliteal pulses and palpation of the posterior tibial vessels and dorsalis pedis. The measurement of ABI is also critical.

Imaging

Although contrast arteriography remains the gold standard for evaluation of patients undergoing lower extremity revascularization,[24] recurrent lesions are often readily detected by duplex ultrasonography. Magnetic resonance angiography (MRA), computed tomography (CT), and angiography may also be useful.

ENDOVASCULAR, SURGICAL, AND MEDICAL TECHNIQUES TO RESOLVE COMPLICATIONS

Thrombolysis/aspiration

When abrupt closure and/or stent thrombosis is detected, angiography via contralateral access is performed to determine the site and flow is reestablished using one or more of the following approaches: selective thrombolysis below the access site, mechanical thrombectomy, and/or suction thrombectomy. In some patients, administration of a thrombolytic via an infusion catheter may not be successful in restoring adequate flow, and the patient may continue to have severe symptoms. Ultimately, femoropopliteal bypass surgery is sometimes necessary when the deep femoral artery and common femoral artery are affected.

Stent migration

When stent migration is detected, usually via Doppler and angiography, a nitinol snare may be introduced from a contralateral femoral approach to retrieve a misplaced stent.

Coil embolization

Coil embolization is rarely, if ever, indicated in femoral popliteal intervention. In emergent situations, such as a bleed or rupture, these complications are usually treated by prolonged balloon inflation or the use of a covered stent (Figures 12.3 and 12.4).

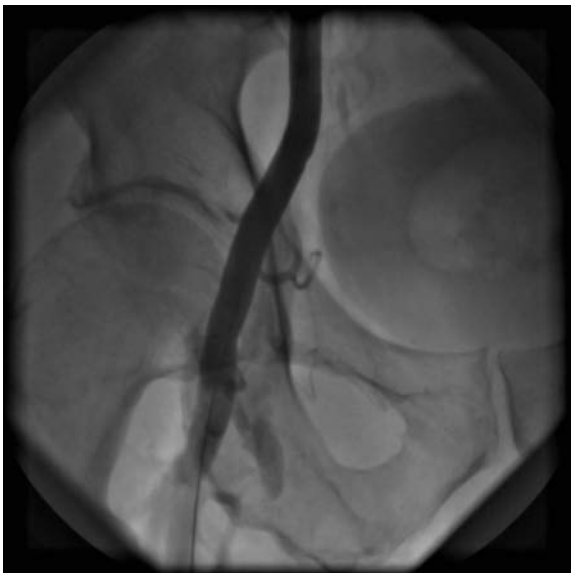

Figure 12.3 This arteriogram illustrates a right common femoral arteriovenous fistula in a patient who had undergone multiple coronary interventions in the past. The patient presented with a loud right femoral bruit and mild claudication with normal ABIs.

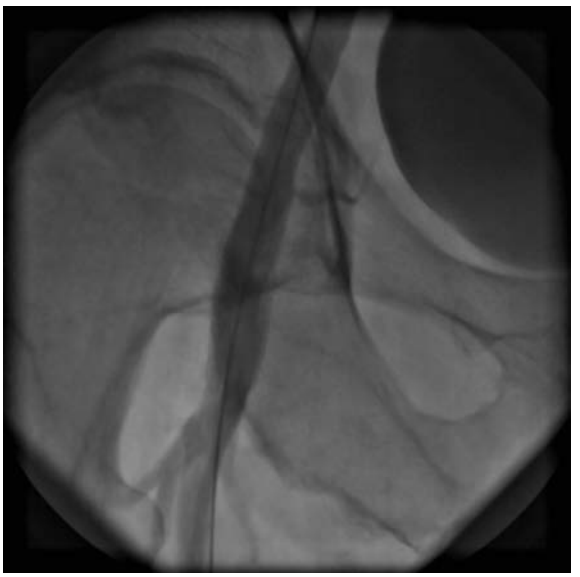

Figure 12.4 The arteriovenous fistula was treated successfully with a Hemobahn covered stent (WL Gore and Associates, Flagstaff AZ).

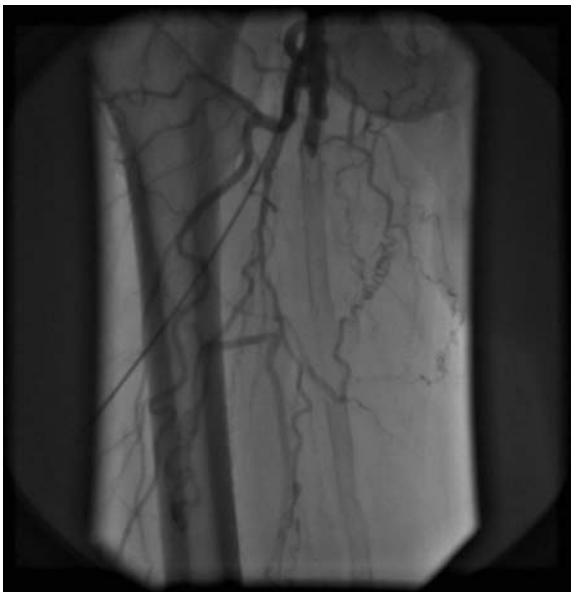

Figure 12.5 This arteriogram of the left common femoral artery and bifurcation delineates a patient with a limb at risk. Note the thrombotic occlusion at the bifurcation of the deep femoral artery. This patient will need immediate revascularization, either percutaneously or via open surgery, otherwise, he will likely lose at least part of his limb.

Surgical intervention

Surgical intervention is indicated when the limb is threatened, and further endovascular intervention is not possible (Figure 12.5).

METHODS TO AVOID COMPLICATIONS

Imaging

Renal toxicity varies according to patient characteristics (renal status, presence of diabetes); those with renal insufficiency may require alternative contrast. Digital imaging may allow smaller amounts of contrast material to be used and reduction in the radiation exposure needed for each image. The use of the subtraction technique with digital imaging may further improve the contrast resolution. Nevertheless, multiple angiographic views are often required to show the severity of a stenosis, and the measurement of translesional pressure gradients and the use of intravascular ultrasound may be helpful adjuncts. Recently, duplex-guided balloon angioplasty has been described as a safe and effective technique for renal patients that allows direct visualization of the puncture site, accurate selection of the proper size of balloon and stent, confirmation of the adequacy of the technique by hemodynamic and imaging parameters, and avoidance of radiation.[29]

Approach

When treating lesions below the inguinal ligament, a contralateral retrograde or an ipsilateral antegrade access may be used. The contralateral approach is often preferable because it avoids potential complications such as dissection or hematoma formation that are sometimes seen with the ipsilateral antegrade approach; also the antegrade approach is awkward and technically challenging for most catheterization labs. The radial approach, though generally easier to perform, is somewhat restrictive because many balloons, atherectomy devices, and stents are simply too short. Multiple lesions should be treated in a distal-to-proximal fashion.

Stent choice

Although balloon-expandable stents provide accurate sizing, self-expanding stents are preferred in the femoropopliteal region because of their flexibility and resistance to external forces in superficial locations. Substantial flexing, such as that occurring at a joint, may lead to compression or kinking; using the shortest device possible may help avoid complications. The use of self-expanding nitinol stents appears to improve patency.[30,31] Stent compression and fracture, though reduced with self-expanding nitinol stents, are still risks when treating long lesions[32] (Figures 12.6–12.9).

The use of coil-shaped stents inside the treated vessel may reduce local trauma by limiting the area of the arterial wall covered by the stent, and self-expandable coil stents are often suitable for tortuous arteries and lesions of the femoral or popliteal artery situated at flexion points or at locations that may be subjected to external compression. Despite these merits, coil stents are not

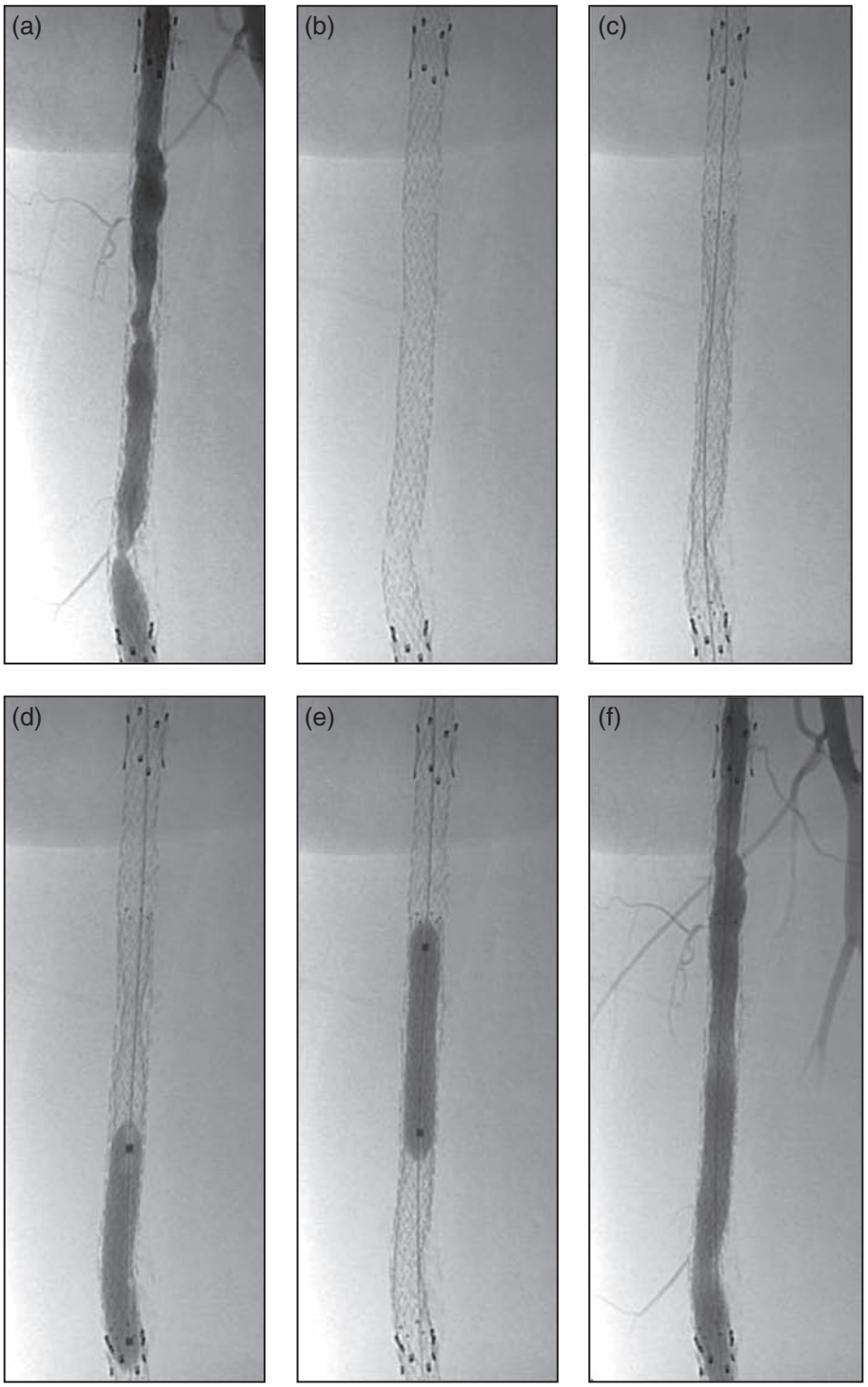

Figure 12.6 (a) The angiogram shows multiple in-stent restenosis. (b) The native frame indicates that the stenoses are correlated to stent fractures. (c) After in-stent placement of a nitinol stent, and focal post-dilation with a 6/20 mm balloon (d–f), a good angiographic result could be achieved. From Heuser and Biamino, eds. Peripheral Vascular Stenting. London: Taylor & Francis, 2005.

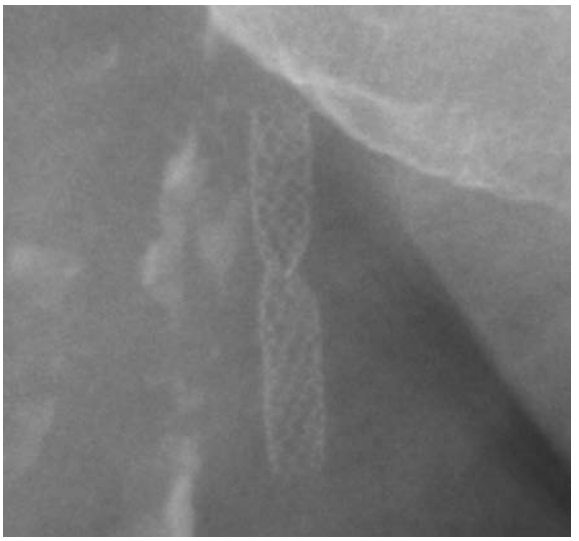

Figure 12.7 Balloon-expandable stent deformed by flexion at the groin. From Heuser and Henry, eds. Textbook of Peripheral Vascular Interventions. London: Martin Dunitz, 2004.

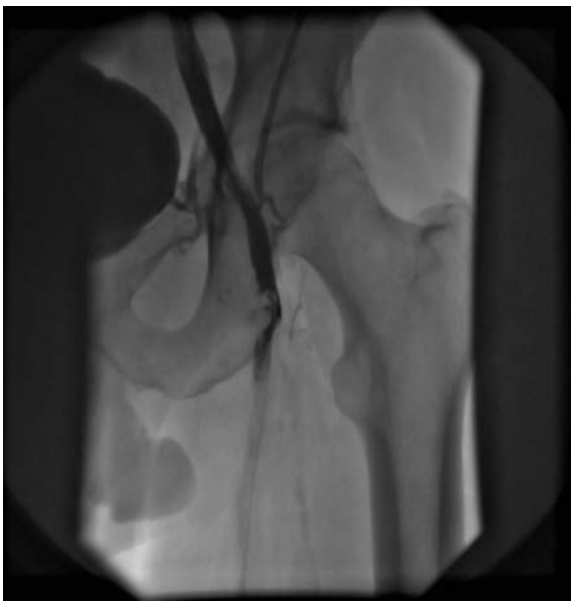

Figure 12.9 This arteriogram illustrates a common problem in patients treated with femoral stents for a long occlusion in the SFA. New technology may reduce the re-occlusion rate in these patients.

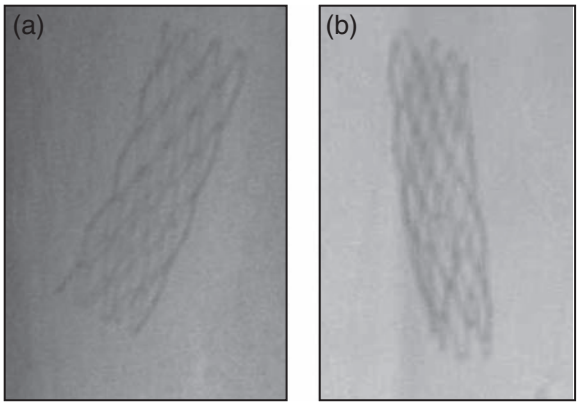

Figure 12.8 (a) Thrombosed Palmaz® stent in the superficial femoral artery. (b) A different angle shows the presence of pressure deformity of the stent. From Heuser and Henry, eds. Textbook of Peripheral Vascular Interventions. London: Martin Dunitz, 2004.

appropriate in heavily calcified and eccentric lesions; conventional balloon-expandable stents may still be preferable in these cases. Some interventionists use coronary drug eluting in the infrapopliteal region. In most cases, these stents can still thrombose and, because of their lack of adequate tensile strength, may be compressed; the use of such stents in this region is still highly controversial and, as yet, investigational.

Prevention of stent thrombosis/distal embolization

The vascular biological response to stent placement in the peripheral circulation may be similar to that in the coronary circulation and, thus, the same antiplatelet regimens used in the coronary vessels are used in peripheral vascular stenting. Clopidogrel has replaced ticlopidine as a drug to prevent stent thrombosis in most centers because it is more easily administered and is generally considered to have a safer hematologic profile. We currently prescribe 4 weeks of clopidogrel following superficial femoral artery stenting, and aspirin is continued indefinitely.

Embolic protection devices have been used for some time in percutaneous interventions in the coronary and carotid arteries. More recently, filter and balloon occlusion devices have been used in

the femoral and popliteal arteries to capture dislodged thromboembolic material during angioplasty and stenting procedures placement – early results ($n = 5$) indicate no apparent difficulties in placing the devices and that all devices were retrieved with substantial debris.[26] Additional study of both filter-type and balloon occlusion devices appears warranted.

Prevention of restenosis

It has been suggested that debulking of lesions may enhance patency, and atherectomy and endovascular endarterectomy have been used in an attempt to improve outcomes (as seen previously in Figures 12.1 and 12.2). The SilverHawk™ coaxial system incorporating cutting and storage chambers (Foxhollow Technologies) has been studied in a registry, and there are early reports of success in debulking short- and medium-length femoropopliteal lesions.[33] However, while the device's debulking capabilities are not at issue, at least one investigative group urges caution, citing a notable risk of dissection, embolic debris, and distal embolization.[26] Results with a mechanical thrombectomy device (Rotarex, Straub Medical, Wangs, Germany) have also been reported, indicating successful treatment of acute, subacute, or chronic peripheral arterial thromboembolic occlusions.[27] However, the investigators caution the device is not recommended for use in heavily calcified lesions, and note that distal embolizations occurred in 10 of 48 patients; six clinically relevant emboli required aspiration in this series.

Medical therapies aimed at interrupting or inhibiting intimal hyperplasia include heparin, low-molecular-weight heparin, aspirin, corticoids, angiotensin-converting enzyme inhibitors, vascular endothelial growth factor, cyclosporin, and other agents. Use of preprocedural aspirin has been shown to reduce abrupt closure during intervention. Traditionally, unfractionated heparin has been used to prevent thrombotic complications in peripheral interventions, but the level of activated clotting time is not well defined. Generally, a level of greater than 300 seconds in the absence of a IIb/IIIa inhibitor has been adopted in most centers. The effects of adjunctive administration of abciximab have been reported to have a favorable effect on patency and clinical outcome in patients undergoing complex femoropopliteal catheter interventions with treatment effects of abciximab maintained at 6-month follow-up in one study.[34] Observational studies with the direct thrombin inhibitor, bivalarudin, indicate that it is safe, effective, and might offer some advantages over heparin such as early sheath removal and possibly a lower major bleeding rate.[35]

The sirolimus-eluting stent (Cordis Endovascular, Miami Lakes, FL) was studied in the SIROCCO trials – most recently, investigators reported a trend for greater efficacy in the sirolimus-eluting stent group but there were no statistically significant differences in any of the variables between the bare and sirolimus-eluting stent groups.

Laser-assisted angioplasty has been shown to be useful in recanalizing long SFA occlusions; however, maintaining patency and quality of life has been reported to require intensive surveillance and prompt repeat intervention.[36] Steinkamp and colleagues[37] noted that, while initial recanalization was more successful with laser-assisted angioplasty, it did not appear to add any long-term benefit over balloon dilatation alone. More recently, a review of data from the Laser Angioplasty for Critical Limb Ischemia (LACI) phase 1 and 2 trials suggests excimer laser-assisted angioplasty is a viable treatment strategy for patients with critical limb ischemia who are otherwise not good candidates for bypass surgery and have limited options for other treatment.[28]

Endovascular radiotherapy in the endolumen of the femoropopliteal segment following percutaneous transluminal angioplasty has been reported to prevent intimal hyperplasia in femoropopliteal arteries and improve patency in some studies.[38,39] While these improvements in patency rates after brachytherapy are encouraging, further study indicated endovascular brachytherapy did not diminish early vascular inflammation in response to angioplasty or stent implantation, and even induced a trend toward an increased inflammatory response; the investigators concluded reduced rates of restenosis after brachytherapy cannot be explained by an anti-inflammatory radiation effect.[40] More recently, it has been reported that while there

appear to be positive short-term effects of adjunctive endovascular brachytherapy, these are not sustained in the longer term and there is no substantial clinical improvement in de novo or recurrent femoropopliteal lesions at up to 5 years.[41]

Cryoplasty incorporates conventional balloon angioplasty and the currently available device (CryoVascular Systems, Los Gatos, CA) uses a double balloon that administers a cold-induced injury at 6–8 atm of pressure. In a total of 102 patients (of whom 31% were each diabetic and active cigarette smokers), the technical success rate was 85.3% with a mean residual stenosis after cryoplasty of 11.2% ± 11.2% ($p < 0.05$ vs baseline). Clinical patency in this group was >80% during the 9-month surveillance period; primary patency determined by duplex US was 70.1%.[42]

While results in the femoropopliteal region are not yet available, intracoronary sonotherapy following angioplasty has been performed using serial ultrasound transducers operating at 1 MHz. Sonotherapy was applied safely and with high acute procedural success, but late lumen loss and neointimal growth were similar to conventional PTCA approaches.[43]

Photodynamic therapy using up to 50 J/cm^2 red light (635 nm) was delivered to the angioplasty site via a laser fiber within the balloon in 7 patients who had previously undergone conventional angioplasty at the same site and had symptomatic restenosis or occlusion between 2 and 6 months.[44] Outcome by duplex imaging indicated the median (interquartile range) peak systolic velocity ratio across stenotic segments was 4.7 (3.7–5.7) before angioplasty and 1.4 (1.0–1.8) at 6 months after intervention ($p = 0.04$) in this small group. At a mean of 48 months, none of the patients had critical limb ischemia or ulceration and there were no arterial complications; one developed mild, non-limiting claudication 18 months after photodynamic therapy.[45]

SUMMARY

Peripheral arterial disease is a common malady in aging populations that causes significant morbidity. The structural and functional properties of the distal arteries predispose them to arteriosclerosis, calcification, and ulceration, and when risk factor modification and medical intervention fail to improve symptoms of claudication and/or ischemia, endovascular therapy is often considered. Although the TASC recommendations for femoropopliteal stent placement do not indicate it should be a primary approach to the interventional treatment of intermittent claudication, stent placement for femoropopliteal arterial disease is widely accepted to prevent residual stenosis, elastic recoil, and flow-limiting arterial dissection following balloon angioplasty. Stent procedures have many advantages over open surgery as they employ local anesthesia, are generally well tolerated, and result in shorter hospitalization and recovery periods. Nevertheless, risks of minimally invasive procedures include embolization, dissection, thrombosis, perforation, bleeding, atherosclerotic stenosis and occlusion, and aneurysm and arteriovenous fistula development.

One of the questions many interventionists have is when is it time to stop. In other words, when you have a dissection or a complication when is the best time to decide to go back and treat the patient at another time or consider referral to surgery. It has been our experience in the antegrade approach or the contralateral approach to the SFA when the vessel is totally occluded or has a complex stenosis, that if there is a significant dissection that is not flow limiting or compromising the deep femoral artery and we have been working to try to enter the true lumen for a significant amount of time, this might be the time to abandon the procedure. This patient might be best served by coming back; the procedure can then be attempted via the popliteal approach to more effectively treat this complicated lesion. We found this approach results in less radiation, less risk to the patient, and a higher degree of success. This may also be a time to share with a vascular surgical colleague the consideration for the surgical approach or perhaps consider a referral to a more experienced interventionist. This would particularly be the case with a thrombotic, calcific, or very resistant lesion. Some interventionists will consider bypass on a younger patient with this histopathology, particularly when there appears to be adequate run-off and the vessel is occluded over a long distance or heavily calcified.

Proper patient selection and appropriate imaging and selection of devices and adjuvant therapies are important determinants of the success of percutaneous interventions. Contrast arteriography remains the gold standard for evaluation of patients undergoing lower extremity revascularization, and self-expanding stents are preferred in the femoropopliteal region because of their flexibility and resistance to external forces in superficial locations. Medical therapy that limits the potential for embolization and thrombosis is an important adjunct, and embolic protection devices are beginning to be used in the femoral and popliteal arteries to capture dislodged thromboembolic material during procedures. Prevention and treatment of restenosis, which is by far the most common complication of percutaneous interventions, currently includes the use of a variety of adjunctive therapies, including drug-eluting stents, local antiproliferative drugs given intraprocedurally, sonotherapy, photodynamic angioplasty, radiation therapy, and cryoplasty. Most of these treatments are in the relatively early stages of development and testing, and it is not yet clear whether lasting protection against restenotic lesions will be afforded. At present, clinicians frequently rely on more than one mode of therapy to treat critical ischemia and reduce the need for amputation in patients with arterial disease in the femoropopliteal segment.

Overall, the interventionist considering endovascular intervention in the femoropopliteal region must be comfortable using contralateral and popliteal approaches and an antegrade stick technique. In addition, he or she must have experience removing emboli and be skilled using a variety of wires, stents, and snares; filter device experience may be useful as well. A close relationship with a vascular surgeon is essential in managing complications such as vascular dissection and perforation.

CHECK LIST FOR EMERGENCY EQUIPMENT

Emergency equipment that should be available for work in the femoral popliteal area include the availability of coils for perforations, covered stents, and an open mind to be able to think on your feet. Sometimes interventionists let their ego get in the way, but a thoughtful approach with the consideration of the patient first is always an important policy.

- covered stent
- coils
- aspiration thrombectomy catheter
- snares
- thrombolytics.

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Complications of tibioperoneal interventions

Erich Minar and Lanfroi Graziani

Introduction to the frequency and type of complications with tibioperoneal interventions • Factors identifying patients at high risk for complications • Complications of specific interventional steps and tools • Methods to detect potential complications • Techniques to resolve complications • Methods to avoid complications • Summary • Check list for emergency equipment for interventions in this specific vessel area

INTRODUCTION TO THE FREQUENCY AND TYPE OF COMPLICATIONS WITH TIBIOPERONEAL INTERVENTIONS

Until recently, scepticism was often expressed concerning the feasibility, effectiveness, and long-term results of catheter revascularization for treatment of infrapopliteal disease. Furthermore, endovascular interventions of the tibial arteries are often viewed as high risk and prone to failure, with fear of enduring the consequences of a limb-threatening complication. Therefore the accepted indication for below-knee endovascular interventions remains primarily the treatment of critical or limb-threatening ischemia,[1] while isolated infrapopliteal endovascular intervention is rarely indicated in patients with intermittent claudication.[2] An additional important indication for below-knee angioplasty is to improve run-off and subsequent long-term patency after femoropopliteal angioplasty/stenting or bypass grafting.

Patients with critical limb ischemia often have multilevel disease with multiple lesions also in the crural vessels, with the consequence of technically demanding surgical procedures requiring femorodistal and even pedal bypasses with a perioperative mortality rate of up to 6% in these mostly high-risk patients.[3] The risks of surgery have led together with the improved technology and the growing literature demonstrating the efficacy of endovascular treatment for critical limb ischemia (CLI) to a steadily increasing application also in the infrapopliteal arteries. However, experience of the interventionalist is even more important than in other regions of the lower leg arteries, and the infrapopliteal vascular bed should definitely not be approached by the novice endovascular interventionalist.

Patients with CLI are usually older than average, have an increased prevalence of diabetes, and often have associated advanced cardiac and cerebrovascular disease. Patients with infrapopliteal lesions alone or in conjunction with femoropopliteal disease are amongst those with the highest likelihood of coronary heart disease. Furthermore, these patients usually have a lot of comorbidities, identifying them as high-risk patients. The natural history of patients with rest pain alone carries a 5-year mortality rate of about 50%.

In general, the rate of complications reported in the literature for infrapopliteal endovascular interventions is astonishingly low concerning these mainly high-risk patients. This may be due

to a rather restrictive indication in the past and to the fact that – because of the fear of limb-threatening complications – in most institutions these interventions have been performed by the most experienced physician.

Complications are reported to occur in 2–6% of cases, and in most series complications at the access site are the most common.[1,4–10] The mortality rate is very low and mainly due to the cardiovascular comorbidity. In the study by Soder et al,[4] the mortality rate after infrapopliteal balloon angioplasty was 1.8%, comparing favorably to the mostly higher perioperative mortality rate for distal bypass surgery. Dorros et al[6] studied a consecutive series of 284 patients treated for critical limb ischemia. They observed 2 (0.7%) in-hospital deaths, and 1 (0.4%) was procedurally related. Emergency vascular surgery became necessary in 3 patients (1%).

Another typical complication is development of transient contrast-induced acute renal failure, due to the high prevalence of diabetes in these patients. In the series of Dorros et al,[6] 20 patients (7%) developed this complication.

Arterial occlusions may occur due to dissection, spasm, or distal embolization. However, the reported incidence is low, at <3%. The embolic occlusion of distal tibial or pedal arteries may severely deteriorate the already existing ischemia. Arterial perforations can occur in up to 3%. These are caused either by the guidewire – inadvertent placement in a small collateral vessel – or at the site of angioplasty, leading to vessel rupture in the most severe cases. Major local bleeding may cause compartment syndrome.

FACTORS IDENTIFYING PATIENTS AT HIGH RISK FOR COMPLICATIONS

Antegrade vascular access is generally associated with an increased risk of complications including severe hematoma, retroperitoneal bleeding, and errant positioning of the sheath. Since this approach is preferred by many interventionalists in patients scheduled for infrapopliteal interventions, a higher rate of access site complications has to be expected, especially in obese patients and in patients with severe vessel wall calcification. Diabetics are generally at increased risk due to the presence of diffusely diseased calcified vessels and due to diabetic nephropathy. The presence of end-stage renal disease has not only a negative prognostic effect on the patency of endovascular interventions, but is also associated with a higher complication rate due to the mostly unfavorable anatomic situation with long-distance lesions and severe calcification. Since many of these patients are also poor surgical candidates, an endovascular treatment is often done as the last option despite this increased risk. Brosi et al[11] reported no major periprocedural complications or in-hospital deaths in a series of 38 patients.

COMPLICATIONS OF SPECIFIC INTERVENTIONAL STEPS AND TOOLS

Crossing even long-distance stenoses can usually be done without major problems also in the infrapopliteal vessels. However, tibial vessels have a significant propensity for spasm, especially in younger patients without calcification. Since spasm may simulate dissection, its evaluation can be difficult.

The use of hydrophilic guidewires increases the risk of unintended subintimal passage and of perforation at the lesion site or of small collateral vessels. Balloon angioplasty can cause dissection, especially in severely calcified vessels. Furthermore, an inadequate luminal opening increases the risk of acute re-occlusion.

Stenoses and short occlusions can usually be crossed intraluminally. However, in longer occlusions subintimal recanalization may become necessary. The principle of this technique, pioneered in the United Kingdom,[12] is to deliberately create a dissection with a hydrophilic guidewire with extension of the dissection until the wire re-enters the patent distal artery. The angioplasty balloon is inflated in the subintimal space. An occlusion is considered suitable for attempted subintimal recanalization if there is a patent distal arterial segment. However, in patients with critical limb ischemia and only one open distal vessel, special care has to be taken to avoid dissection beyond the distal open segment to preserve the possibility for distal vascular surgery in case of failed endovascular recanalization. Complications such as distal embolization

or perforation occur in approximately 5% of cases.[13] Hayes et al[14] have reported that the risk of perforation is significantly increased with subintimal angioplasty.

Treatment of proximal thrombotic or embolic occlusions with thrombolytic agents may cause further distal embolization (see also Figure 13.2) Patients may also experience increased pain during thrombolysis caused by embolization into distal arteries or into muscle vessels.

Several new methods are currently under clinical investigation for recanalization of complex lesions or for prevention of restenosis.[15] At least some of these approaches have the potential to become established adjunctive interventional methods in the infrapopliteal territory. The use of the cutting balloon in the infrapopliteal vessels was associated with a 20% rate of intimal dissection and inadequate hemodynamic result, necessitating use of adjunctive stenting.[16] At present, they may have niche indications such as treating ostial lesions or lesions from intimal hyperplasia.

Atherectomy devices are increasingly used also in the below-knee arteries. Results of treatment of such lesions in the TALON (Treating Peripherals with Silverhawk: Outcomes Collection) registry were reported recently.[17] The rate of perforation or embolization was reported to be low, at <2%. Zeller et al[18] reported 1 (3%) procedural complication, in which an intermittent occlusion of the target vessel occurred after an unsuccessful attempt to cross the lesion with the atherectomy device.

Laser-assisted angioplasty has been widely used for treatment of critical limb ischemia. Laird et al[19] have reported favorable results with a low complication rate. However, no data were reported separately for the lower leg arteries.

Until recently, stenting of the crural vessels was only recommended in case of complication,

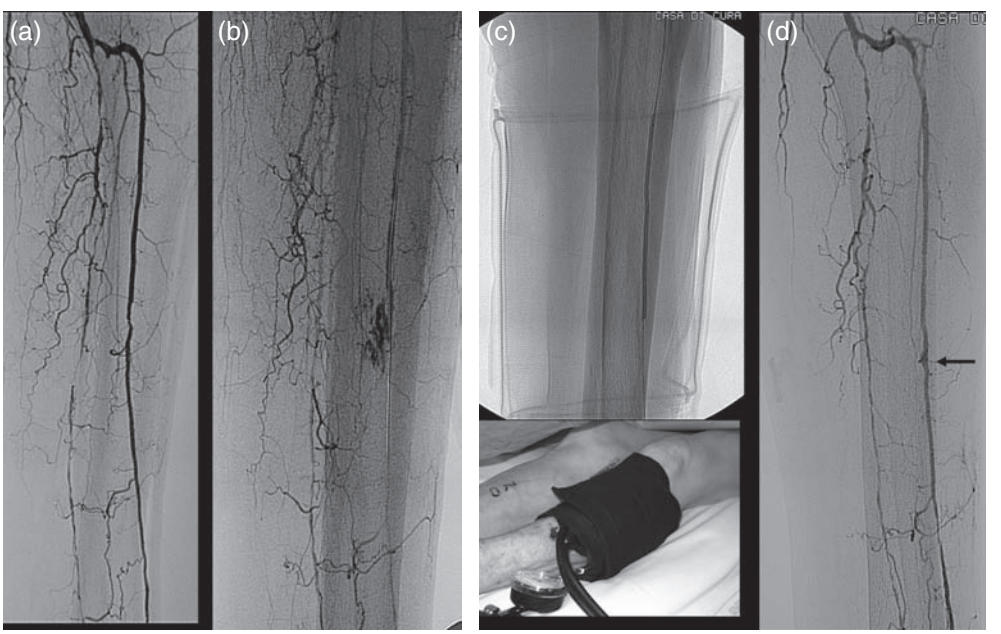

Figure 13.1 (a) Angiography demonstrating a focal stenosis of the anterior tibial artery (ATA) associated with stenosis of the tibioperoneal trunk and short-segment occlusion of the posterior tibial and long-distance occlusion of the peroneal artery. It was planned to recanalize the anterior and posterior tibial artery. (b) After angioplasty of the ATA by a monorail 2.5 × 20 mm coronary-type balloon catheter, inflated at 12 atm for 180 seconds, control angiography demonstrated rupture of the vessel at the angioplasty site. (c) Inflation of a long over-the-wire balloon for 3 minutes at 6 atm. Further compression was done externally by suprasystolic inflation of a blood pressure cuff at the level of the perforation. (d) The control angiogram demonstrates no further contrast extravasation.

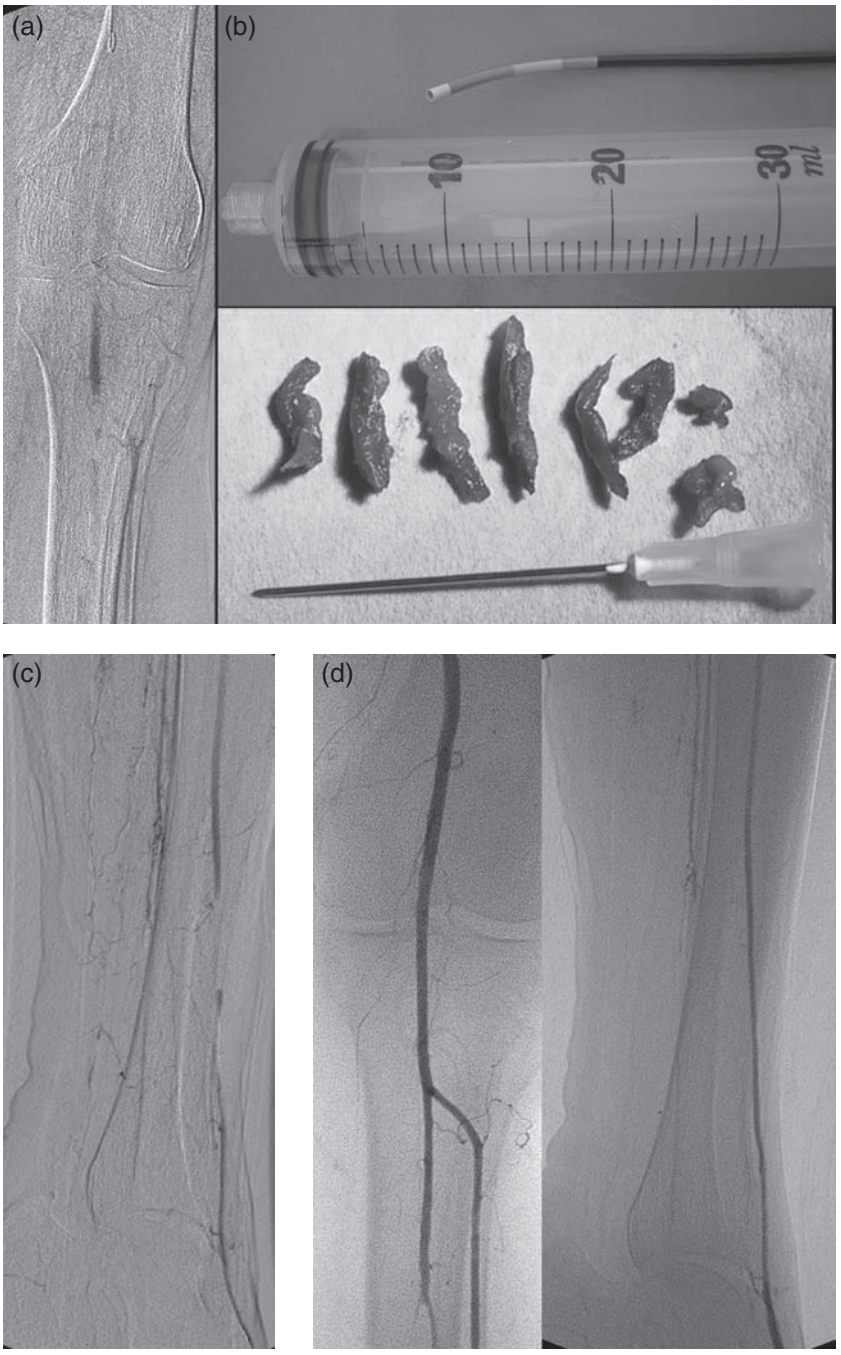

Figure 13.2 (a) Subacute embolic occlusion of the popliteal trifurcation. (b) Treatment by aspiration thrombembolectomy. (c) Angiographic control demonstrates further embolization – due to thrombus fragmentation – in the distal anterior tibial artery. At this level the thrombus was aspirated using a 6 French coronary guiding catheter. (d) Final angiography demonstrating an optimal result with no residual thrombus at the popliteal trifurcation and anterior tibial artery with direct flow to the foot.

e.g. dissection. However, recently studies have also been published concerning stent implantation for the treatment of focal infrapopliteal lesions to improve long-term patency.[9,20,21] No site-specific complications were reported. The choice of the appropriate stent has been unclear until now. While in other vascular regions self-expanding or balloon-expandable stents are recommended, currently no clear recommendations can be given for the crural vessels. Due to limited availability of self-expanding stents with an appropriate dimension, mainly balloon-expandable coronary stents are currently used. Such balloon-expandable stents can be used without problems, since the course of the tibial and peroneal arteries is relatively protected. Furthermore, until now there have been no reports concerning compression from outside forces of a balloon-expandable stent implanted in the infrapopliteal vessels.

METHODS TO DETECT POTENTIAL COMPLICATIONS

Preinterventional angiogram is the optimal method to identify good candidates for endovascular treatment. However, even in cases of unfavorable morphology, it is often necessary to recommend primary endovascular treatment due to the risks of surgery, especially in high-risk patients. An optimal angiogram of the distal tibial and crural vessels is obligatory to recognize patency of the distal segments and to detect a new occlusion caused by the intervention. At the end of the intervention, an angiogram with a long series is necessary to recognize even small perforations.

The postinterventional follow-up is primarily done clinically for evaluation of improvement or further deterioration of limb ischemia. Control of the patency can be done by duplex sonography. However, in cases of severe calcification, morphologic judgment may be impossible. In these cases one has to rely on the flow pattern in the distal tibial or pedal arteries. In our laboratory we avoid immediate – for about 4 weeks – measurement of ankle pressure with suprasystolic inflation of a cuff in patients with intervention in the distal lower leg arteries.

TECHNIQUES TO RESOLVE COMPLICATIONS

Dissections can effectively be treated by stent implantation. Perforation requires temporary balloon occlusion for a few minutes. Furthermore, inflation of a blood pressure cuff in the region of the vessel perforation can also be recommended to support rapid sealing of the perforation (see Figure 13.1). Coil embolization is rarely necessary. If control angiography demonstrates further blood extravasation, implantation of a bare metal or even covered stent may become necessary. In case of arterial wall rupture caused by extraluminal position of the balloon or atherectomy devices, prolonged balloon inflation may not be sufficient and implantation of a covered stent is then the treatment of choice. Reversal of the anticoagulation should be avoided because of the risk of thrombotic occlusion. Distal embolic occlusions usually respond to thrombolysis ('lacing' of the clot may shorten the duration time of necessary thrombolysis and support further aspiration) and/or aspiration thrombectomy (Figure 13.2). Some authors also recommend use of a mechanical thrombectomy device (such as the AngioJet). In the case of persistent occlusion caused by atheromatous debris stent implantation can be recommended to re-establish flow.

METHODS TO AVOID COMPLICATIONS

Use of modern devices (fine wires and small, low-profile balloon catheters adopted from coronary technology) and great operator experience are the best prerequisites to avoid major complications.

An antegrade approach is preferred by many interventionalists since it is often the easiest approach for intervention in the crural arteries. However, this increases the risk of access site complications. Therefore a 4 Fr sheath should be used when simple balloon angioplasty – or even the placement of small stents – is planned. This makes subsequent hemostasis safer and simpler. In obese patients and in patients with severe calcification at the puncture site, the contralateral approach should be chosen primarily. The use of non-kinking sheaths, guiding catheters, and low-profile balloons enables successful intervention from the contralateral approach in most cases.

Furthermore, a long 5 Fr sheath can be used as a guiding catheter. The use of a distally placed guiding catheter may be of value to provide proximal support with the use of rapid exchange catheters.

In case of technical failure with inability to cross the lesion with the guidewire, a retrograde tibial access using a micropuncture kit is recommended as a possible alternative approach.[22] However, this percutaneous access requires sufficient caliber of the anterior or posterior tibial artery below the ankle. Furthermore, this kind of intervention should only be tried by an experienced operator, since potential complications may damage the single patent run-off vessel and worsen surgical options due to lack of identifiable distal anastamotic sites. Since the infra-popliteal arteries are sensitive to manipulation with a risk of spasm, liberal use of antispasmodic agents (such as an intra-arterial bolus application of 0.1–0.2 mg nitroglycerin, 30–60 mg papaverine, 12.5 mg tolazoline, or 10 mg nifedipine orally) is often recommended at the beginning of the procedure to avoid the risk of severe spasm leading to thrombosis. Strict anticoagulation with heparin (5000 IU at the beginning of the procedure and eventual further application after control of the activated clotting time (ACT) in prolonged interventions) is obligatory.

Coronary 0.014-inch wires are recommended to cross stenotic lesions, especially for very distal lesions. In case of occlusion, the use of hydrophilic 0.018-inch wires may become necessary. Since hydrophilic wires have a higher risk for perforation, they should be used with special caution and exchanged for a standard wire after successful passage of the lesion. Furthermore, the distal tip of the guidewire should always be kept in view to avoid perforation by inadvertent placement in a collateral vessel.

Treatment of long-distance lesions should be done with balloon lengths up to 12 cm to avoid repeated inflations. In long lesions we prefer to use the Amphirion balloon catheter. This is a small-diameter, long balloon with excellent trackability, designed specifically for the tibial arteries. The Amphirion is available in diameters ranging from 1.5 to 4 mm, with lengths up to 12 cm with a 0.014-inch platform. The 0.018-inch wire compatible Cordis Savvy is another popular balloon for infrapopliteal vessels.

The appropriate choice of balloon size according to the diameter of the artery is of critical importance to avoid severe dissections or vessel perforation/rupture. In severely calcified arteries, predilation with a smaller balloon can be recommended to reduce the risk of vessel perforation.

Despite the lack of studies concerning optimal antithrombotic treatment during and after infrapopliteal interventions, a combined antiplatelet therapy with aspirin and clopidogrel/ticlopidin can be recommended due to the similar diameters of the tibial and coronary arteries, and the proven efficacy of this regimen after coronary interventions. Such treatment seems especially important after stent implantation.

SUMMARY

Treatment of critical limb ischemia is the only generally accepted indication for below-knee endovascular interventions. The risks of surgery in these mostly high-risk patients (diabetics, renal insufficiency) have led, together with the improved technology, to a steadily increasing application of endovascular interventions in the infrapopliteal arteries as well.

Complications are reported to occur in 2–6% of cases, and in most series complications at the access site are the most common. A 4 Fr sheath should be used for the antegrade approach when simple balloon angioplasty – or even the placement of small stents – is planned. The use of modern devices (fine wires and small, low-profile balloon catheters adopted from coronary technology) and great operator experience are the best prerequisites to avoid major complications.

Coronary 0.014-inch wires are recommended to cross stenotic lesions, especially for very distal lesions. In case of occlusion, the use of hydrophilic 0.018-inch wires may become necessary. The use of hydrophilic guidewires increases the risk of unintended subintimal passage and of perforation at the lesion site or of small collateral vessels. The appropriate choice of balloon size according to the diameter of the artery is of critical importance to avoid severe dissections or vessel perforation/rupture.

Dissections can effectively be treated by stent implantation. Perforation requires temporary balloon occlusion for a few minutes.

A combined antiplatelet therapy with aspirin and clopidogrel/ticlopidin should be applied.

CHECK LIST FOR EMERGENCY EQUIPMENT FOR INTERVENTIONS IN THIS SPECIFIC VESSEL AREA

- covered stent
- thrombolytics
- aspiration thrombectomy catheter
- coils.

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14

Complications in the percutaneous management of failing hemodialysis fistulas and grafts

Dierk Vorwerk

Introduction to the frequency and type of complications • Complications of specific interventional steps and tools • Acute complications • Methods to avoid complications • Conclusion • Check list for emergency equipment

INTRODUCTION TO THE FREQUENCY AND TYPE OF COMPLICATIONS

Interventional radiology in failing hemodialysis fistulas and grafts has been – in the meantime – accepted as a valid alternative to surgical revision. The literature does not show a significant difference concerning technical outcome, complication rate, and follow-up patency between surgical revision and an interventional radiologic approach.[1–3] Most procedures are safe, easy to perform, and benign in outcome. In the majority of cases a transvenous access is used, severe bleeding complications therefore remain rare. Nevertheless, there are typical complications in percutaneous interventions in dialysis connections; the type, rate, and severity depend on the underlying problem, the method of treatment, and the means of access. Furthermore – albeit still very rare – there are some typical complications that are potentially life-threatening or disabling, such as pulmonary embolism, paradoxic arterial embolism, and septicemia. Others occur that require surgical repair.

Most shunt procedures are performed as an acute and emergency treatment, but in conscious and informable patients, raising open and sometimes delicate questions about the ways in which patient information and consent should be approached. As related questions, however, depend on the jurisdiction of each individual country, it is difficult to give clear answers in that complex field.

General complication rate

It is somewhat difficult to give a uniform overview about complication rates from the literature as they are reported and classified in heterogeneous ways. Some authors, for example, count venous ruptures among complications, while others regard them as technical failures that require further treatment, but not as complications.

Nevertheless, most of the complications that have been reported are relatively benign and do not require further surgical or medical treatment. Life-theatening situations such as clinically significant pulmonary embolism or paradoxic arterial embolism may occur, but due to the underlying character of the shunt failure they are typically associated with treatment of shunt thrombosis.

There is scant literature dealing exclusively with the rate of complications of percutaneous

shunt treatment. Beathard et al[4] reported on a large collection of data from 14 067 cases that were treated in different ways, including both shunt thromboses and stenosis. They found a total rate of 3.54% for complications in general; 3.26% were classified as minor while 0.28% were classified as major. Turmel-Rodrigues et al[5] reported on a mixed group of 1118 shunt procedures. They found a rate of 2% for major complications such as uncontrollable rupture with fistula loss (2 cases), formation of pseudoaneurysms at the site of dilatation or puncture requiring surgery (5 cases), infection and bacteremia (5 cases), severe hematoma requiring surgical evacuation (2 cases), pulmonary embolism (1 case), mesenteric infarction (1 case), significant blood loss (1 case), iododermitis (2 cases), metabolic acidosis (1 case), and pulmonary edema (1 case). However, they did not count arterial embolism during declotting as a complication as they claimed that all events were treated by aspiration. Technical problems occurred with venous rupture in 83 cases (7.7%), with the highest rate in upper arm fistulas. Venous ruptures were partly treated by stent placement, with two events of stent dislodgement requiring retrieval.

Thrombosed shunts

Complications seem to be more frequent in shunt declotting techniques. Sofocleous et al[6] found 48 complications among 579 cases of percutaneous shunt treatment in grafts (8.5%). These included 12 venous ruptures, 4 graft dissections, 7 small hematomas, 12 graft extravasations and one distant hematoma, 8 arterial emboli, 2 pulmonary emboli, one intestinal angina, and one death related to the procedure. While the majority was related to bleeding complications at the site of access or dilatation, some very typical complications for thrombectomy procedures did occur – although in a relatively small amount of 2%.

Lazzaro et al[7] compared mechanical thrombectomy using the percutaneous thrombectomy device (PTD) device as a sole instrument for mechanical thrombectomy with a historical group where the PTD device together with a Fogarty balloon was used in order to remove the arterial plug and to pull it into the graft. They had a rate of 6% of arterial emboli in the PTD alone group versus 2% in the PTD Fogarty group. Venous rupture occurred in 6% versus 2% and one case of sepsis was found. This counted for a total of 9 complications out of 104 procedures (9%).

Turmel-Rodrigues et al[8] described one case of pulmonary embolism, one subacute pseudoaneurysm, one significant blood loss, and 5 venous ruptures in 93 cases of thrombectomy of native fistulas (8% including venous rupture, 3% without). Myayama et al[9] described minor complications in 20% of 26 patients with thrombosed Brescia–Cimino fistulas, but this included procedural events such as venous rupture in 12% and development of a hematoma in 8%. Liang et al[10] reported just 2 cases of venous rupture and 2 cases of radial arterial emboli in a group of 42 thromboses of Brescia–Cimino fistulas treated by percutaneous means, which counts for a total complication rate of 10%, or 5% excluding venous rupture. Rajan and Clark[11] found 2 complications among 30 treatments for thrombosis of native fistulas: one small hematoma and one small pseudoaneurysm (7% in total).

COMPLICATIONS OF SPECIFIC INTERVENTIONAL STEPS AND TOOLS

Barth et al[12] did not find significant differences in complications comparing random hydrodynamic thrombectomy and spray lysis in thrombosed hemodialysis grafts. Vesely et al[13] compared rheolytic thrombectomy using the Angiojet™ device with surgery in the treatment of thrombosed grafts in a randomized trial with 153 treatments enrolled. They did not find a significant difference in the complication rate, with 14.6% in the Angiojet™ group and 14.1% in the surgery group.

Immature fistulas

In the percutaneous treatment of immature fistulas, an overall complication rate of 4%, with minor complications in 3% and major complications in 1%, was described by Beathard et al[14] analyzing procedural results of 100 cases. Turmel-Rodrigues et al[15] described two significant complications out of 69 procedures including bacteremia and a pseudoaneurysm formation (2.8%). They also described 9 cases of venous rupture (n = 13%)

where 2 required further treatment by placement of a stent graft.

Transarterial access

Most authors use a transvenous access to treat shunt failure. There are few references available where a transbrachial arterial access was used as the primary access technique. In those, a higher risk of bleeding complications is likely. Manninen et al[16] reported a complication rate of 12% exclusively dealing with access problems, including 6 minor hematomas but 4 pseudoaneurysms of the brachial artery and 2 persistent arterial bleedings, of whom 4 needed surgical treatment. According to Trerotola and Turmel-Rodrigues[17] therefore, transarterial access should remain reserved to special cases where a transvenous access is not possible or failed.

ACUTE COMPLICATIONS

Technical complications

Venous rupture at the site of balloon inflation is a relatively frequent technical complication and occurs in 2 to 8% of cases.[6,8,11] It is more frequent in the treatment of immature fistulas, occurring in up to 13%. Venous stenoses in shunts and grafts are frequently more rigid than in arteries and formed by scarring tissue. However, venous rupture is unpredictable but occurs more frequently in upper arm veins than in lower arm veins.[5]

Usually rupture is benign and extravasation is self-limiting in the majority of cases (Figure 14.1). The primary means of treatment is prolonged balloon inflation at the site of rupture. If this is not sufficient, or rupture is flow-limiting, the use of native stents is recommended; some authors also prefer the use of stent grafts instead. In our own experience, the use of stent grafts as the only effective means to treat a ruptured vein is very rarely necessary, but polytetrafluoroethylene (ePTFE)-coated stent grafts may be used as an alternative to native stents as they seem to be promising concerning their tendency of restenosis.

Rajan et al[11] used Wallstents to treat venous rupture in 9 of 414 angioplasties, indicating a stent rate of 2%. Turmel-Rodrigues et al[5] used stents and stent grafts in 16 of 83 venous ruptures (18%). Related to all interventions, the stent rate was about 1.5% for venous rupture (Figure 14.2).

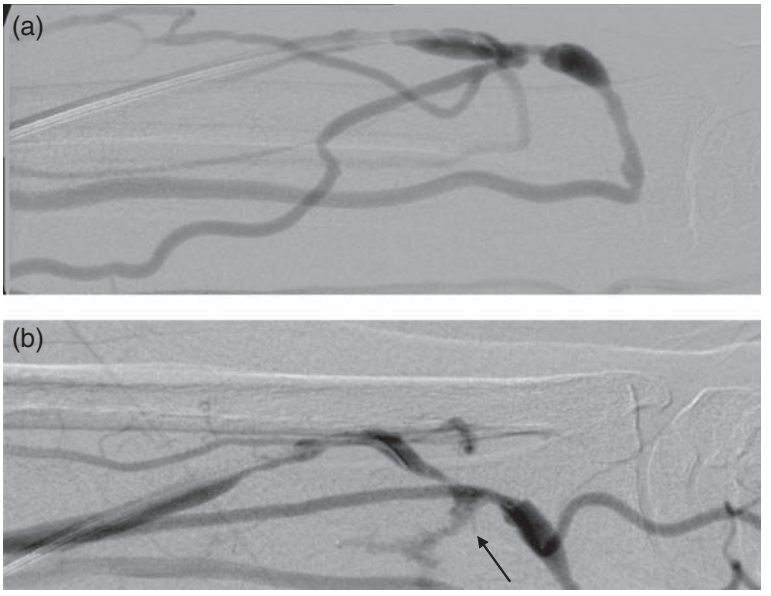

Figure 14.1 Venous rupture. (a) Native lower arm fistula with a stenosis in the proximal vein. (b) After PTA, venous rupture (arrow) occurs, that was successfully treated by prolonged PTA.

Venous dissection (Figure 14.3) with compromise of the venous lumen but no blunt extravasation may occur as a variation of venous rupture and may require stent placement. Both venous rupture and venous perforation, which may occur during an attempt to cross a tight stenosis, may lead to a complete blockage of the venous lumen, making recanalization from the same approach impossible. In such a case, a second access from the opposite venous segment – or from an arterial approach if the dissection happens close to the anastomosis – should be used.

Arterial dissection is a very rare event and should be treated similarly as in all peripheral arteries by prolonged balloon angioplasty eventually combined with stent placement.

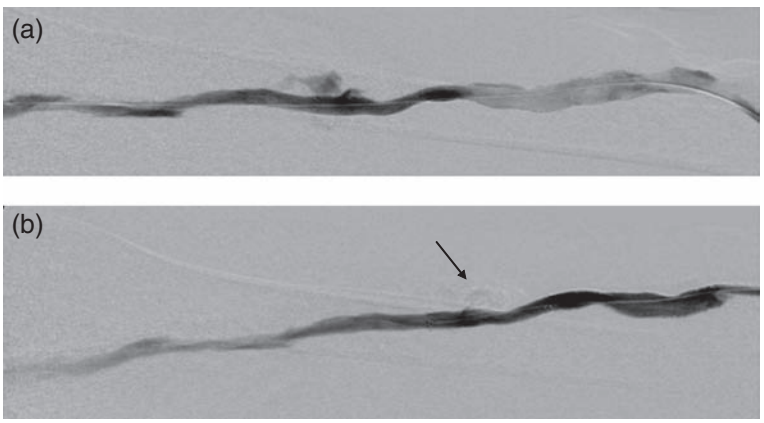

Figure 14.2 Venous rupture and stent. (a) Rupture of the upper cephalic vein after PTA. (b) After stent implantation following unsuccessful prolonged PTA, rupture is sealed (arrow).

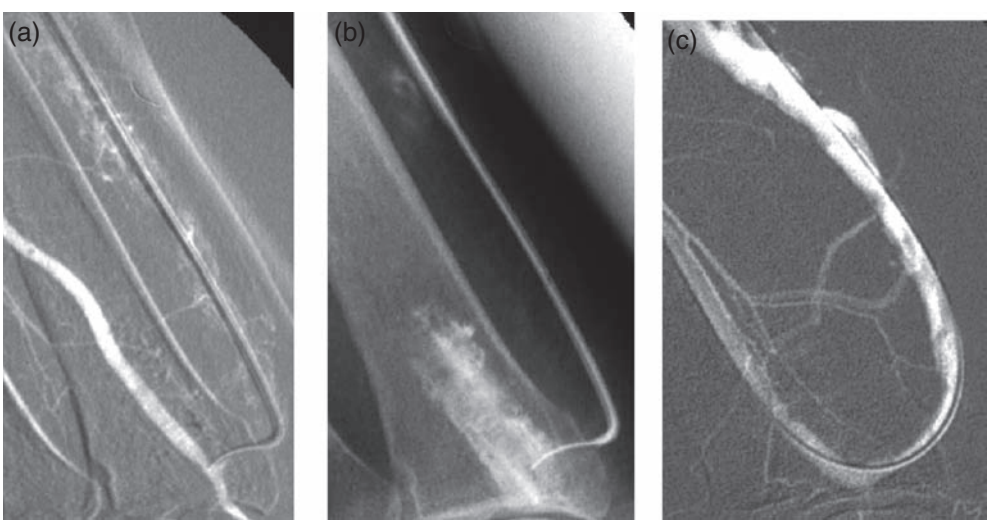

Figure 14.3 Venous dissection in an occluded forearm fistula. (a) After retrograde cannulation of the lower cephalic vein the guidewire is not able to enter into the artery crossing the occlusion. (b) After contrast an extravasal depot of contrast is seen, indicating dissection. (c) Repeat cannulation finally enters into an endoluminal pathway and into the radial artery.

In some stenoses, conventional balloons do not open completely despite high pressures up to 18 atm. This may lead to incomplete opening of the lesion and residual stenosis (Figure 14.4). In those cases, high pressure balloons that may be dilated up to 30 and 40 atm may be used as well as cutting balloons.[18] Cutting balloons do not improve long-term patency in a general shunt population but offer a technical option in cases with rigid stenoses.[18,19]

Bleeding problems

Bleeding may occur at different locations. It may follow venous rupture and is self-limiting in most of these incidences. From our experience, bleeding may be more severe in upper arm vein ruptures, as skin and subcutaneous tissue may be looser than at the forearm. The same is true for bleeding from the point of access. As especially for thrombectomy, larger diameter sheaths such as 8 Fr are used, bleeding control is sometimes time-consuming and difficult.

We routinely use subcutaneous purse string sutures to narrow the puncture channel and to reduce bleeding time.[20] This works very well in areas with scarring tissue, which is almost always present in puncture areas of shunts in use for a long time. In patients with immature shunts, however, or patients with very loose subcutaneous tissue, this method may fail and massive bleeding may occur. Prolonged compression and sometimes surgical evacuation may then become necessary.

As a sequela of bleeding or rupture, late formation of a pseudoaneurysm eventually occurs.

Embolization

Arterial embolization

Arterial embolization rarely occurs during recanalization of lower arm arteriovenous fistulas. Antegrade flow from the feeding artery usually prevents dislodgement of thrombus material into the radial artery.

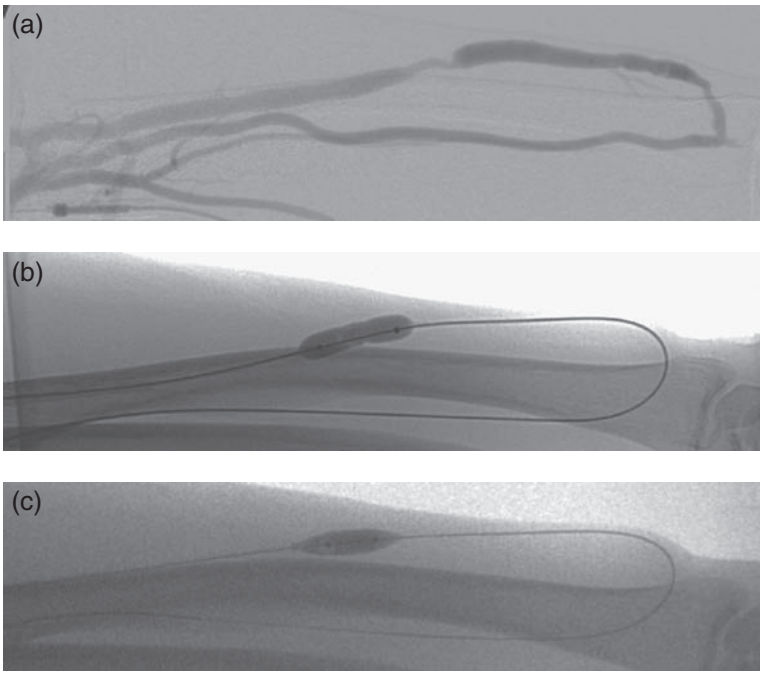

Figure 14.4 Rigid stenosis. (a) Stenosis of the lower cephalic vein in a native fistula. (b) By use of a conventional balloon, the stenosis does not open completely, despite pressures of 18 atm. (c) Cutting balloon completely opens at the stenotic side, overcoming the rigid stenosis.

More often, arterial embolization occurs when treating an upper arm brachiocephalic shunt of implant grafts. The nature of the arterial anastomosis to a bigger arterial vessel as a side-to-end anastomosis facilitates dislodgement of thrombus material into the brachial artery. Its rate is relatively high. Lazzaro et al[7] described a rate of 2 to 6% using the PTD device. Smits et al found three arterial emboli in 68 treatments using different mechanical devices (4%).[21]

Some of these emboli may remain asymptomatic. It is, however, recommended to remove them as early as possible as in most dialysis patients peripheral arteries are delicate. In upper arm native fistulas, treatment is relatively easy by retrograde puncture of the upper cephalic artery. By this access a guidewire is inserted into the brachial artery in an antegrade fashion and a suitable manual aspiration catheter is guided close to the point of embolic occlusion. The thrombus is then sucked out from the artery and dislodged into the vein or outside of the body through the sheath. A sheath with a removable hub is recommended.

In implant grafts, removal of arterial emboli is usually more difficult due to the very acute angulation between the arterial graft limb and the brachial artery. Trerotola et al[7] described a simple backbleeding technique where the brachial artery proximal to the arterial graft anastomosis is occluded by a balloon while the patient starts exercising his ipsilateral hand. By collaterals a reversed flow is created that dislocates the embolus into the graft out of the artery.

If this approach fails, aspiration embolectomy can be performed (Figure 14.5). For this purpose, a kink-resistant cross-over sheath (6–7 Fr) is guided across the arterial anastomosis through which an aspiration catheter can be safely introduced without the risk of kinking.

Pulmonary embolism

Pulmonary embolization (PE) rarely becomes symptomatic in patients undergoing shunt and graft declotting procedures. However, single events are reported from many series and there is also the description of fatal outcome.[22]

Smits et al[21] described one case out of 68 (1.5%) with symptomatic PE; Sofocleous et al[6] did not describe a single case among 579 sessions and Turmel-Rodrigues et al[5] found one case out of 1118 treatments (0.09%). However, there is also a certain subset of patients who experience silent events of PE without becoming symptomatic.

Petronis et al[23] performed perfusion scans before and after mechanical thrombectomy in 13 patients but found signs of new filling defects in only one patient. Smits et al[21] analyzed 23 of their patients in the same way before and after mechanical or pharmacomechanical thrombectomy and found signs of PE in 8 cases (35%).

It is questionable whether thrombolysis instead of mechanical thrombectomy prevents PE. In an animal experimental setting, Trerotola et al[24] have tested mechanical thrombectomy using the PTD device against spray lysis and found signs of PE in lung scans after recanalization of grafts in 18% of dogs in the PTD group but in 91% of the spray-lysis group. However, Kinney et al[25] compared spray lysis with urokinase versus spray lysis with heparin saline solution only in 27 patients. They found signs of new PE in 18% of patients where urokinase was used but – significantly more – in 64% where heparinized saline was used. All cases remained clinically silent. Interestingly enough, they compared baseline perfusion lung scans with those after treatment and described abnormal baseline scans in 70.4%. These findings state the old knowledge that patients with arterio-verious fistulas and grafts frequently experience events of PE even without shunt thrombosis.

Harp et al[26] investigated whether recurrent thrombectomy treatment may lead to chronic pulmonary hypertension potentially due to silent recurrent embolization. They compared patients with one or more thrombectomies to healthy persons and those with end-stage renal disease but no thrombectomies. They found a higher incidence for pulmonary hypertension in patients with end-stage renal disease, but no incidence of a higher rate in patients having undergone thrombectomy treatment.

To conclude, there is a small but existing risk of symptomatic pulmonary embolism after thrombectomy in shunts. There seems to be an

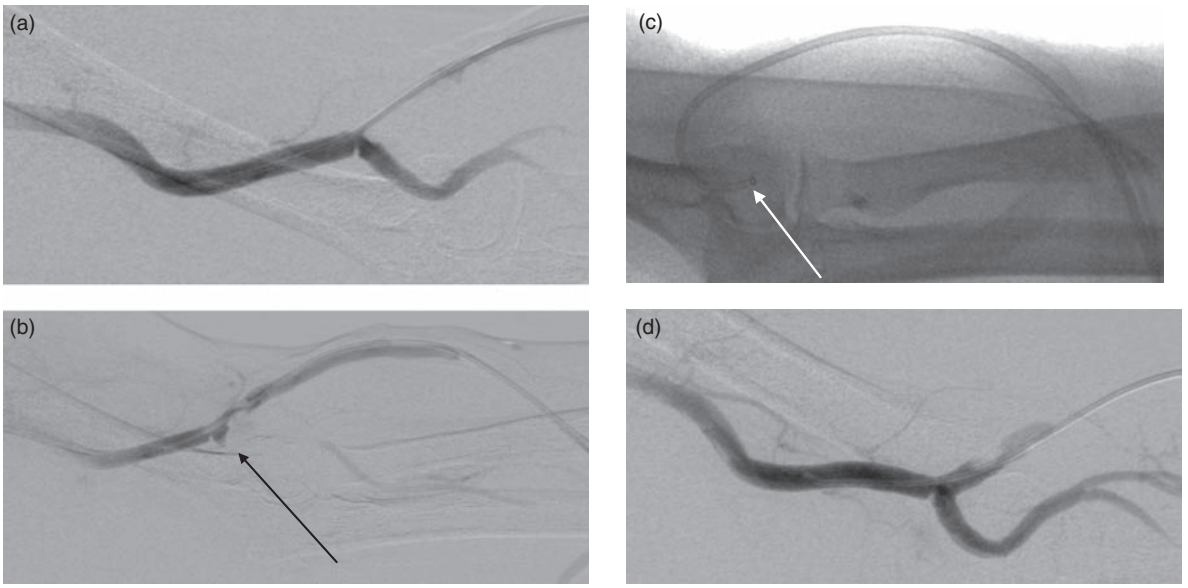

Figure 14.5 Arterial embolization. (a) Angiographic appearance of the arterial anastomosis of an implant shunt. Shunt is still occluded but brachial artery is open. (b) After mechanical thrombectomy, brachial artery is occluded by an embolus (arrow) but shunt flow is partly restored. (c) A kink-resistant cross-over sheath with removable hub has been introduced into the brachial artery (arrow) through which a 6 Fr aspiration catheter was advanced. (d) After aspiration, brachial artery is patent again. Note residual clot in the proximal loop.

even higher risk to experience silent PE which – from our current knowledge – is not likely to lead to late complications. Unfortunately, single cases have been reported who developed paradoxal cerebral emboli or mesenteric schemia which may result from paradoxal thrombus dislodgement. Besides case reports on paradoxal cerebral emboli,[27,28] Turmel-Rodrigues et al[5] reported one case of mesenteric infarction out of 1118 treatment sessions (0.09%) and Sofocleous et al[6] described one case of mesenteric angina out of 579 cases (0.14%).

Infection

Infection and septicemia may complicate treatment of shunt thrombosis in some cases. If a local infection is apparent, percutaneous intervention is contraindicated. In some cases, however, infection is not apparent, the site develops infection after intervention, or part of the occluding material is superinfected. In those cases, septicemia may occur. Turmel-Rodrigues et al described 5 cases out of 1118 interventions (0.45%).[5] Very rarely, a stent may undergo secondary infection. There is one case report published on a superinfected stent in the subclavian vein of a dialysis patient.[28]

Stent complications

After a stent has been placed, complications are rare. Acute stent thrombosis in central or upper arm veins is extremely rare as a sufficient flow usually keeps them patent. In grafts, rethrombosis also involves a stent at the venous anastomosis if early graft thrombosis takes place.

Stent dislocations from central veins into the right heart or the pulmonary circulation have been described, but remain rare, if the stent is long enough to make enough contact with the venous wall and is of a sufficient diameter.

METHODS TO AVOID COMPLICATIONS

Due to the variety and different nature of the complications, avoidance is sometimes difficult. Of course, general rules of percutaneous intervention

need to be obeyed, for example no gross oversizing of balloons and no advertent massive force should be obtained. Venous rupture, however, is difficult to predict and is not strictly related to high pressures. Thus, it is recommended not to apply high pressure onto a resistant stenosis because otherwise the intervention might fail.

If mechanical instruments for thrombectomy are used they should be over-the-wire instruments to prevent perforation or rupture. Rupture is usually simple to control either by prolonged dilation, stent, or stent graft placement.

Bleeding problems are also unpredictable in most cases. In patients with immature shunts, however, or patients with very loose subcutaneous tissue, a subcutaneous string purse suture should be avoided or used with care, not to oversee larger subcutaneous bleeding. In rare instances, surgical assistance is required.

Inadvertent arterial embolization in implant loop shunts and upper arm shunts is mostly due to incautious injection of contrast medium into the graft or the vein without sufficient outflow. With increased pressure, parts of the thrombus might then be squeezed out of the graft into the open artery. Thus, imaging of partially blocked grafts should always be performed as antegrade angiography from an arterial injection point. Also, manipulations within a thrombus require the use of straight or slightly curved catheters and wires; J-shaped instruments may push parts of the thrombus into the artery.

Venous and pulmonary embolization is – unless no paradoxal embolization occurs – relatively benign if the thrombus remains small. To prevent dislodgement of larger portions of organized thrombus, it is recommended to place a tourniquet around the upper arm during thrombectomy and to clear the vein as completely as possible from remaining clots up to this point before venous outflow is opened again.

CONCLUSION

Stenosis and thrombosis of hemodialysis fistulae and grafts represent the most frequent complications of hemodialysis accesses.

In conclusion, mechanical thrombectomy with all its variations proved to be an effective percutaneous method for thrombectomy in hemodialysis grafts and native fistulas, achieving results comparable to alternative methods such as lysis therapy. What particular type of treatment should be used depends on the experience of each operator, the clinical situation, the extent of thrombosis, and the type and age of the occlusion.

Percutaneous techniques have become the approach of first choice in many institutions and surgical thrombectomy has been limited to special cases. Outcome in the overwhelming majority of cases is benign and the nature of complications is usually minor and simple to treat by percutaneous means. Complications exist, however, but should not prevent interventional radiologists from being active in this interesting field of interventional radiology.

CHECK LIST FOR EMERGENCY EQUIPMENT

In order to be sufficiently prepared for the management of complications the following instruments should be in stock:

For venous rupture
self-expanding stents (8–12 mm), stent grafts (8–12 mm), preferably self-expanding.

Arterial embolization
aspiration catheters, equipment for thrombolysis, stable and long cross-over sheath (8 or 9 Fr).

Venous thrombus removal
Aspiration catheters (8–9 Fr), thrombectomy devices, tourniquets.

As dialysis patients are usually older, multimorbid, and of fragile constitution, a structure for emergency treatment and the possibility of in-house admission should be available.

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15

Venous interventions

C Binkert

Introduction • Factors identifying patients at high risk for complications • Complications of specific steps and tools • Methods to detect potential complications • Techniques to resolve complications • Methods to avoid complications • Summary • Check list for emergency equipment

INTRODUCTION

Various interventions are performed in the venous system. In general the intervention is performed to restore blood flow through a stenotic or occluded vein segment. Depending on the location, the chronicity, and the cause of the obstruction, thrombolysis, angioplasty, or stenting is performed. In contrast to the arterial system, vein closure is rarely performed. Exceptions are embolizations of insufficient gonadal veins or occlusion of varicose veins in the leg. Unfortunately the literature about venous intervention is scarce and reports about complications are even more infrequent and consist mostly of case reports or small series. The largest numbers are available in angioplasty of the venous anastomosis of hemodialysis grafts. A large series reported 14 (2%) ruptures in 683 procedures.[1] The lack of reported adverse events could be interpreted to suggest that venous interventions are comparably safe. The goal of this chapter is to address complications specific to venous intervention and how to resolve them.

The complications in the venous system differ from the arterial system mainly because of the lack of high blood pressure. There are hardly any substantial venous access site bleedings despite the use of remarkably large access sheaths. In cases of bleeding from an access site, manual compression is usually all that is needed. In case of a severe access site bleeding an inadvertent injury to the adjacent artery must be considered. With the use of ultrasound guidance the venous access complications can be markedly reduced.[2,3] Because of the low pressure in the venous system severe bleeding complications are uncommon and often associated with an additional problem such as coagulopathy or bleeding into a cavity.

Access site thrombosis was reported to be between 2 and 28% for filter placement.[4] These numbers include data from the time when the introducer systems were considerably larger than today. With the smaller introducer profile the rate has dropped to the point where it is no longer reported in most publications.

Unlike the arterial system, the venous system consists of an extensive network of collaterals. The collateral venous network can compensate for many segmental venous occlusions or thromboses. Often a segmental vein occlusion does not cause any clinical symptoms and is therefore not necessarily perceived as a complication. The difference in the vein wall configuration compared to the arterial wall results in different types of complications if damaged. Dissections, quite common in the arterial system, are very uncommon in veins. A case report describes a rare circumstance of a venous dissection caused by a malpositioned return needle during dialysis.[5] Vein injuries rather manifest as perforation, rupture, or occlusion instead.

FACTORS IDENTIFYING PATIENTS AT HIGH RISK FOR COMPLICATIONS

Patients with severe comorbidities such as coronary artery disease, congestive heart failure, or chronic obstructive pulmonary disease have an increased risk for any procedure including venous intervention. However, because alternative surgeries carry an even higher risk for these patients, endovascular intervention is generally the better option for these patients. Besides the general medical conditions, there are some specific factors which can increase the risk of venous interventions. These factors include all conditions which increase the risk of bleeding. An increased bleeding risk is most commonly secondary to anticoagulation. In these cases waiting till the bleeding risk is back to normal is often the best choice. Other reasons for a prolonged bleeding time are liver failure or less common hereditary coagulopathies. In the latter instances, correction of the bleeding risk with fresh frozen plasma or specific factors is indicated. The opposite, a hypercoagulopathy, can also increase the risk of venous intervention by causing thrombosis during intervention. Careful administration of heparin is advisable in these cases, including monitoring the heparin effect with repeat measurements of the activated clotting time (ACT).

Vein wall weakness can also lead to an increased risk of vein rupture during interventions. Chronic steroid treatment, recent surgery, or ablation[6] can weaken the venous wall. In case of recent surgery, the risk will decrease over time, therefore waiting 2–4 weeks before intervening in an area of prior surgery is advisable. In case of chronic steroid use, careful manipulation of material through the veins is important in order to avoid complications such as a vein rupture (Figure 15.1). In case of additional risk factors, the risks and benefits of a venous intervention have to be evaluated individually before proceeding.

COMPLICATIONS OF SPECIFIC STEPS AND TOOLS

Similar to arterial revascularization, the first step to re-open a vein is to advance a wire through the obstruction. This step itself hardly ever causes any problems because the hole, even in the wrong place, is too small to cause a significant hemorrhage. This is still true when a sharp recanalization technique is used. For sharp recanalizations typically a 21 gauge metallic mandrel is used through which a sharp stylet can be passed (Cook).[7] Sharp recanalizations have a high-risk of severe hemodynamic complications, including hemothorax and/or pericardial tamponade (Figure 15.2). A recent report of 12 patients treated with sharp recanalization showed major complications in 3 patients (25%).[7] After guidewire placement the next step is usually to advance a catheter, most commonly a 5 French catheter, through the obstruction. Through the catheter a venogram is typically performed to confirm the appropriate position of the catheter beyond the obstruction. If a wrong path is recognized at this point, simply pulling the catheter and abandoning the procedure can prevent a serious complication. The critical step is the inflation of the balloon to open up the obstruction.

During angioplasty a vein can rupture (Figure 15.3). Possible causes for a vein rupture are balloon oversizing or a rupture of the balloon itself.[8] The burst of a balloon can damage the surrounding vessel wall, which is also described in the coronary literature.[9,10] It is advisable to use an inflating device to monitor the balloon pressure, and high-pressure balloons, in case of a resistant stenosis. An area of increased risk of rupture is the cephalic arch (Figure 15.4). One article described a 6% rupture rate at the cephalic arch during angioplasty.[11] Besides rupture of the vein, the step of balloon inflation can cause a substantial amount of bleeding if the course of the guidewire was extraluminal. Figure 15.2 illustrates how the step of angioplasty of an extraluminal path can cause an immediate severe complication, while nothing happened when the guidewire and catheter were advanced.

Balloon angioplasty is usually the treatment of choice in the venous system. In certain instances, angioplasty alone is not enough, however. Such instances are immediate recoil, extrinsic compression, or rare cases of dissection after angioplasty. In these cases the placement of a stent can be helpful. Generally self-expanding stents are preferred over balloon-expanable stents in the venous system in order to adapt to the changing vein diameter during respiration and to avoid irreversible collapse

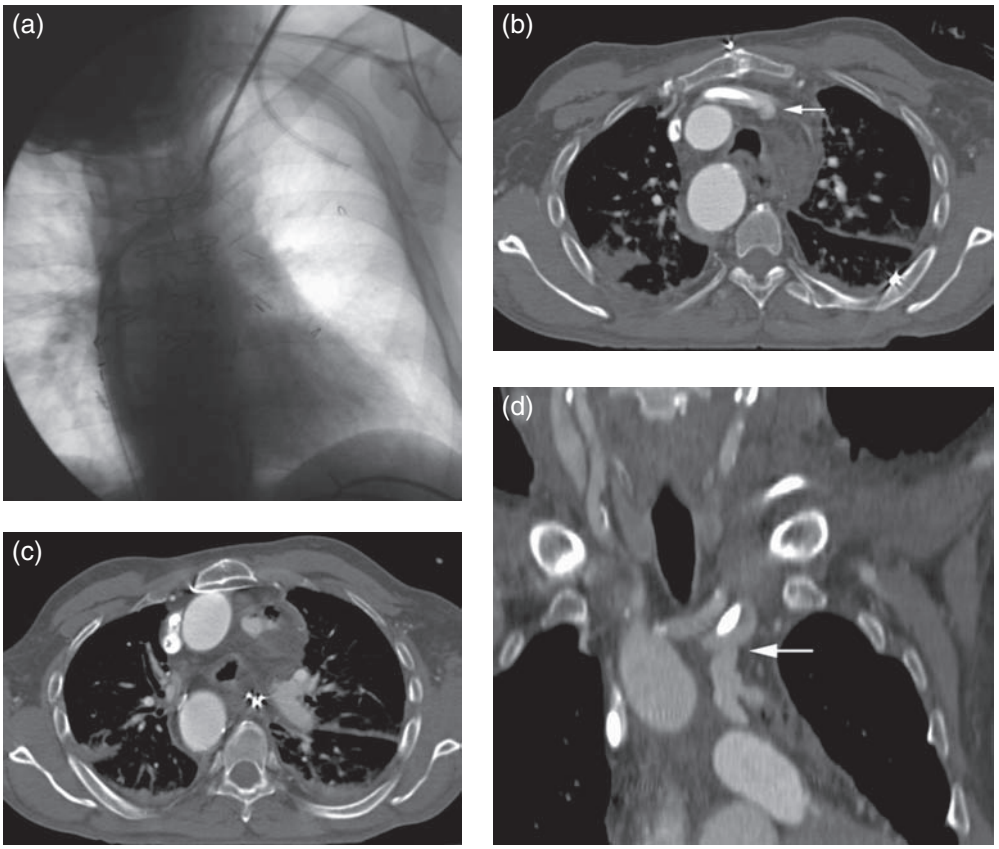

Figure 15.1 56-year-old man with heart–lung transplant 8 years previously. He developed renal insufficiency secondary to cyclosporine therapy. He presented for tunneled hemodialysis catheter. During insertion of the peel-away sheath the guidewire was bent and dilator pointed into the mediastinum. A quick hand-injected venogram showed regular flow of contrast through the brachiocephalic vein (a). Because of pain and an episode of hypotension a few hours later a CT was performed showing rupture of the left brachiocephalic vein (arrow, b) and a mediastinal hematoma with air from the recent catheter placement (c). The rupture in the trajectory of the traumatically inserted dilator is better visualized on coronal reconstruction (arrow, d). The patient was admitted to ICU for observation. He did well without any further intervention and left the hospital 2 days later.

by compression. The use of self-expandable nitinol stents is somewhat limited by the available sizes. The largest diameter available is 14 mm from different companies (Luminex, Bard Peripheral; Zilver, Cook, or Smart, Cordis). For larger diameters alternatively the Wallstent™ from Boston Scientific (up to 24 mm) or the Gianturco-Rosch Z™ stent from Cook (up to 35 mm) can be used. As a side note for interventionalists in the US: the nitinol stents are approved for biliary use and the larger stents for tracheo-bronchial use.

While rupture during angioplasty is the most feared complication during venous revascularization, stenting has its own complications. Stent complications include collapse, fracture, migration, thrombosis, and perforation. Collapses or fractures most commonly occur when the stent is repeatedly compressed, for example in the subclavian vein between the first rib and the clavicle.[12] Migration is most likely when stents are undersized or when using Wallstents. Wallstents have a tendency to migrate when the edges of the stent are not well embedded (Figure 15.5). Retrieval of a migrated Wallstent is illustrated in Figure 15.5. Similar Wallstent retrieval is also described in the literature.[13] The sharp edges of the Wallstent can cause damage to the vessel wall, which is most dangerous close

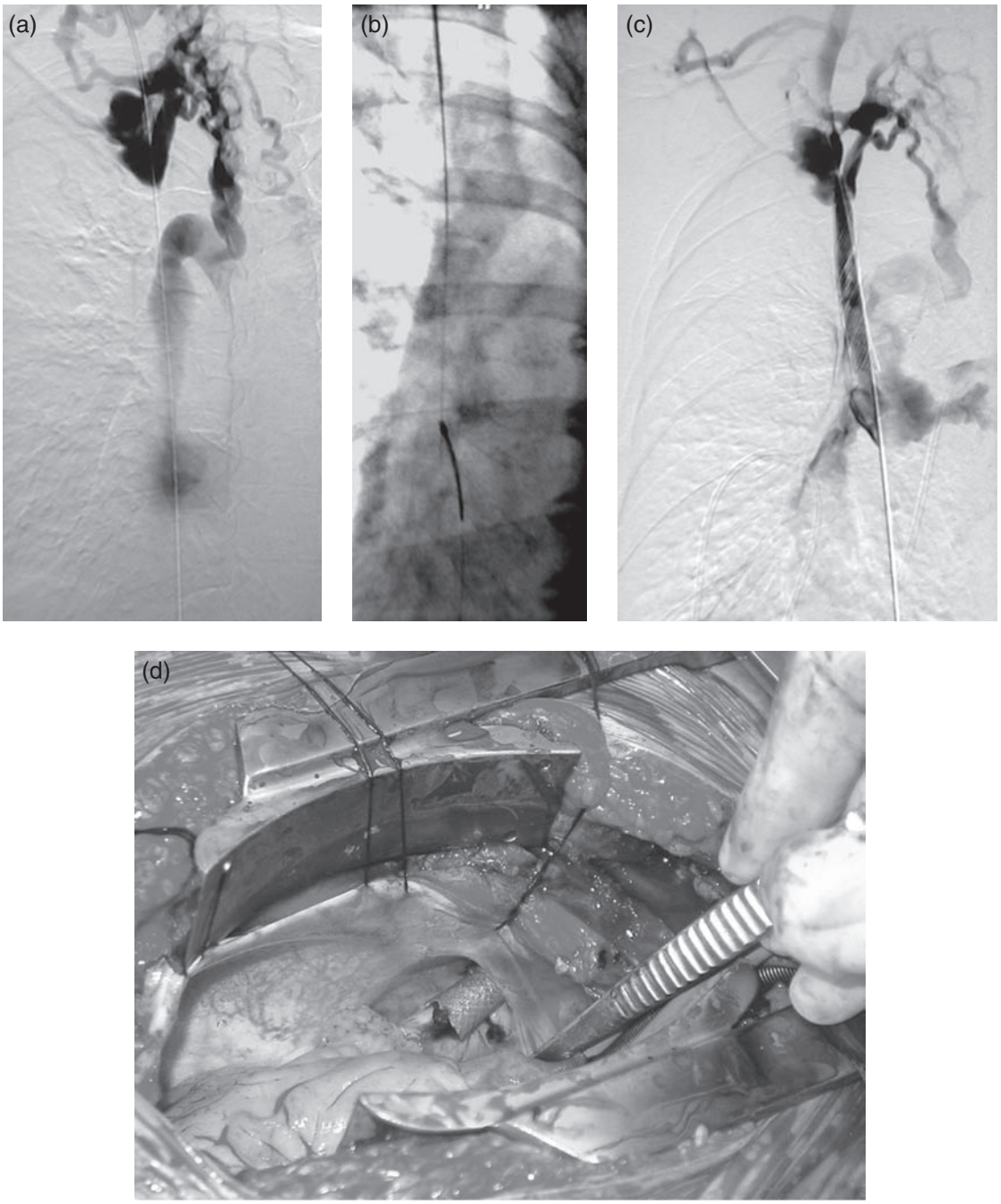

Figure 15.2 43-year-old woman with cystic fibrosis and head swelling secondary to chronic SVC occlusion. Initial venogram shows a short occlusion of the right brachiocephalic vein (a). Sharp recanalization was performed and the wire was snared in the SVC to achieve through-and-through access (b). After angioplasty to 8 mm the patient developed a cardiac tamponade. The balloon was re-inflated and an emergency pericardiocentesis was performed. The patient stabilized and a 14/40 mm Wallgraft was placed with the intention to cover the rupture site, but follow-up venography continued to show contrast leaking into the pericardium (c). A balloon was re-inflated and the patient was brought to the operating room where open repair was perfomed. Strangely, the Wallgraft was found to end in the pericardium without a hole in the heart or SVC (d). The patient recovered well from a cardiovascular perspective, but she could not be extubated secondary to her underlying lung disease and expired 27 days later.

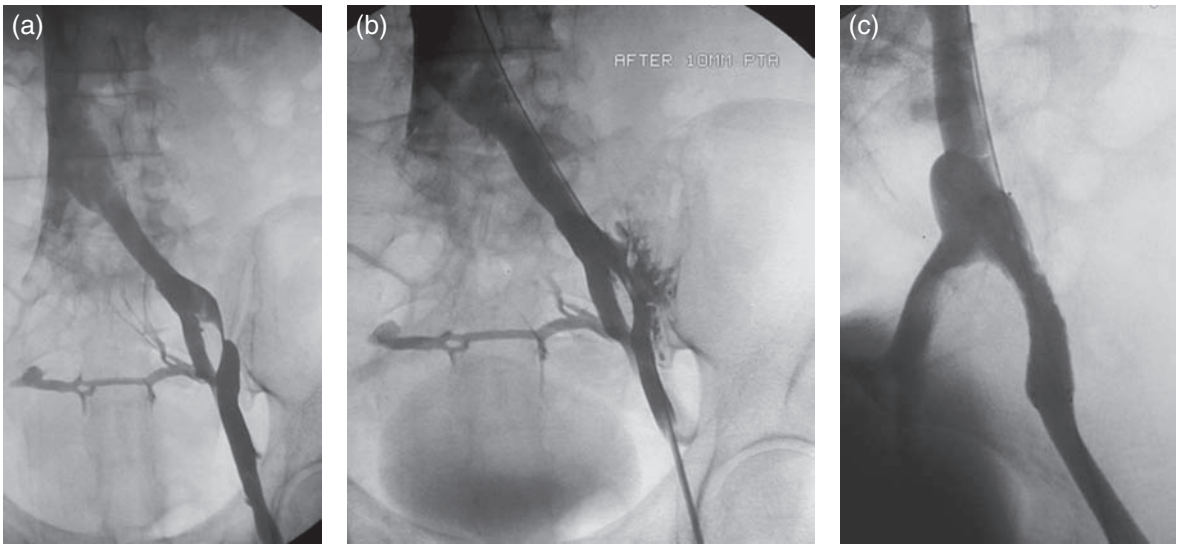

Figure 15.3 44-year-old woman with persistent left leg swelling. Initial venogram shows a high-grade stenosis of the external iliac vein close to the internal iliac vein inflow (a). After angioplasty to 10 mm the vein ruptured with diffuse extravazatioin into the surrounding tissues (b). A bare stent (Smart 12/40 mm) was placed to seal the rupture (c). The patient left the hospital after an overnight observation.

to the heart. Damage to the superior vena cava or right atrium can lead to cardiac tamponade, which can be fatal[14] if not immediately decompressed with a pericardial drain.[15] Cardiac tamponade can occur even 6 months after Wallstent placement.[16] Venous perforation can also occur when two stents are compressing the tissue in between. This condition led to two fatal outcomes with simultaneous caval and esophageal stent placement.[17]

Balloons and stents are the most commonly used tools for venous intervention. Other tools include caval filters and coils. Possible filter complications include filter migration,[18] filter fracture, caval penetration with injury to adjacent structures such as the aorta[19] or duodenum,[20] or caval occlusion.[21] The incidence of these complications is likely higher because many of them are asymptomatic and go undetected.

As mentioned earlier, embolization of veins is rarely performed. Particulate embolization is not feasible because in the venous system the blood flow runs from small to large vessels and particles would end up in the pulmonary circulation when released into the vein. Coil embolization is occasionally performed. One area of such embolization is insufficient gonadal veins.[22] There is a chance that a coil could dislodge with the flow to the pulmonary arteries. A single coil into the pulmonary artery would likely be asymptomatic. However, snare retrieval can be attempted to avoid the risk of pulmonary artery thrombosis. The snare technique is widely used to remove foreign bodies from the pulmonary circulation.[23,24]

Endovascular thrombectomy of acute deep vein thrombosis, despite being controversial, is increasingly performed. Thrombectomy can either be performed mechanically or pharmacologically,[25] or in a combined technique using the power-pulse spray technique.[26] The complications of mechanical thrombectomy are rupture of the vein similar to angioplasty. Catheter-directed thrombolysis has additional risks of local or distant bleeding. In a study of 473 patients, major bleedings were reported in 11%.[27] Most of the major bleeds were either at the venous insertion site or in the retroperitoneum. However, in the same study two intracranial hemorrhages (0.4%), one of them fatal, occurred. More recently, smaller studies report no major complication using combined mechanico-pharmacologic techniques.[25,26]

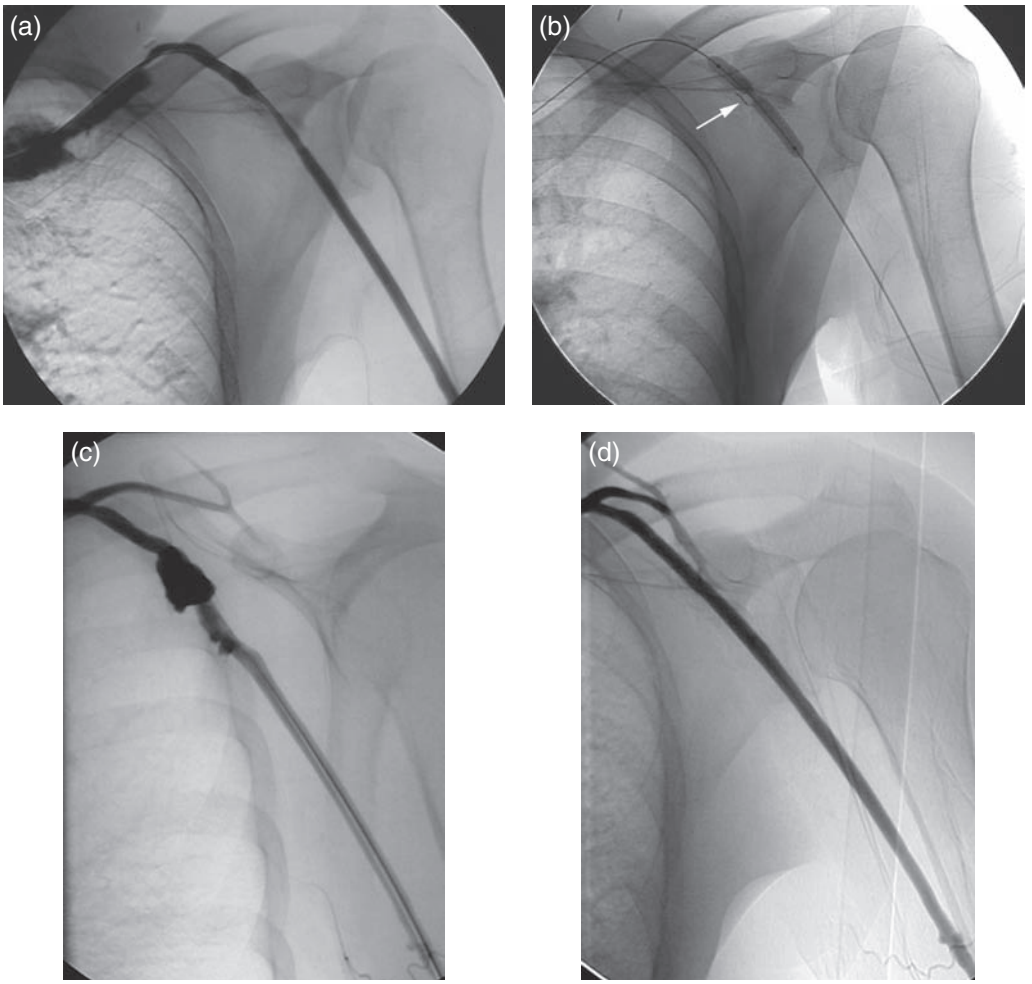

Figure 15.4 52-year-old man on hemodialysis. He presented with a central stenosis of a left brachio-cephalic graft (a). During angioplasty to 6 mm a tight waist was seen (arrow, b). After angioplasty the cephalic vein ruptured (c). Prolonged balloon inflation for 10 minutes was unsuccessful, therefore an 8/40 mm Wallgraft was placed which sealed the rupture (d). The stent graft was patent at 3 months' follow-up.

With either mechanical or pharmacologic thrombectomy there is a risk of pulmonary embolism. In a larger series symptomatic pulmonary embolisms were seen in 6 patients (1%), one fatal.[27] With the availability of retrievable filters many interventionalists place an optional caval filter prophylactically before thrombus removal. It has been shown that retrievable filter can effectively avoid new pulmonary embolism during treatment of deep vein thrombosis.[28] Filter placement is maybe even more important when using newer, more aggressive thrombolysis techniques. Recently a case with a large pulmonary embolism after power-pulse spray thrombolysis was reported.[29]

METHODS TO DETECT POTENTIAL COMPLICATIONS

Before discussing methods to detect complications, it should be emphasized that good imaging before an intervention can help to minimize complications during the intervention. Contrast-enhanced cross-sectional imaging (CT and/or MRI) helps proper planning of the intervention including determination of the best access site,

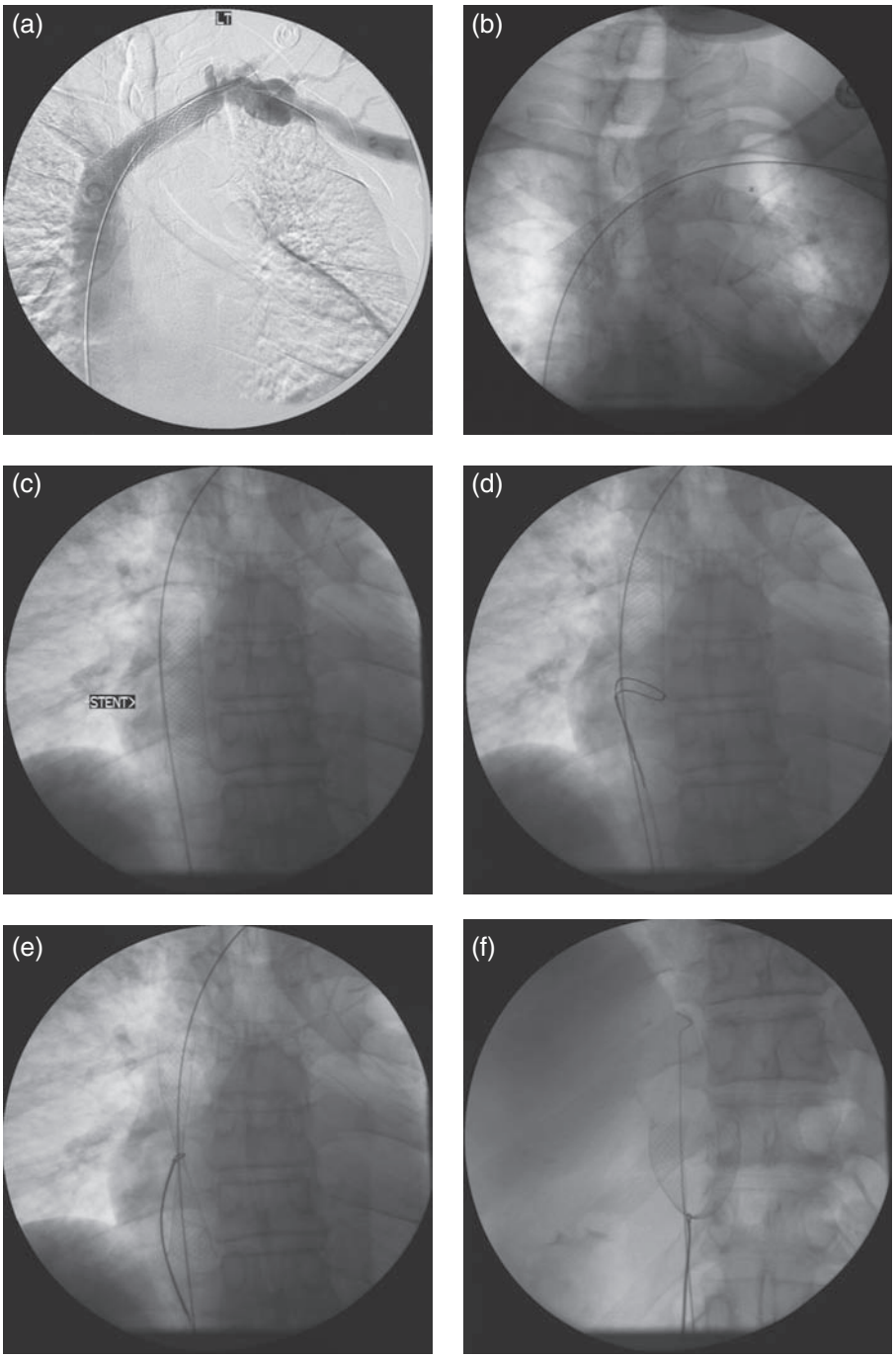

Figure 15.5 60-year-old woman with end-stage renal disease and left arm AV access. A 16 mm Wallstent was placed in the left brachiocephalic vein (a). The Wallstent opened the stenosis well, but remained in a funnel shape with the central struts not engaging the subclavian vein. Shortly after placement the Wallstent started to migrate towards the right atrium (b) and a little later the stent was in the right atrium (c). A gooseneck snare was then advanced around the stent (d) and closed at the center of the Wallstent (e). The Wallstent was then removed through the femoral access (f). The patient had no sequelae from the procedure. In a further procedure the left brachiocephalic vein was stented using a self-expandable nitinol stent. Courtesy of R Torrance Andrews, MD; University of Washington.

assessment of the cause of the obstruction, and the strategy to cross the lesion. In addition, the vein diameter and the length of the stenosis/occlusion can be measured, which helps in selection of the appropriate balloon or stent before the procedure.

At the beginning of any complex case a scout film should be taken in order to better recognize changes during the intervention. Venography should be performed using a power injector in order to properly fill the vein. A low-volume hand injection can miss even a quite large rupture easily (Figure 15.1). Hemodynamic monitoring is of limited use for early detection of venous complications. Unlike in the arterial system, venous bleeding is usually slow and significant blood loss occurs over longer periods of time. Exceptions are bleeding into the pericardium, as shown in Figure 15.2, which resulted in immediate cardiac arrest.

If in doubt, cross-sectional imaging should be performed to assess an ongoing problem.[15] As illustrated in Figure 15.1, a rupture of a central vein with a large hematoma was missed on hand-injected venography. The patient remained hemodynamically stable, but was admitted to the intensive care unit for observation.

TECHNIQUES TO RESOLVE COMPLICATIONS

Bleeding is the most common complication from venous interventions. The treatment of bleeding ranges from observation (Figure 15.1) to emergency surgery (Figure 15.2). It can be difficult to choose the appropriate method because venous bleeds can develop over time. It is important for the interventionalist to have pre-thought strategies in place to quickly control the acute bleeding before contemplating further treatment options. These automatisms include immediate re-inflation of the angioplasty balloon at the site of bleeding or manual compression if applicable. These initial measures can sometimes be all that is needed to control the bleeding, but more importantly they give time to rethink the options for further steps. Prolonged balloon inflation, typically with the same balloon used for angioplasty, is a simple first step. The success of prolonged balloon inflation for rupture hemodialysis access was reported at 29%.[30]

If prolonged balloon inflation is not successful a bare[1] or covered stent can be placed to cover the rupture or bleeding site (Figure 15.4). Self-expandable stents are preferable over balloon-expandable stents to adopt to the changing size of a vein during respiration and to exert a continuous force for optimal wall adaptation. The stent length should be chosen to cover the rupture site by at least 2 cm on each side. When using a bare or covered stent appropriate oversizing of the device is important. Oversizing by 10–20% or 2–3 mm is recommended. Too much oversizing can be a problem for bare and covered stents. If a bare stent is too oversized the increased radial force could potentially lead to a worsening of the vein rupture. When using a too oversized covered stent there is a risk that the cover material will not fully adapt to the vein wall. If redundancy of the cover material persists the rupture may not be sealed properly, Similar to the nitinol bare stents, the available sizes of self-expanding covered stents are limited to a diameter of 10 mm Fluency (Bard Peripheral), 13 mm Viabahn (Gore) or 14 mm Wallgraft (Boston Scientific). Alternatively a piece of an aortic stent graft can be used.[31]

In contrast to bleeding issues, venous thrombosis can occur during venous interventions. This is most common when working in an arteriovenous access graft, because the graft has no side branches. Native veins hardly ever thrombose during a procedure, especially when appropriate anticoagulation with heparin is used. However, acute stent thrombosis has been described.[32] In case a thrombosis occurs, mechanical or pharmacologic thrombolysis can be performed to resolve the clot. Because of the acuity of the clot, dissolution of the clot is typically fairly easy. The simplest way is to spray a thrombolytic agent into the fresh clot. A very practical way is to use a vial of 2 mg alteplase (Cathflow Activase, Genentech, South San Francisco, CA) which was designed for central catheter lysis. Expensive mechanical devices are rarely needed to dissolve acute thrombosis which occurs during a procedure. In case of thrombosis it is important to make sure the patient is appropriately anticoagulated with heparin. The use of an activated clotting time can be helpful to adjust the correct heparin dose. In addition, it is important to try

to treat the underlying problem, which is likely a venous obstruction or a hypercoagulable situation, in order to avoid rethrombosis.

Despite the advancement in endovascular technology open surgical solutions should always be considered. In certain cases, such as in the case described in Figure 15.2, open surgery is the life-saving solution. In other circumstances, surgical options can possibly be less invasive and quicker than an endovascular approach. An example would be a foreign body stuck in the common femoral vein. Endovascular options would likely require another large access, whereas surgical removal is straightforward. A good collaboration between the interventionalist and surgeon is important, especially if riskier central vein interventions are performed.

METHODS TO AVOID COMPLICATIONS

Careful planning of every intervention is the best way to prevent complications. Planning should include as many technical details of the intervention as possible, including special patient factors such as comorbidities, prior interventions or surgeries, and anatomic details. Ideally, alternative plans should be developed for every step of the intervention. In the way of: 'what if?' A well-defined strategy makes it easier to stop and adapt during a case when things are not going the way they are supposed to go. During the planning the achievability of the intervention should be assessed and alternative options should be considered. The interventionalist should always keep in mind that doing nothing is also an option, especially if the patient is not very symptomatic. For venous intervention the endovascular approach is often less invasive and as effective as surgery. However, there are situations where the surgical option is preferable. The best example is the venous thoracic outlet syndrome, also called the Paget–von Schrötter syndrome. In this condition the subclavian vein is compressed between the first rib and the clavicle. This condition, which would better be named thoracic inlet syndrome, is best treated with surgical resection of the compressing bone structure. Stenting of the subclavian vein has a high risk of stent malfunctioning, especially in young and active individuals, and should therefore be avoided.[12]

SUMMARY

Venous interventions are overall safe and effective. The key to avoid complications is good pre-procedural planning, assessment of every single step during the procedure, and automatisms in case a complication occurs. If a problem such as an extraluminal guidewire is recognized early, a possible complication can be avoided. Automatisms such as re-inflating the balloon or manual compression can help to gain time to decide about the next step. Most complications can be dealt with by endovascular means. Nevertheless, a surgical back-up is important, especially when working in the central venous system close to the heart.

CHECK LIST FOR EMERGENCY EQUIPMENT

Large diameter angioplasty balloons

- 12–26 mm Atlas PTA Dilation catheter (Bard Peripheral, Tempe, AZ).

Occlusion balloons

- 20–40 mm Equalizer (Boston Scientific, Natick, MA).

Large bare stents

- 16–24 mm Wallstent (Boston Scientific, Natick, MA).
- 20–35 mm Gianturco Rosch Z stent (Cook, Bloomington, IN).

Covered stents

- 10–14 mm Wallgraft (Boston Scientific, Natick, MA).

Aortic stent graft extensions

- 23, 26, 28.5 mm aortic extender (Excluder, WL Gore & Associates, Inc, Flagstaff, AZ)
- 22–32 mm main body extension (Zenith, Cook, Bloomington, IN).

Large diameter sheath to accommodate above devices

- 16–24 Fr Check-Flo introducers (Cook, Bloomington, IN).

Snares

- 15 mm and 25 mm Amplatz Goose Neck Snare (ev3, Plymoth, MI)

- 12–20 mm and 18–30 mm EN snare (interv Medical Device Technologies, Inc, Gainesville, FL).

Retrievable filters for protection during thrombolysis

- Recovery G2 (Bard Peripheral, Tempe, AZ)
- Gunther Tulip (Cook, Bloomington, IN)
- Optease (Cordis, Miami Lakes, FL).

Thrombolytics

- 2 mg alteplase (Cathflow Activase, Genentech, South San Francisco, CA).

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Complications in

PERIPHERAL VASCULAR INTERVENTIONS

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Minimal invasive endovascular treatment of peripheral arteries is one of the most rapidly evolving techniques in interventional therapies. Advanced technologies enable treatment of more complex lesions in severely diseased patients. Increasing evidence suggests that particularly in high risk patients endovascular solutions offer substantial advantages compared to vascular surgical procedures. Nevertheless, growing numbers of procedures are associated with an increased incidence of complications. Knowledge of specific complications in different vessel areas will support the interventionist in preventing such adverse events and if necessary provide considerable reassurance if such complications need to be resolved.

Complications in Peripheral Vascular Interventions systematically covers specific complications in peripheral vascular interventions. Typical and atypical complications are described for all peripheral vessel areas and methods how to handle these events are outlined. This excellent text is divided in two parts: part I reviews general aspects on complications in peripheral interventions, part II covers the specific vessel areas.

Each chapter on the specific vessel areas includes

- Introduction on the frequency and kind of complications in this vessel area
- Factors identifying high risk patients for these complications
- Complications of specific interventional steps and complications for specific interventional tools
- Endovascular techniques to resolve these complications
- Methods to avoid these complications
- Summary
- Check list for an emergency equipment for interventions in this specific vessel area

Complications in Peripheral Vascular Interventions focusses on practical tips for the interventionist in the cath-lab, reviews complicated cases and outlines different strategies in real-life cases, thus to sharing the experience of high-volume interventionists with the reader.