Arterial Complications in Patients with Cancer

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Abstract

Complications of peripheral arterial disease in cancer patients are associated with increased morbidity and mortality. Medical management with modification of vascular risk factors remains the first line of treatment for cancer patients with arterial occlusive disease. Endovascular or surgical revascularization is indicated for patients who have critical limb ischemia or disabling claudication symptoms. In this article, we review the management of peripheral arterial disease in cancer patients, and present a series of common and rare case examples of arterial complications that can occur during or after oncologic therapy.

Keywords

Angiography • Angioplasty • Arterial disease • Cancer • Endarterectomy • Limb ischemia • PAD • Radiation • Stenting • Vascular

Introduction

Cardiovascular complications are a common cause of morbidity and mortality in patients undergoing oncologic treatment. The presence of a malignancy is known to be associated with a state of hypercoagulability and increased risk of venothromboembolism (VTE) in patients diagnosed with cancer [1–3]. Certain chemotherapeutic drugs have known potential deleterious cardiovascular side effects [4, 5]. The field of cardio-oncology has emerged as an important subspecialty in our fight against cancer [5, 6]. However, the management of arterial complications in cancer patients, not directly related to the heart, remains ill defined and controversial.

The prevalence of peripheral arterial disease (PAD) in older patients diagnosed with cancer is estimated to be roughly 15–40% [6]. The incidence of acute arterial thrombosis in cancer patients is infrequent but has been linked to advanced cancer stage and poor prognosis [7, 8]. Some experts have suggested that palliative expectant treatment may be the most appropriate management for cancer patients who develop arterial complications due to their associated dismal survival rate [8–10]. In contrast, other groups have shown good outcome in treating arterial complications in cancer patients [11, 12]. In this article, we review the management of PAD in patients diagnosed with cancer and present a series of common and rare case examples of arterial complications that can occur during or after oncologic therapy.

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PAD Epidemiology and Clinical Significance

Approximately 8.5 million people over the age of 40 in the United States have atherosclerotic PAD, including 12–20% individuals over the age of 60 [13, 14]. Most patients with chronic PAD are asymptomatic, with a minority presenting with symptoms of classic intermittent claudication, and less than 5% have critical limb ischemia [15, 16]. The lifetime risk of limb-loss for the majority of patients with PAD is less than 5%, reflecting the relative "stable" or "slow-progression" nature of the disease. The clinical importance of PAD is more related to it being a marker of atherosclerotic disease at other sites rather than it causing limb loss. Individuals suffering from PAD are at a much higher risk of morbidity and mortality from complications related to cardiac and cerebrovascular complications than individuals without PAD [17]. In general, studies have shown that antiplatelet and statin therapy can reduce the rate of myocardial and ischemic stroke events in PAD patients [18, 19]. However, there are still no good clinical predictors to indicate PAD progression in the affected limbs.

For the subgroup of patients with chronic critical limb ischemia, the more severe form of the disease, the 1-year risk of limb-loss can exceed 25%. Typically, chronic critical ischemia occurs as a result of multi-level arterial occlusive disease (affecting more than one artery segment), or is due to extensive tibial artery disease. Intervention on the occluded aorto-iliac or femoro-popliteal segments, either by endovascular or surgical techniques, or a combination of both approaches (hybrid), can achieve high limb-salvage rates. Revascularization for patients with tibial arterial occlusive disease remains a challenging task.

Up to 10% of patients with critical limb ischemia can have concomitant malignancy [20]. It is well recognized that patients with critical leg ischemia who also harbor a malignancy have shorter survival than patients with critical leg ischemia who do not have a malignancy. It is unclear whether death in patients with concomitant malignancy and critical leg ischemia is due to the underlying malignancy or related to their cardiovascular co-morbidities. Moreover, the limb-salvage outcome for these patients are not well reported in the literature, and there remains a need for determining the optimal management cancer patients with critical leg ischemia.

Diagnostic Evaluation

The diagnosis of arterial insufficiency in cancer patients can often be delayed, due to the presence of confounding factors such as cancer-related pain or symptoms of peripheral neuropathy caused by chemotherapy drugs. However, a presumptive diagnosis of arterial insufficiency can usually be made after a thorough history and physical examination. The symptoms of intermittent leg claudication in the hip, thigh or calf muscles, precipitated by walking and relieved by rest, are typically reproducible. The symptom of ischemic rest pain in the foot with recumbency, which wakes the patient from sleep and is relieved by dangling of the affected foot, is a reliable indicator of severe arterial insufficiency. On exam, the loss of palpable pulses in the affected extremity is a diagnostic sign of PAD. Typically palpable pulses will be lost below the level of complete arterial occlusion. Other chronic signs of moderate to severe leg ischemia include loss of hair and atrophic muscles in the affected limb. Other chronic signs of severe ischemia include dependent rubor, and tissue loss such as non-healing wound or tissue necrosis. Patients who suffer acute limb-threatening ischemia (ALI) typically complain of new sudden onset of leg pain, coldness, pallor, numbness and weakness.

Measurement of the ankle-brachial index (ABI) can usually confirm and estimate the severity of ischemia, or rule out ischemia if normal (0.9–1.1). Duplex utrasonography is the fist vascular imaging modality of choice for patients with suspected PAD, as it provides real-time dynamic visualization of the aorto-iliac, femoro-popliteal and tibial arteries. High-resolution CT angiogram can be used for further evaluation when vascular duplex ultrasound is non-diagnostic. In patients with iodine contrast allergy or severe renal insufficiency, we use MR angiogram as an alternative diagnostic imaging modality. Conventional selective contrast arteriography is currently performed primarily as part of a therapeutic endovascular intervention and is rarely required in the diagnostic work-up.

The Trans-Atlantic Society Consensus, also known as the Inter-Societal Consensus, TASC II classification of PAD has been widely adopted, both in clinical practice and research communities, nationally and internationally [21]. The TASC II classification allows for stratification according to the location and severity of disease. TASC II classification divides PAD anatomical involvement into aorto-iliac, femoro-popliteal, and infra-popliteal segments. In TASC II classification, PAD disease extent ranges from A, B, C to D, in increasing severity, and includes single short partial segmental occlusion to multiple long complete occlusions. In addition, the TASC guidelines for the management of PAD have emerged as a valuable resource for vascular specialists from across different disciplines. Currently, medical therapy is still the first line of treatment for patients with PAD. Endovascular interventions are typically considered for symptomatic PAD patients with TASC II A or B lesions. Surgical interventions remain the accepted method of revascularization for TASC II C or D lesions, even though endovascular techniques are increasingly being used for more extensive disease. When endovascular intervention is deemed unsuitable or fails, surgical revascularization remains a good secondary option for limb-salvage.

Medical Management

The recommended medical therapy for PAD in cancer patients follows the same guiding principles as for PAD patients without concomitant cancer diagnosis. Lifestyle modifications are effective and well-validated interventions for symptomatic PAD, with tobacco cessation and supervised exercise demonstrated to improve functional performance, and quality of life scores, while reducing symptoms [22, 23]. In addition, best medical therapy is recommended for all patients with PAD including antiplatelet, statin, and control of blood pressure and diabetes. Optimal medical therapy has been shown to reduce the incidence and fatality of cardiovascular events such as stroke or myocardial infarction in patients with PAD, and should be continued throughout oncologic treatment unless otherwise deemed contra-indicated [24, 25]. For cancer patients undergoing chemotherapy that can cause severe thrombocytopenia, antiplatelet agents can be withheld temporarily to minimize bleeding risk, but should be resumed when the platelet count returns to a level greater than 50,000/μL. Similarly, PAD patients needing oncologic surgical resection can temporarily stop antiplatelet medication but should resume it as soon as the risk of postoperative bleeding subsides. Cilostazol and pentoxifylline are the only two agents specifically approved for the treatment of intermittent claudication in the USA. Both drugs inhibit platelet aggregation, and have rheologic, and vasodilatory effects. Cilostazol and pentoxifylline can be stopped during oncologic treatment without significant increased cardiovascular risk.

In general, we encourage patients with mild to moderate symptoms of intermittent claudication to continue to exercise. In addition, we provide patients with reassurance that the risk of limb loss is minimal and that the claudication pain is harmless. Revascularization can be considered in cancer patients with severe disabling claudication symptoms to relieve symptoms but is best delayed until after completion of oncologic treatment. In contrast, cancer patients who show evidence of critical ischemia, such as ischemic rest pain or tissue loss in the affected extremity, have a high risk of limb loss and should be evaluated urgently for revascularization.

Surgical Versus Endovascular Revascularization

Vascular reconstructive surgery remains the gold-standard treatment for patients with symptomatic PAD and critical leg ischemia. The two most common synthetic graft materials used in vascular bypass reconstruction are polyester (Dacron) and polytetrafluoroehtylene (PTFE); the former is traditionally used as the conduit choice for aorto-femoral bypass and the latter for femoro-popliteal bypass. However, autogenous saphenous vein is still the preferred graft for infra-inguinal reconstruction, as it has higher patency rates when compared to synthetic grafts in this location [26]. In general, long-term patency of aorto-femoral bypass procedure is approximately 80–85% over 5 years [27]. The long-term patency of infra-inguinal bypass reconstructions is roughly 50–80% [26, 28]. Although endovascular interventions have not been shown to produce superior results over open surgical revascularizations, a practice shift toward an "endovascular approach first" has undeniably taken place over the last two decades [29, 30]. It is generally recognized that repeated interventions are more common after endovascular treatment than after surgical revascularization. However, the minimally invasive nature of the endovascular approach, which is associated with less morbidity when compared to surgical bypass, has made the former a more attractive and popular option to patients and providers.

Advances in endovascular techniques and devices have continued to improve the success of endovascular interventions. Endovascular interventions for aorto-iliac occlusive disease are known to produce high success rates and durable results. Comparatively, the reported outcomes of endovascular interventions for infra-inguinal occlusive disease remain variable. Several different types of endovascular tools including balloons, stents, and other devices are now commercially available. The novel drug-coated balloon and drug-eluting stent platforms have shown promising short and intermediate term results in PAD treatment [31–33]. The anti-proliferative effect of paclitaxel and everolimus, (the two drugs currently used in this technology) has been shown to be associated with reduced rates of binary restenosis and target revascularization [31, 34, 35]. Vascular stents are either self-expandable or balloon-expandable. We prefer to use balloon-expandable stents to treat ostial common iliac artery lesions, for their higher radial force, better visibility, and more predictable placement, when compared to self-expandable stents. In contrast, we preferentially use the more flexible self-expandable stents to treat lesions in the external iliac artery, which can be more tortuous and are subject to external forces. Covered stents (also known as stent-graft) are increasingly used in the treatment of PAD. The principal advantages of the covered stents over bare metal stents include the exclusion of thrombus and coverage of vessel rupture. The superior long-term outcome of covered stents over bare metal stents in the treatment of aorto-iliac and femoro-popliteal occlusive disease remains to be proven [36–39]. The presence of graft material (PTFE) on the covered stents is thought to provide a mechanical barrier to prevent intimal proliferation and stent fracture, two factors that have been associated with in-stent restenosis in the femoro-popliteal lesions. The larger diameter of the covered stents (for vessel diameters

greater than 6 mm) still require larger size delivery sheath compared to the smaller sheaths for bare metal stents of comparable size.

For patients undergoing concomitant oncologic treatment, the advantage of a quicker recovery after endovascular intervention over surgical bypass is obvious. Patients can typically resume chemotherapy or radiation therapy within 1–2 weeks after endovascular intervention. In contrast, we recommend waiting approximately 3–6 weeks following surgical bypass before resuming or starting chemotherapy to allow adequate time for wound healing. Radiation treatment can usually take place safely away from the operative wounds within 2–3 weeks after surgery. Anti-platelet therapy has become standard adjuvant treatment following endovascular and surgical revascularization, although the anti-platelet agent of choice (aspirin versus clopidogrel) and duration of therapy remains variable. In general, we recommend lifelong aspirin after surgical bypass. On the other hand, we recommend clopidogrel after endovascular stenting for 3–6 months and lifelong aspirin subsequently.

Acute Limb-Threatening Ischemia

The three most common causes of acute limb threatening ischemia are: (1) acute thromboembolism from cardiogenic or other sources, (2) acute arterial graft or stent thrombosis (in patients who had prior vascular intervention), and (3) acute native arterial thrombosis with or without prior chronic atherosclerotic occlusive disease. The initial management of patients who develop ALI remains controversial. The treatment of patients who have concomitant malignancy and acute limb-threatening ischemia is even more debatable. Guarded survival outcomes and higher morbidity rates have been reported for patients who have surgical revascularization for ALI with concomitant malignancy compared to patients without a malignancy diagnosis [8–10]. However, Tsang et al. reported more favorable results in patients with concomitant malignancy who underwent surgical revascularization for ALI [11]. Similarly, we have shown more promising results in patients who develop ALI with concomitant malignancy, using selective treatment strategies including endovascular approach, surgical revascularization, or medical therapy alone or in combination [12].

Our current approach is to tailor treatment to cancer patients who develop ALI based on the severity of ischemia, the patient's performance status, and associated comorbidities. Surgical revascularization generally achieves reperfusion within 3–6 h. It is our preferred method of revascularization for patients who have severe immediately threatened limb ischemia, requiring prompt limb reperfusion. Surgical procedures to restore arterial flow range from simple thrombo-embolectomy for acute thromboembolism, to more extensive endarterectomy and bypass reconstruction for acute on chronic arterial thrombosis. Endovascular approach, including pharmaco-mechanical thrombectomy and catheter directed thrombolysis, usually takes up to 8–24 h to achieve revascularization. We recommend endovascular intervention for patients with ALI in whom the longer time to revascularization is deemed acceptable. Immediately following successful endovascular recanalization, adjuvant balloon and/or stent angioplasty is commonly required to maintain vessel patency. The advantages of endovascular approach over surgical treatment are well recognized, including less morbidity and quicker recovery. In our experience, inconsequential ecchymosis and minor bleeding at access sites are common occurrences with catheter directed thrombolytic therapy, but fortunately the incidence of major bleeding and intra-cranial hemorrhage has been low. In addition to the typical absolute contra-indications to catheter directed thrombolysis including active bleeding, recent major surgery or stroke, we consider thrombocytopenia (platelet count <100,000/μL), intra-cranial metastatic disease from renal cell cancer, thyroid cancer, or melanoma primary tumors as relative contra-indications to catheter directed thrombolysis.

Following treatment for ALI, long-term therapeutic anticoagulation is recommended to prevent recurrent thromboembolic complications in patients who have chronic atrial fibrillation or valvular heart disease. Long-term anticoagulation is similarly indicated for patients with established hypercoagulability. We have traditionally used subcutaneous low molecular weight heparin injection as the chronic anticoagulation therapy of choice for cancer patients. However, oral direct thrombin inhibitors have recently become available and are emerging as a comparable and more attractive option for patients. The long-term use of anticoagulation after vascular intervention for ALI in patients with a malignancy but without cardiogenic embolic source is not well described. We have empirically recommended a 3–6 month period of anticoagulation for these patients.

Radiation Induced Vasculopathy

Late onset radiation induced vasculopathy can develop several years after high-dose external beam radiation therapy for various kinds of cancer. It is postulated that radiation can cause acute injury to the vasa vasorum and endothelium, that leads to subsequent accelerated atherosclerosis and formation of occlusive plaque in irradiated vessels [40]. Radiation vasculopathy appears to affect the major arteries more frequently than the vein counterparts.

Radiation induced carotid disease is discussed elsewhere in this book. The external iliac artery appears to be the most commonly affected pelvic vessel in women who had radiation treatment for cervical and vulvar cancer [41, 42]. Radiation induced vasculopathy can also involve other any major artery that is within the index radiation field, such as the axillary or femoral artery in the treatment of breast cancer, limb sarcoma, myeloma, lymphoma, and etc. We recommend expectant medical therapy with exercise, aspirin and statin therapy for patients who have non-critical ischemia related to radiation induced vasculopathy.

Vascular intervention is reserved for limb-salvage in patients who have symptoms and signs of critical limb-threatening ischemia. These patients can present with acute, subacute, or chronic insidious ischemic symptoms. Endovascular interventions including catheter directed thrombolysis and arterial stenting have produced satisfactory results, but are associated with high rate of re-interventions. Surgical bypass has resulted in seemingly better long-term graft patency and lower re-intervention rates, and can be offered to patients in whom endovascular interventions have failed or are not feasible. In general, surgical bypass options involving extra-anatomical bypass procedures such as cross-over bypass from the contralateral common femoral artery to ipsilateral common femoral artery, or axillary-femoral artery bypass are preferred to avoid the risks associated with operating in a previously irradiated abdomen or pelvis. However, aorto-bifemoral bypass remains an option for patients with limb-threatening ischemia due to severe bilateral aorto-iliac occlusive disease not amenable to endovascular intervention. Much work lies ahead of us to determine the pathogenesis of radiation-induced vasculopathy in order to improve our management and ultimately prevent its development.

Chemotherapy and Vascular Thrombosis

Several chemotherapy drugs have been reported to increase risk of VTE, arterial thrombosis or both in cancer patients, although the mechanism of causing thrombosis for various agents is yet fully elucidated [4, 43]. Currently, Cisplatin, an alkylating agent, and Bevacizumab, a monoclonal antibody targeting the vascular endothelial growth factor (VEGF) are two widely used drugs in the treatment of solid malignant neoplasms that have been associated with increased risk of myocardial infarction, stroke and peripheral arterial thrombosis [44, 45]. The newer tyrosine kinase inhibitors (TKI), Imatinib, Nilotinib and Ponatinib, recently established as highly effective front-line therapies for chronic myeloid leukemia (CML), have also been linked to increased risk of peripheral arterial thrombosis [46]. However, in a recent case-controlled study using the Surveillance, Epidemiology, End-Results (SEER) cancer registry and Medicare claims data, investigators showed that elderly patients with CML have greater rates of myocardial infarction, stroke, pulmonary embolism and peripheral artery disease than age-matched non-cancer patients from the same region [47]. These event rates were not higher in the TKI-treated patients suggesting that risk for the vascular events in the patients with CML was more related to underlying cardiovascular risk factors of patients with CML and not with TKI treatment.

Treatment of Arterial Complications at the University of Texas-M.D. Anderson Cancer Center

The following are the synopsis of ten patients with critical limb ischemia recently treated at The University of Texas--M.D. Anderson Cancer Center. We review their clinical presentation, management, and outcome. Vascular imaging and photographs of the cases are shown. In addition, we provide brief pertinent expert comments on each case. We selected these ten cases as examples of common and rare arterial complications seen in patients who either have concomitant active malignancy or are cancer survivors.

Case #1. Metastatic Esophageal Cancer and Chronic Critical Leg Ischemia

A fifty-six year-old Caucasian male was referred to our institution for treatment of stage IV distal esophageal adenocarcinoma with distant metastasis to the left arm triceps muscle. The patient was a former smoker and had chronic renal insufficiency. The patient had right external iliac artery stenting and multiple failed left leg bypass graft procedures (Fig. 9.1a–d). Initially, the patient only reported left leg claudication and intermittent symptoms of ischemic rest pain in the left foot. Vascular assessment showed ABI in the severe ischemic range and multilevel arterial occlusive disease. However, the viability of the left ischemic leg was not immediately threatened. We first recommended medical therapy with aspirin, cilastazol, and statin. Chemotherapy with 5-FU and Herceptin was started. Subsequently, the patient showed remarkable oncologic response to systemic chemotherapy, becoming symptom-free from his cancer after approximately 18 months of treatment. The patient remained on maintenance chemotherapy and resumed full-time work.

At 20 months after cancer diagnosis, the patient became more incapacitated by progressive claudication symptoms and experienced worsening ischemic rest pain in the left foot. Vascular work-up showed chronic occlusion of left external iliac, common femoral, and superficial femoral arteries with

reconstitution of the distal below-knee popliteal artery via collateral from patent profunda artery (Fig. 9.1e). On the right, there was severe stenosis of the right external iliac artery. The decision was made to proceed with revascularization of the left leg for limb-salvage. We opted for a hybrid procedure with stenting of the right common (using 8 × 27 mm balloon-expandable stent) and external (7 × 10 mm covered self-expandable stent-graft) iliac arteries (Fig. 9.1f), and concomitant redo cross-over right common femoral artery to left profunda artery bypass using an 8 mm heparin-bonded PTFE graft. The patient recovered well after hybrid surgical revascularization with resolution of both ischemic rest symptoms and claudication. Postoperative duplex image of fem-fem PTFE graft and left profunda shows satisfactory appearance and flow (Fig. 9.1g, h). Maintenance chemotherapy was resumed after a 6-week interruption. The patient is currently at 5 months after revascularization without symptoms of leg claudication or rest pain. Unfortunately, a recurrent malignant stricture in the distal esophagus has been diagnosed and further oncologic treatment is being considered at the time of writing this manuscript.

Comments: Even though this patient had severe chronic leg ischemia when he was first diagnosed with metastatic esophageal cancer, we prioritized his cancer treatment to prolong his survival over the limb ischemia. Revascularization was delayed until after the patient showed clinical response to chemotherapy. An alternative revascularization option for this patient would have been an aorto-bifemoral bypass reconstruction, but this would have interrupted the patient's maintenance chemotherapy for a longer post-operative

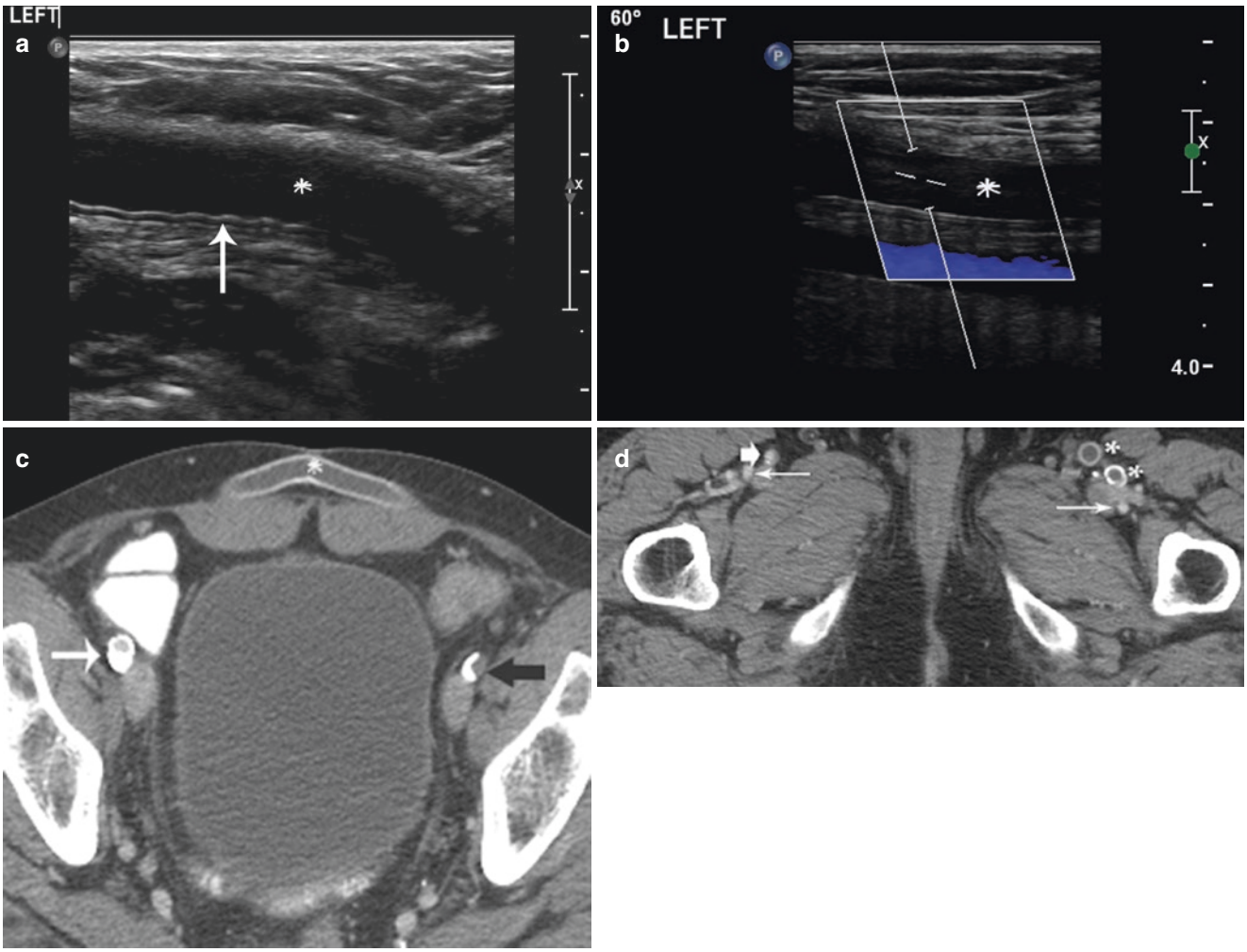


Fig. 9.1 Metastatic esophageal cancer and chronic critical leg ischemia. (**a**) Gray-scale ultrasound image shows an occluded supra-pubic cross-over femoro-femoral synthetic bypass graft; *asterisk*, lumen of graft (filled with hypoechoic thrombus), and *arrow* points to wall of graft. (**b**) Colorflow ultrasound image shows an occluded left femoral-popliteal synthetic graft; *asterisk*, lumen of graft (filled with hypoechoic thrombus). *Blue colorflow* is seen in the native femoral vein adjacent to the graft. (**c**) Axial CT image shows the occluded native left distal external iliac artery (*black arrow*) and a calcified and narrowed distal right external iliac artery (*white arrow*). (**d**) Axial CT image shows the occluded synthetic grafts (*asterisk*) with bright rims in the left groin; *long arrows* point to the respective patent native profunda arteries. The *short arrow* denotes the patent right superficial femoral artery.

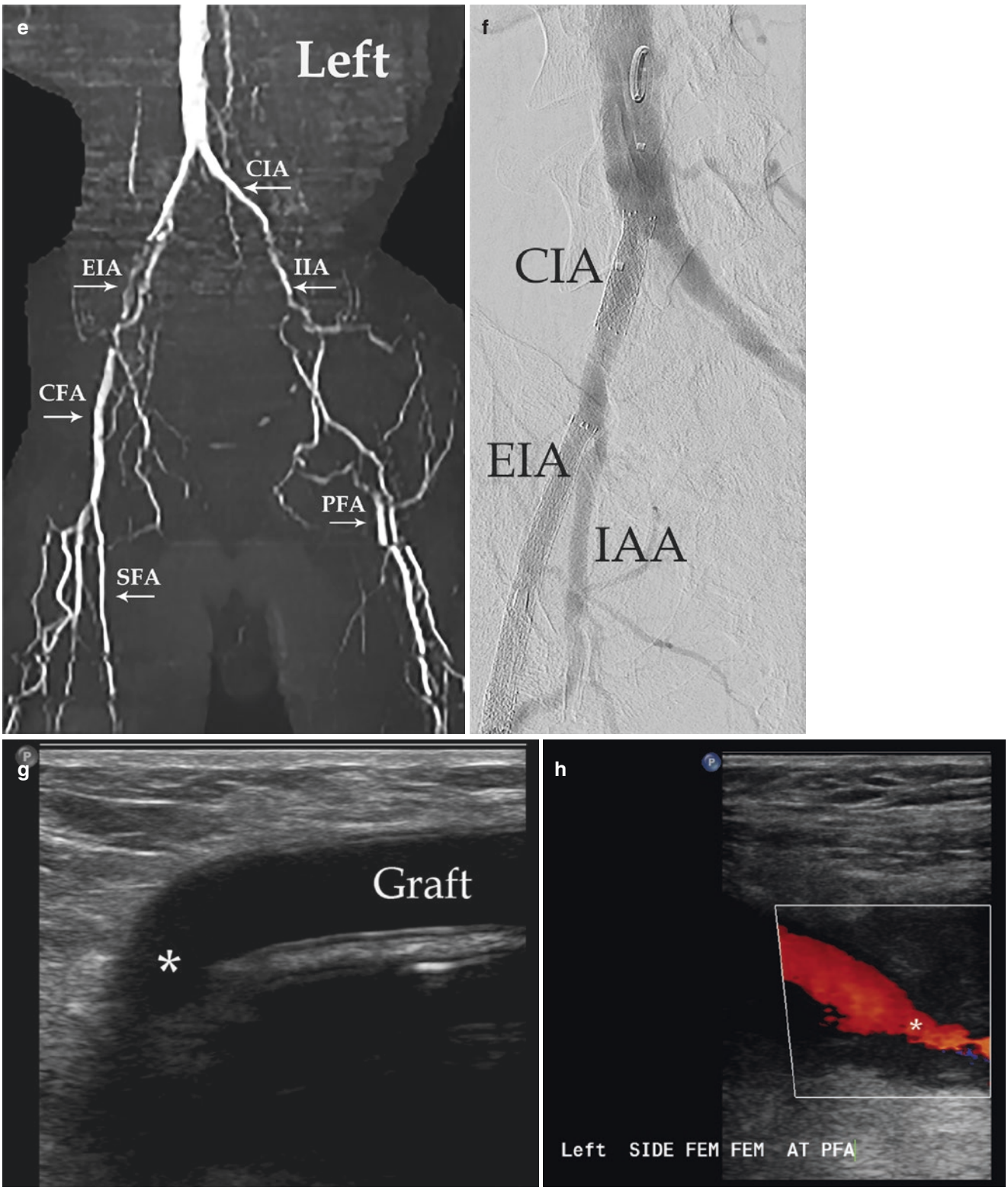


Fig. 9.1 (continued) (**e**) Reformatted MRA image reveals patency of the distal abdominal aorta and bilateral common iliac arteries (CIA). The right external iliac artery (EIA) is severely diseased and the left external iliac and common femoral arteries are occluded. The right common femoral (CFA), profunda and superficial femoral (SFA) are patent. On the left, numerous branches of the internal iliac (IIA) and profunda (PFA) arteries are seen. (**f**) Right iliac stenting was performed as part of a hybrid revascularization procedure to provide inflow to a new cross-over right to left femoro-femoral bypass graft. Stents are shown in the right common iliac (CIA) and external iliac (EIA) arteries; IAA, internal iliac artery. (**g**) Gray-scale ultrasound image shows the new cross-over femoro-femoral synthetic graft showing the right femoral-graft anastomosis (*asterisk*). (**h**) Colorflow ultrasound image shows the new femoro-femoral synthetic graft at the left graft to profunda femoral artery (PFA) anastomosis (*asterisk*)

recovery. It is also noteworthy to mention that the patient's ischemic leg symptoms resolve following the inflow procedure and distal bypass of the left femoral and popliteal artery occlusion was not required.

Case # 2. Acute Femoral Artery Thromboembolism in a Patient with Metastatic Renal Cell Cancer

A fifty-eight year-old Caucasian woman presented to the emergency room with 24-h history of acute right leg ischemic symptoms including pain, numbness and weakness. The patient had started Axitinib (a tyrosine kinase inhibitor—TKI) treatment for progressive metastatic renal cell cancer to the lungs. The patient had radical right nephrectomy 7 years prior and partial left nephrectomy for bilateral renal cell cancer 4 years later. Duplex ultrasound showed acute occlusion of the right common femoral and superficial femoral arteries with distal reconstitution (Fig. 9.2a, b). We performed surgical thromboembolectomy removing occluding clots from the femoral artery bifurcation (Fig. 9.2c, d). Her native iliac, femoral, popliteal and tibial arteries were otherwise normal without significant plaque disease. After successful revascularization, the patient was initiated on long-term anticoagulation, transitioning from unfractionated intravenous heparin to warfarin. Cardiac work-up showed normal sinus rhythm and normal left ventricular ejection fraction without evidence of a thrombus or valvular heart disease. The patient resumed Axitinib few weeks after thromboembolectomy and was kept on warfarin. However, she developed intermittent hemoptysis the following year and systemic anticoagulation was discontinued. Two years after the

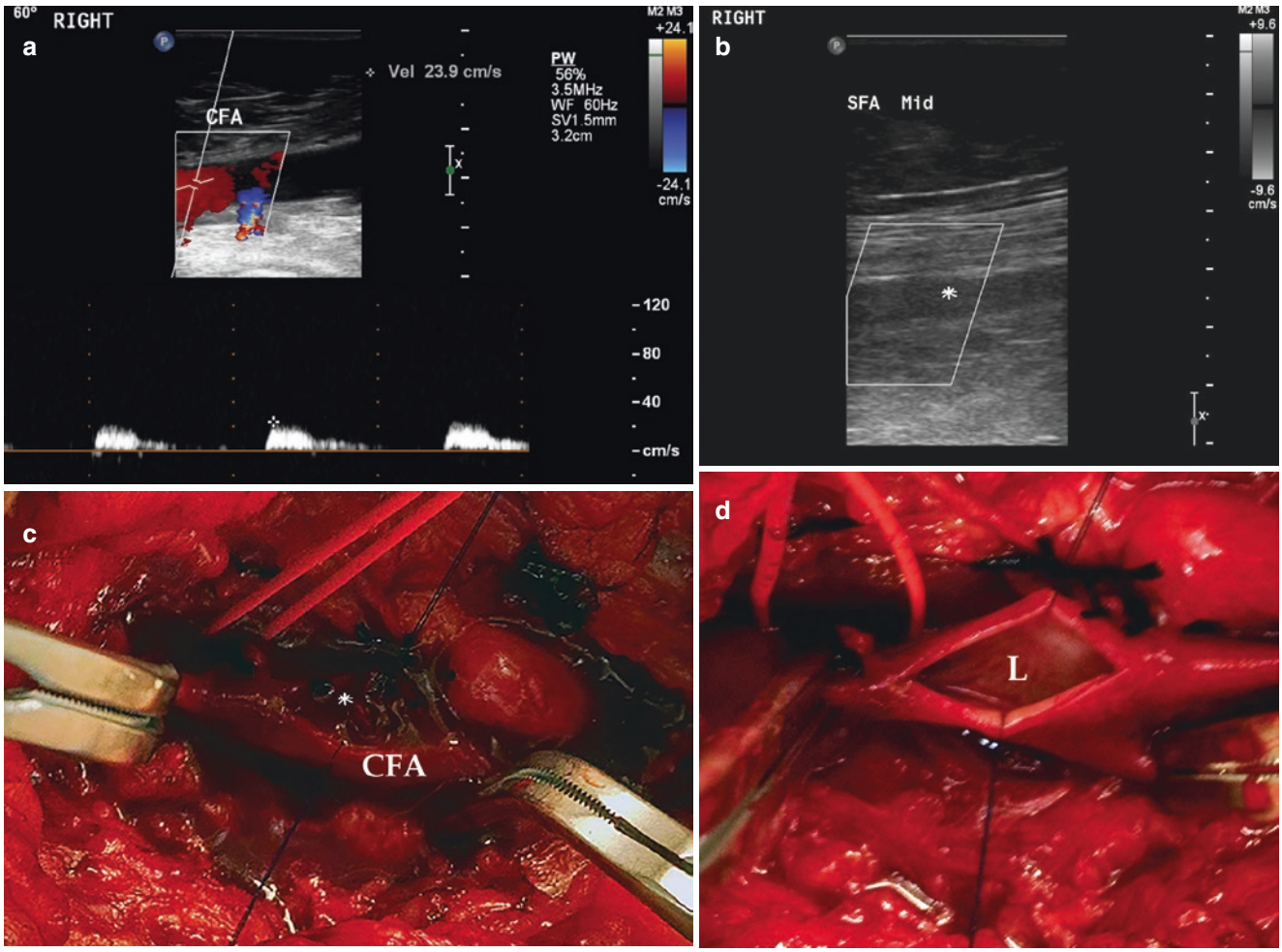


Fig. 9.2 Acute femoral artery thromboembolism in a patient with metastatic renal cell cancer. (**a**) Ultrasound image shows blunted low flow velocity in the common femoral artery. (**b**) Gray-scale ultrasound image shows the occluded superficial femoral artery (SFA) with lumen filled by hypoechoic thrombus (*asterisk*). (**c**) Intra-operative photograph shows fresh clots (*asterisk*) inside the lumen of opened common femoral artery (CFA). Artery is temporarily clamped proximally and distally during thromboembolectomy. (**d**) Intra-operative photograph of the CFA after removal of the clots demonstrates the normal appearance of the luminal surface (L) and vascular wall

acute thromboembolic event, the patient's metastatic disease has progressed to the brain. The patient also developed new onset of atrial fibrillation and cardiomyopathy. She has been started on Cabozantinib (a newer TKI approved for advanced renal cell cancer) and is currently resuming anticoagulation.

Comments: At the time the acute arterial thromboembolic event, it was not clear whether the acute arterial thrombosis was related to hypercoagulability, TKI drug, or an embolism from a cardiogenic source. At that time, the patient had normal echocardiogram and was in sinus rhythm. The patient has had no recurrent arterial thromboembolic event while remaining on TKI, even when anticoagulation was stopped. In this case, the exact cause or source of the thromboembolic event remained undetermined even though the patient subsequently developed atrial fibrillation.

Case # 3. High-Grade Invasive Bladder Cancer and Subacute Left Leg Ischemia After Neoadjuvant Chemotherapy

A sixty-five year-old woman former heavy smoker was referred to our institution for treatment of high-grade invasive urothelial cancer. Prior trans-urethral partial resection of the tumor resulted in bladder perforation and neodajuvant chemotherapy was recommended prior to definitive cystectomy (combination of Methotrexate, Vinblastine, Adriamycin, and Cisplatin). The patient completed five cycles of chemotherapy but developed insidious onset of left leg disabling hip and calf claudication, ischemic rest pain, and left foot numbness toward the end of chemotherapy. The patient denied antecedent claudication symptoms. Prior CT imaging showed non-occlusive arteriosclerotic plaque disease in the aorta and bilateral iliac arteries. Repeat CT imaging demonstrated interval occlusion of the left common and external iliac arteries (Fig. 9.3a). An incidental right lower lobe pulmonary embolus was also found on CT. Cardiac evaluation was negative.

We performed catheter-directed thrombolysis and successfully recanalized the left common and external iliac arteries (Fig. 9.3b). A focal residual stenosis in the left external iliac artery was stented (Fig. 9.3c). The patient was kept on therapeutic low molecular weight heparin and aspirin after revascularization. She underwent radical bladder cystectomy with neo-bladder urinary diversion and bilateral pelvic node dissection 2 weeks after the endovascular intervention. The patient made remarkable progress after oncologic surgery. She completed 4 months of anticoagulation and remained on aspirin. She returned to full-time work within couple of months. One year following her oncologic surgery, the patient developed locally advanced tumor recurrence. She also reported recurrent left leg claudication symptoms. Re-occlusion of the left iliac arteries and stent was confirmed on imaging. As she did not have symptoms or signs of immediate limb-threatening ischemia, the patient declined repeat vascular intervention. Unfortunately, it was deemed that further oncologic treatment would not benefit the patient and she passed away approximately 2 years after the initial cancer diagnosis.

Comments: We postulate that this patient was likely hypercoagulable. The combination of high-grade malignancy and aggressive chemotherapy both contributed to the acute arterial thrombosis. Interestingly, the patient did have a normal duplex ultrasound of the stented left iliac artery at 6–9 months after stent placement, suggesting that the vascular re-occlusion may have been due to cancer-related hypercoagulability state. It is conceivable that re-occlusion of the left iliac arteries and stent could have been prevented if anticoagulation had been maintained.

Case # 4. Renal Cell Cancer and Severe Aorto-Iliac Occlusive Disease

A sixty-seven year-old male presented with chronic progressive disabling hip and calf claudication bilaterally, new onset of severe ischemic rest pain in both feet, and non-healing right toe ulcer. Vascular work up demonstrated chronic occlusion of the infra-renal aorta and bilateral common iliac arteries on CT angiogram (Fig. 9.4a), and an incidental finding of a large exophytic right renal mass. Because of the incapacitating ischemic pain in his legs, the patient was unable to begin oncologic therapy. Therefore, we elected to proceed first with surgical revascularization to relieve the ischemic pain in his legs. Following successful axillary-bifemoral bypass grafting, the patient's pain resolved and his performance status improved rapidly (Fig. 9.4b, c). Although the patient had metastatic disease, the cancer was deemed oncologically "stable", and a debulking radical right nephrectomy was recommended. The patient underwent oncologic resection approximately 3 months after the extra-anatomical surgical bypass without complications. The patient was then kept on surveillance until progression of metastatic disease was noted in imaging approximately 2 years after the initial cancer diagnosis, at which time he was started on Pazopanib. His axillo-bifemoral bypass remains patent at 26 months (Fig. 9.4d, e).

Comments: This patient's chronic aorto-iliac occlusion was not amenable to endovascular intervention. One alternative option would have been concomitant surgical aorto-bifemoral bypass and radical right nephrectomy. However, major concomitant surgery was initially deemed not beneficial, in light of the metastatic disease, uncertain cancer behavior, and poor performance status at presentation. Although primary chemotherapy without oncologic resection was the initial recommended oncologic therapy, because of the observed "stability" of the cancer and patient's improved performance status after surgical revascularization, the oncologic strategy changed to surgical tumor resection.

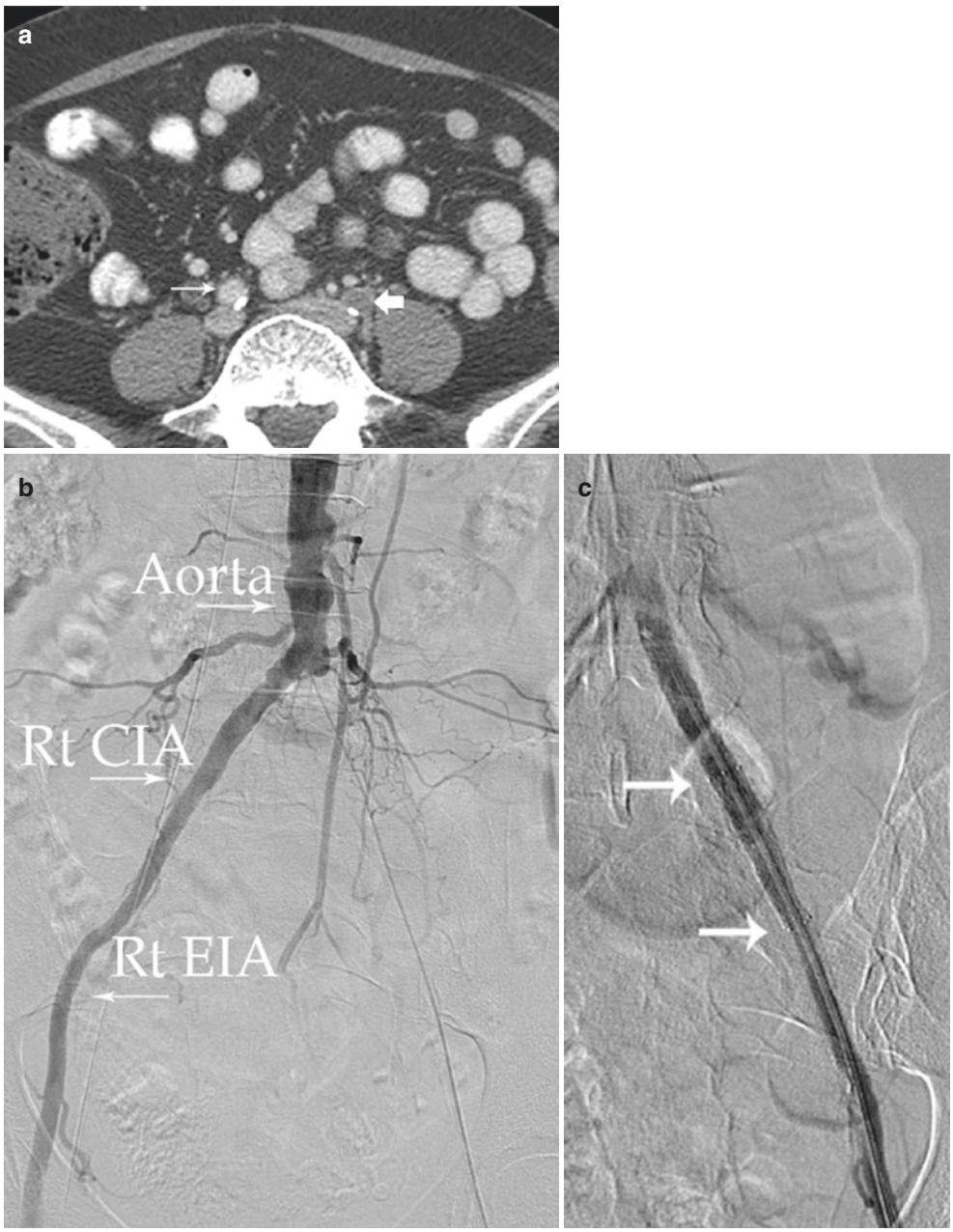
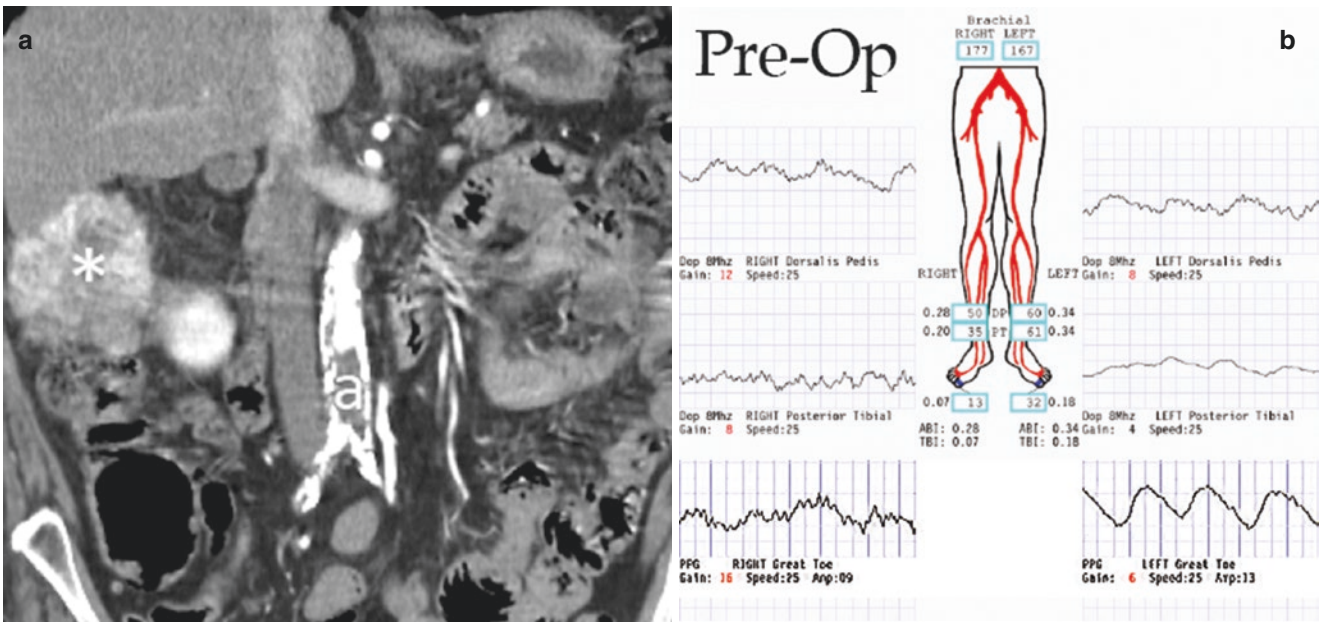


Fig. 9.3 High-grade invasive bladder cancer and subacute left leg ischemia after neoadjuvant chemotherapy. (**a**) Axial CT image shows no contrast filling of the occluded left common iliac artery (*short arrow*) and patent right common iliac artery (*long arrow*); calcified plaque is seen in the posterior wall of both iliac arteries. (**b**) Digital substraction angiographic (DSA) image shows total occlusion of the left common and external iliac arteries (no contrast filling). The distal aorta is irregular with non-occlusive plaque disease. The right (Rt) common (CIA) and external iliac (EIA) arteries are patent without significant luminal stenosis. (**c**) DSA image of the stented left common/external iliac artery (*arrows* point to the proximal and distal edges of stent); no contrast filling of occluded left internal iliac artery

Case # 5. Blue Toe Syndrome and Lung Cancer

A sixty-eight year-old man developed right leg DVT and was started on rivaroxaban. Further work-up found non-small cell lung cancer (NSCLC). The patient underwent right upper lobectomy. Pathological and clinical staging was IIIA with repeat PET/CT showing residual disease in the mediastinum after surgical resection. The patient was scheduled to receive concurrent chemoradiation therapy 6 weeks post-operatively. He developed painful blue toe syndrome involving mostly the first and fifth left toes just prior to starting chemoradiation (Fig. 9.5a, b). Vascular work up revealed normal pedal pulses. CT angiogram showed minimal plaque disease in the aorto-iliac and infrainguinal arteries. Aspirin therapy was added to anticoagulation. The ischemic pain and discoloration in the affected toes resolved with expectant management. Patient tolerated three cycles of Carboplatin and Paclitaxel without further vascular complications (at the time of this writing).

Comments: Blue toe syndrome is typically due to an atheroemboli, or a microemboli occluding a small distal digital vessel. The embolic source is usually an atherosclerotic



Lower Arterial Segmental Pressures

c

Post-Op

Right			Left
158		Brachial	156
99	- 0.63	Ankle (PT)	112 - 0.71
91	- 0.58	Ankle (DP)	106 - 0.67
78	- 0.49	1st Toe	88 - 0.56

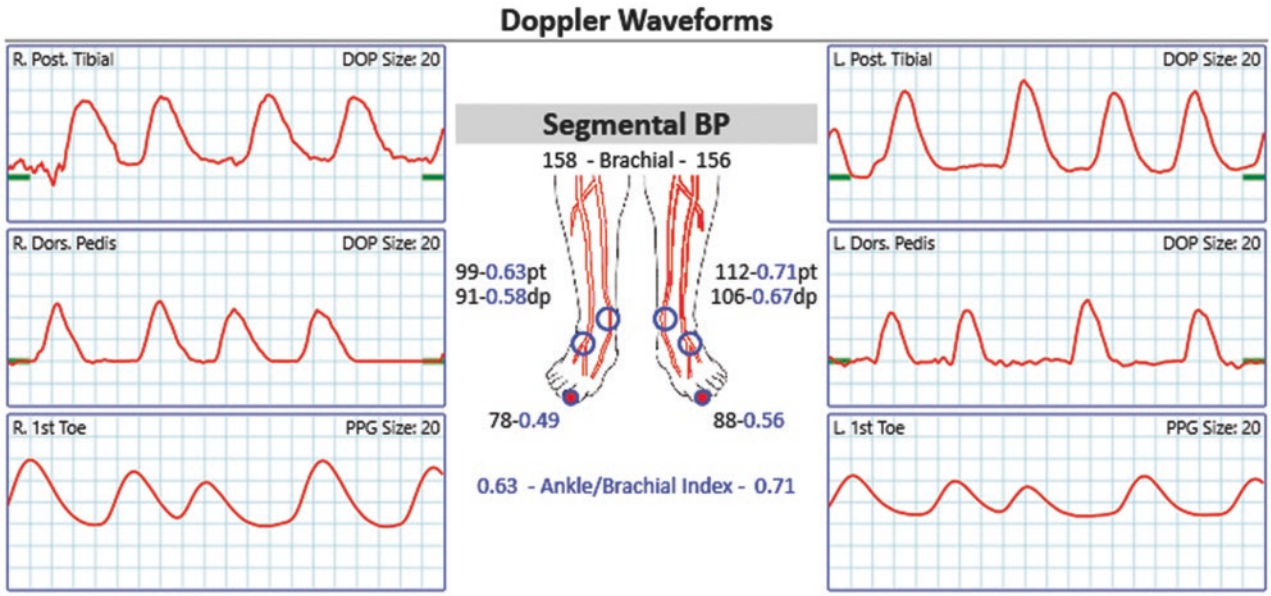


Fig. 9.4 Renal cell cancer and severe aorto-iliac occlusive disease. (**a**) Coronal CT image of abdomen shows heavily calcified occluded aorto-biiliac arteries (**a**) and large exophytic mass (*asterisk*) in superior pole of the right kidney. (**b**) Physiologic arterial testing shows severely reduced preoperative ankle-brachial indexes (ABI): 0.28 on right and 0.34 on left. (**c**) Post-operative ABIs are increased: 0.63 on right and 0.71 on left.

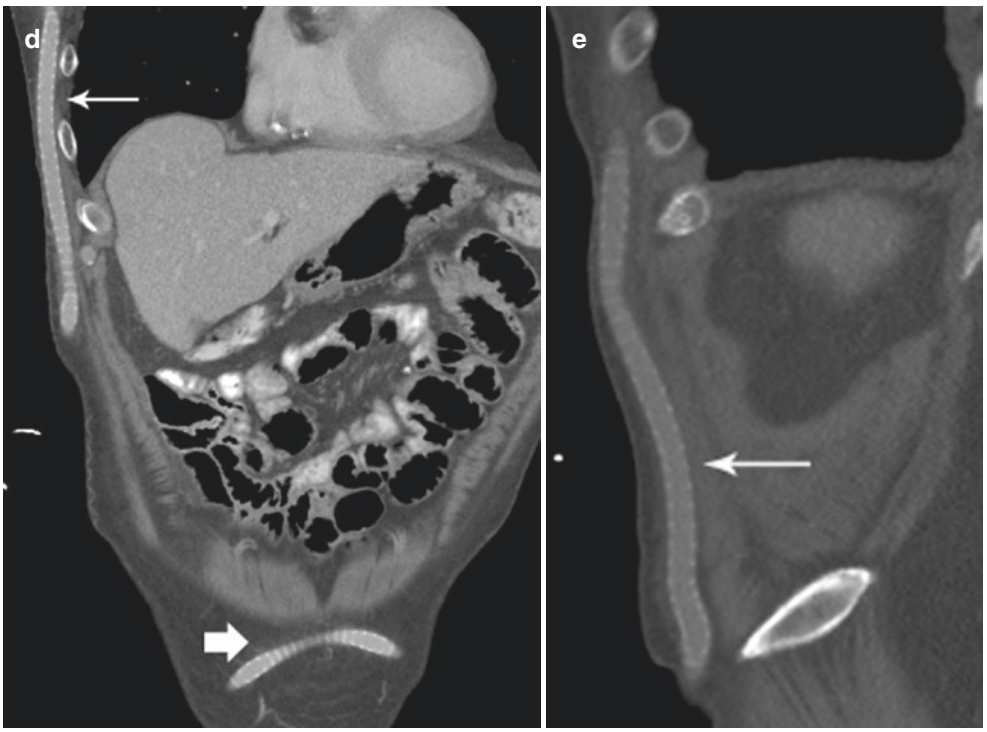


Fig. 9.4 (continued) (**d**) Coronal CT image shows patent axillary (*thin arrow*) and femoral (*short arrow*) segments of the extra-anatomical bypass reconstruction. (**e**) Patent axillary segment of axillo-bifemoral bypass graft (*arrow*) is shown on sagittal CT image

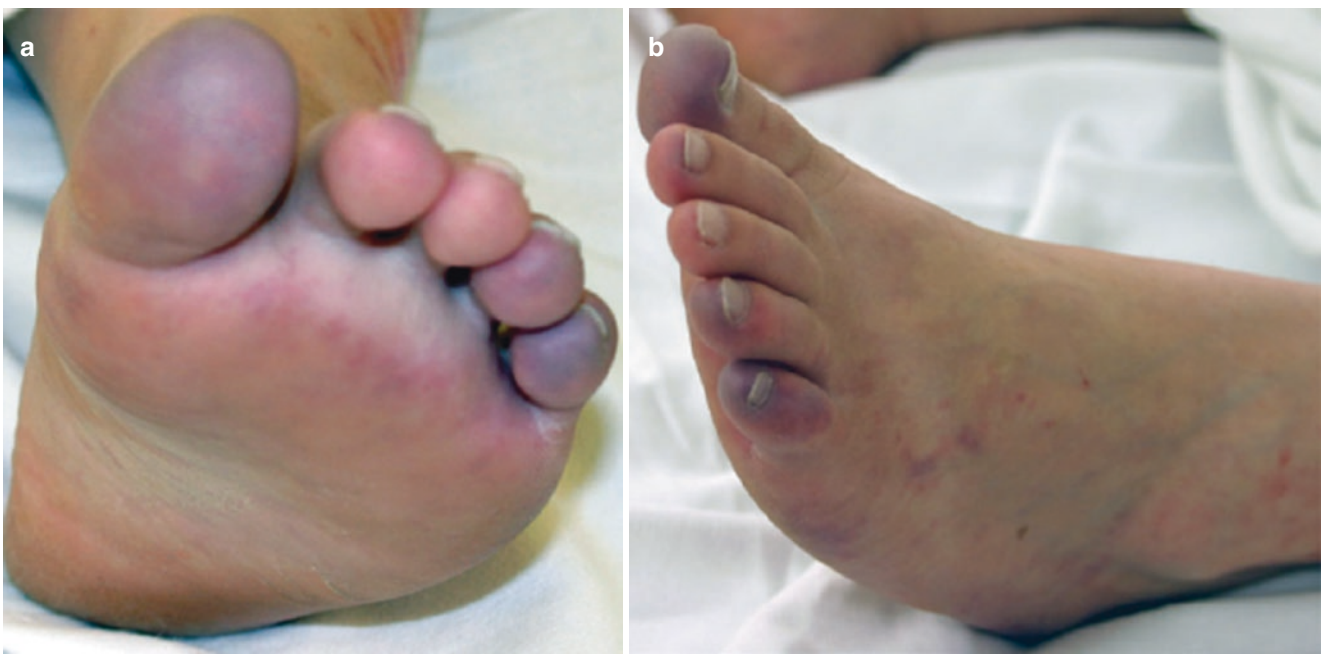


Fig. 9.5 Blue toe syndrome and lung cancer. Photographs of the patient's left foot show blue discoloration of the ischemic first and fifth toes on plantar (**a**) and dorsal (**b**) views

plaque in a proximal large vessel such as the aorta or iliac arteries. The classic description refers to ischemia of one or more toes in the absence of large vessel occlusive disease. We have observed blue toe syndrome in patients with various types of solid tumors. We generally recommend antiplatelet and statin therapy for blue toe syndrome.

Case # 6. Multiple Myeloma and Acute on Chronic Critical Leg Ischemia

This is the case of a Caucasian male diagnosed with multiple myeloma in 1995. The patient had external beam radiation to right hip and sacrum. He received three cycles of melphalan and prednisolone therapy in 1995 and remained on maintenance cyclophosphamide treatment ever since. The patient reported a 15 pack-years history of tobacco smoking but quit in 1990. In addition, he has well-controlled longstanding non-insulin dependent diabetes and essential hypertension. The patient developed an acute right parietal ischemic stroke in 2011, at the age of 66, and had right carotid endarterectomy for severe proximal internal carotid artery stenosis. The patient was kept on aspirin, statin, anti-hypertensive, metformin, and cyclophosphamide maintenance therapy. In 2013, the patient develops insidious onset of right leg ischemic rest pain, numbness, foot drop and a non-healing wound at the base of the fifth toe (Fig. 9.6a), although he had had chronic bilateral leg claudication. Vascular work-up showed severe occlusive disease of the right common femoral artery bifurcation including proximal superficial femoral (SFA) and profunda arteries, and severe distal right SFA stenosis (Fig. 9.6b–f). We performed hybrid revascularization with extensive right common femoral artery bifurcation endarterectomy and reconstruction with patch angioplasty of the proximal profunda and SFA (Fig. 9.6g–j); concomitant stenting of the right mid to distal SFA was done using covered self-expandable stent-graft (Fig. 9.6k–m). The patient recovered well with good revascularization and eventual healing of ischemic toe wound (Fig. 9.6n, o).

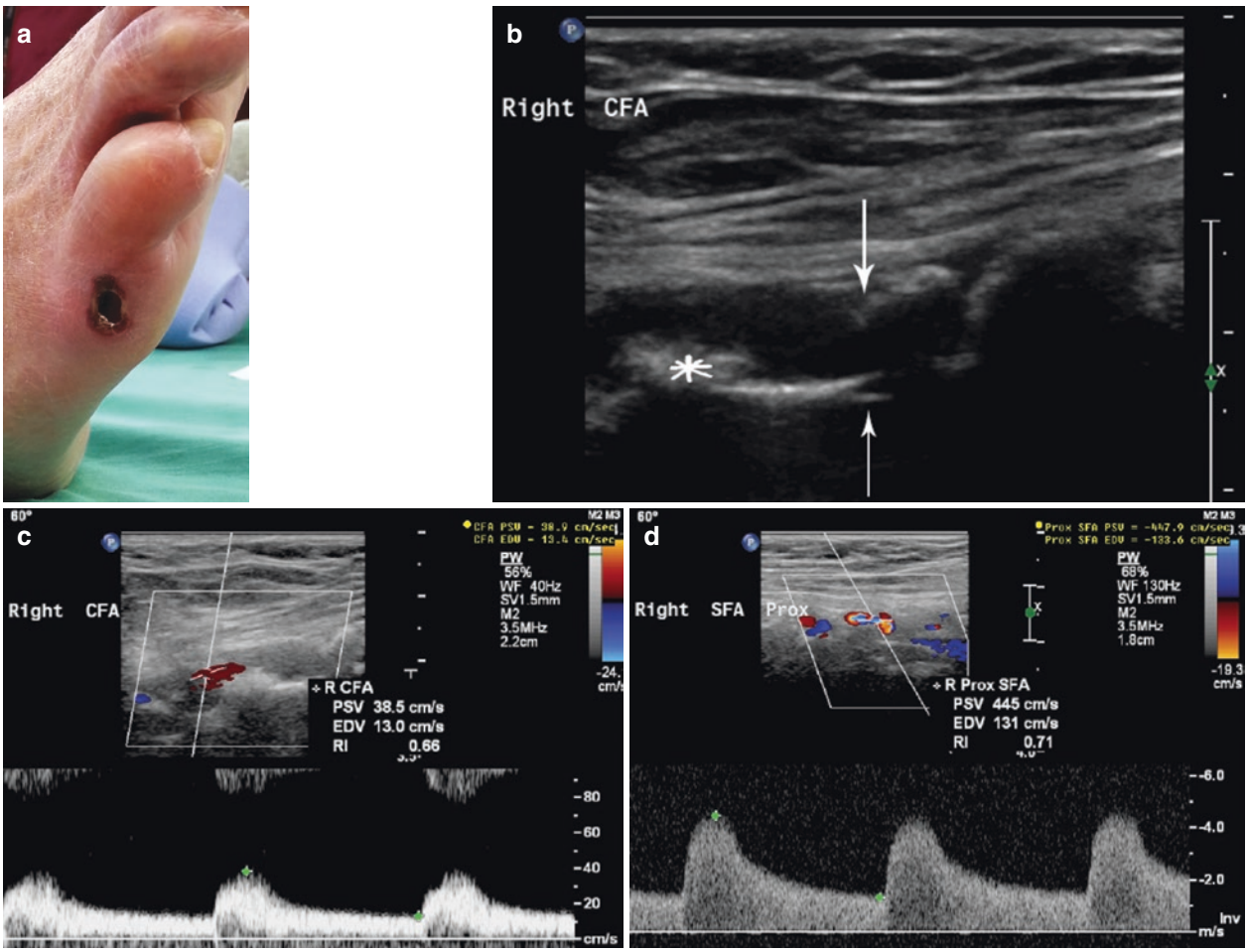


Fig. 9.6 Multiple myeloma and chronic critical leg ischemia. (**a**) Photograph of right foot shows signs of chronic ischemia: non-healing wound at base of the fifth toe, thin skin, muscle atrophy, and toe discoloration. (**b**) Gray-scale image of right common femoral artery (CFA). The *arrows* point to the vessel walls and *asterisk* marks the location of a dense plaque. (**c**) Markedly reduced Doppler flow velocity is shown in the CFA beyond the occluding plaque. (**d**) Increased flow velocities in the proximal superficial femoral artery (SFA) indicate severe vessel stenosis.

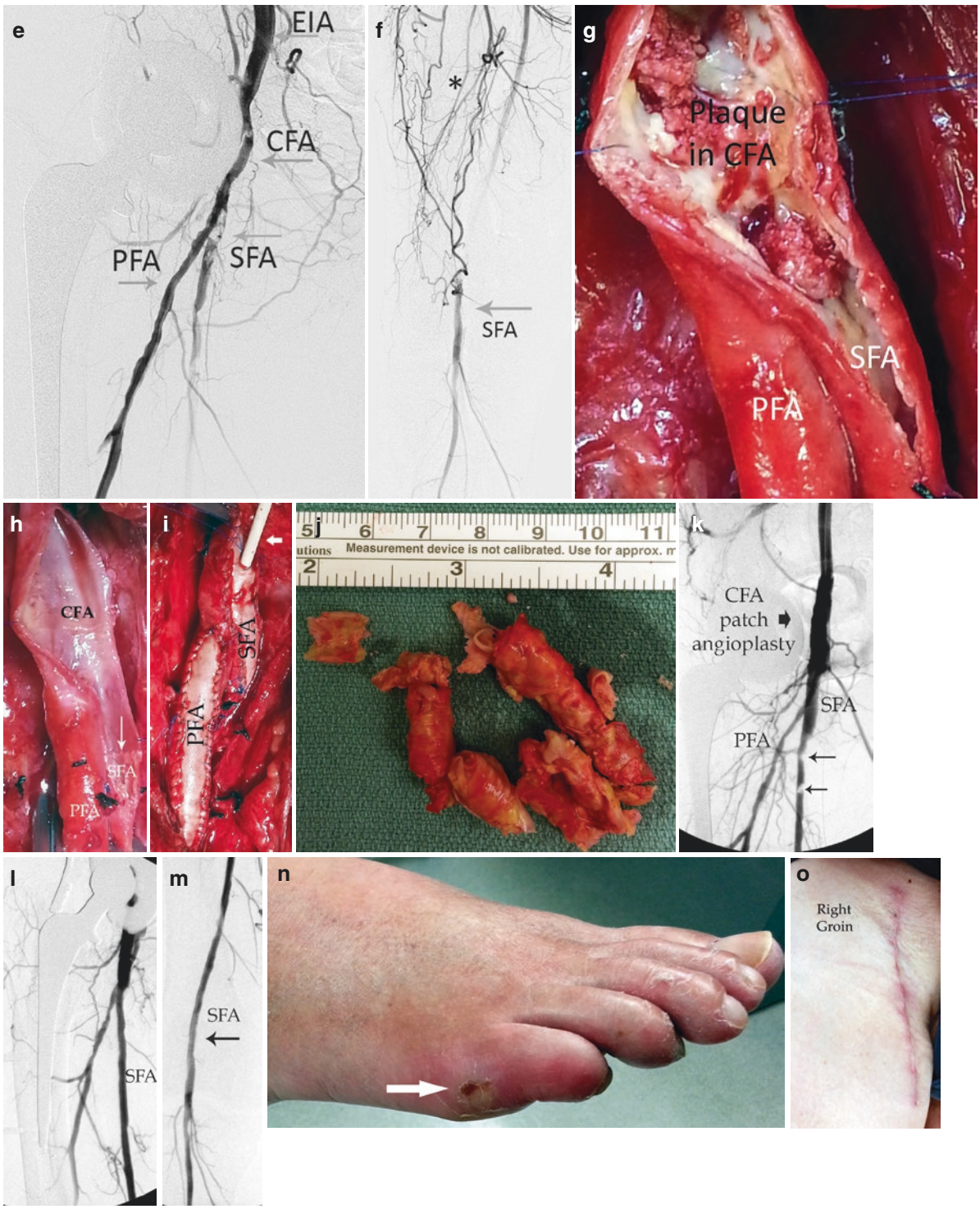


Fig. 9.6 (continued) (**e**) DSA image shows widely patent external iliac artery (EIA), narrowed CFA, nearly occluded proximal SFA, and patent profunda femoral artery (PFA). (**f**) DSA image shows large profunda branches (surrounding *asterisk*) reconstituting flow in the distal SFA. (**g**) Intra-operative photograph depicts an arteriotomy in the CFA extended through the proximal SFA and shows extensive calcified eccentric occluding plaque disease. (**h**) Intra-operative photograph shows luminal surface of CFA after removal of the plaque and endarterectomy; *arrow* points to the distal transition point with residual intimal thickening in the SFA; in this image the PFA is still intact. (**i**) Intra-operative photograph shows reconstructed patch reconstruction of the SFA and PFA after endarterectomy. *Arrow* points to a vascular sheath placed in an antegrade fashion for hybrid endovascular stenting of the remaining SFA stenoses. (**j**) Multiple fragments of the endarterectomized plaque specimen are shown. (**k**) DSA image demonstrates residual severe stenoses in the SFA distal to the patch angioplasty (*arrows*) after patch angioplasty reconstruction of the femoral artery bifurcation. (**l**) Completion DSA image shows satisfactory appearance of proximal to mid SFA stenting. (**m**) Completion DSA image shows satisfactory appearance of distal SFA stenting (*arrow* points to stent). (**n**) Photograph demonstrates healing of toe wound (*arrow*) after revascularization. (**o**) Hybrid revascularization including concomitant femoral endarterectomy and reconstruction and SFA stenting was completed through a single right groin incision

The patient subsequently developed similar symptoms of ischemic rest pain in the left leg and underwent similar hybrid revascularization successfully in 2015. The following year, the patient sustained acute myocardial infarction following right hip redo replacement and had drug-eluting stents placed in the right coronary artery. Dual antiplatelet therapy was added. Just over 12 months after right coronary artery stenting, the patient now reports that he has been recommended to undergo coronary artery bypass for multivessel coronary artery disease.

Comments: This case underscores the systemic nature of atherosclerotic disease. In this patient, the first cardiovascular manifestation was an embolic stroke from severe carotid artery disease. He then had bilateral extremity revascularization for severe multilevel arterial occlusive disease and subsequently coronary revascularization. All these events took place within 5–6 years while the patient remained on maintenance chemotherapy (cyclophosphamide) for multiple myeloma. Anecdotally, this case demonstrates that long-term survival is possible for patients with cardiovascular risk factors and active cancer. Regarding the treatment of severe common femoral bifurcation occlusive disease, surgical endarterectomy and reconstruction remains the treatment of choice. In this case, hybrid revascularization allowed concomitant surgical reconstruction of the common femoral artery bifurcation and stenting of the tandem proximal and distal SFA occlusive lesions. Adjunct femoral artery stenting is less invasive with clear advantages over the traditional femoro-popliteal bypass with less post-operative pain and swelling.

Case # 7. Ulcerated Squamous Cell Skin Cancer in Patient with PAD

A sixty-eight year-old woman presented with cutaneous squamous cell cancer in a chronic painful large ulcerated wound in her right calf (Fig. 9.7a). Work-up showed prior infrarenal aortic graft reconstruction for abdominal aortic aneurysm and chronic occlusion of the right superficial femoral artery with reconstitution of the above-knee popliteal artery and 2–3 vessel run-off (Fig. 9.7b, c). We staged her treatment. First, we performed surgical revascularization with a femoral to popliteal artery bypass using ipsilateral great saphenous vein graft (Fig. 9.7d). Wide surgical resection of the cutaneous cancer was subsequently done with skin engrafting (Fig. 9.7e).

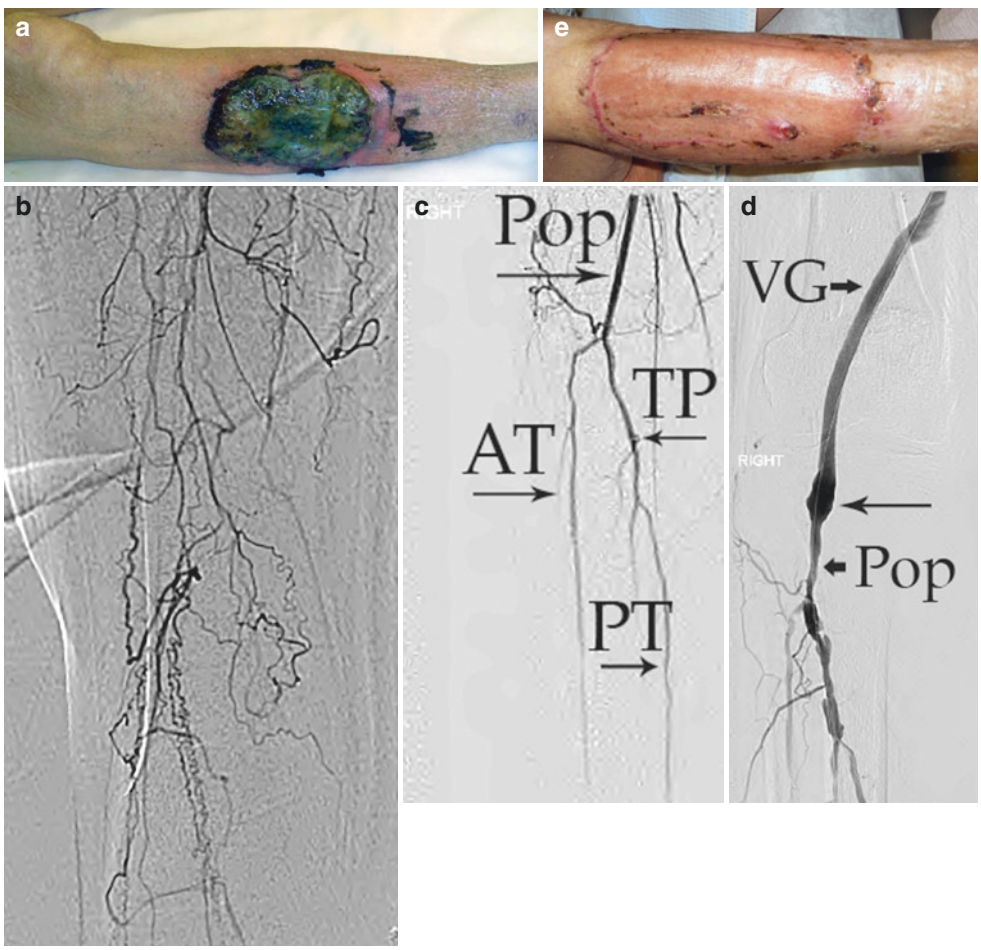


Fig. 9.7 Ulcerated squamous cell skin cancer in patient with PAD. (**a**) Photograph shows the large ulcerated skin growth. (**b**) DSA image of mid thigh demonstrates large collateral network from profunda branches secondary to chronic occlusion of the superficial femoral artery. (**c**) DSA image shows reconstituted popliteal (Pop), patent anterior tibial (AT), tibio-peroneal (TP) trunk, and posterior tibial (PT) arteries. (**d**) Completion DSA image after femoro-popliteal artery bypass shows satisfactory appearance of the vein graft (VG; *short arrow*). *Long arrow* points to the distal anastomosis. (**e**) Photograph shows healed skin graft wound following wide tumor resection

Comments: Endovascular recanalization of the long chronic right superficial femoral artery was not possible. However, staged surgical revascularization and wide oncologic resection allowed for limb-salvage, as opposed to the alternative option of major limb amputation.

Case # 8. Radiation Induced Femoral Artery Occlusion Following Surgical Resection and Radiation Treatment for Extremity Desmoid Tumor

A thirty-seven year-old woman presented with insidious onset of severe left leg pain for several months. Her past history included surgical resection of desmoid tumor in the left posterior thigh and adjuvant high dose external beam radiation at age of 16. Approximately 15 years later, the patient was found to have local recurrence in the left posterior thigh and had a second round of high dose external beam and repeated surgical resection. In addition, multiple subsequent orthopedic interventions were required to treat non-union pathologic fractures of left femur (Fig. 9.8a, b). Meanwhile, the patient continued to receive systemic single agent chemotherapy including Tamoxifen first, then Imatinib (TKI), and lastly Sorafenib (TKI) for recurrent regional disease. At the time of the vascular complication, Sorafenib was on hold due to other side effects. Vascular work-up showed critical ischemia of the left due to radiation induced long occlusion of the left superficial femoral artery with reconstitution of the popliteal artery (Fig. 9.8c–f). We performed left common femoral to below-knee popliteal artery bypass using ipsilateral saphenous vein graft for limb-salvage. The left leg bypass graft is still patent 2 years after reconstruction (Fig. 9.8g, h). The patient remains active and has resumed Sorafenib for progressive regional disease.

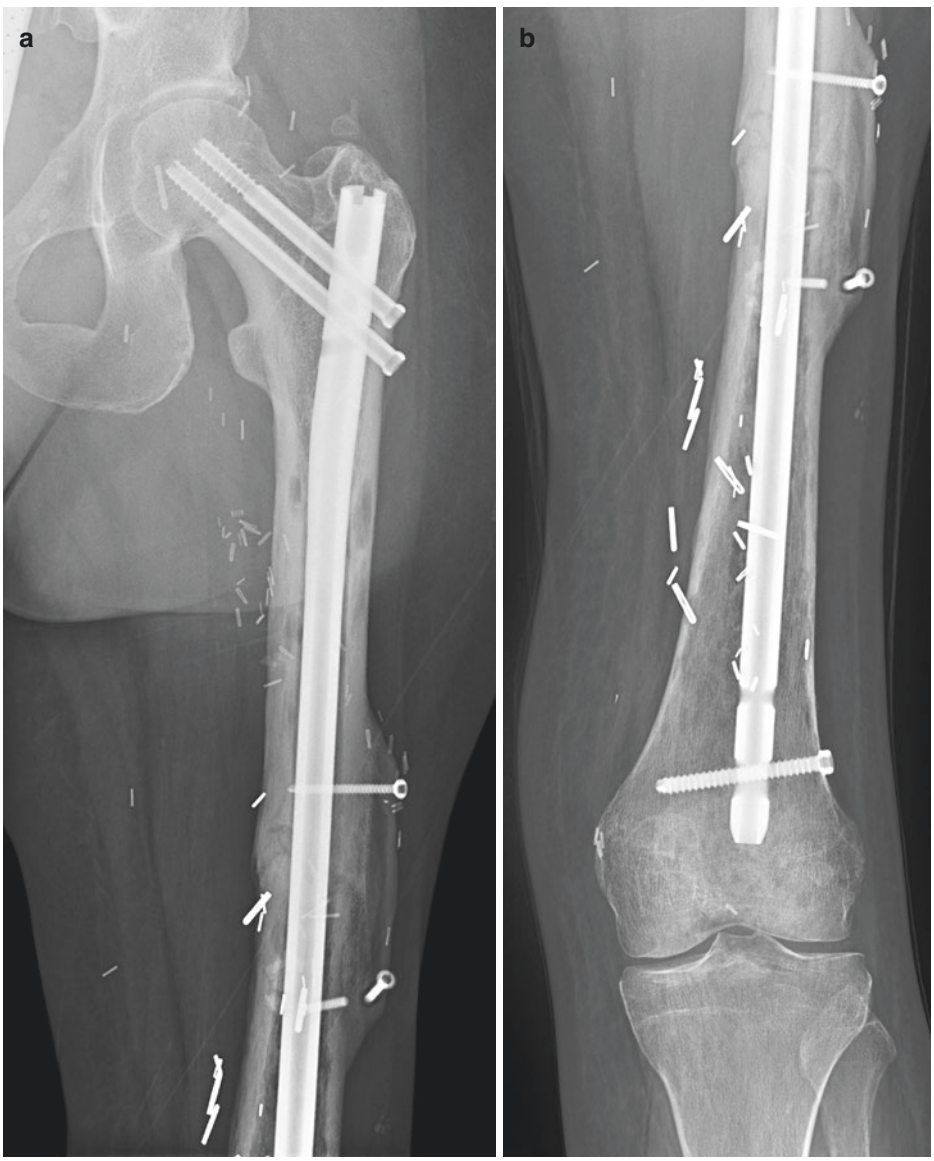


Fig. 9.8 Radiation-induced femoral artery occlusion following surgical resection and radiation treatment for lower extremity desmoid tumor. (**a**) Radiograph shows top part of intramedullary rod fixation of the left femur for non-union. (**b**) Radiograph shows lower part of intramedullary rod fixation of the left femur for non-union.

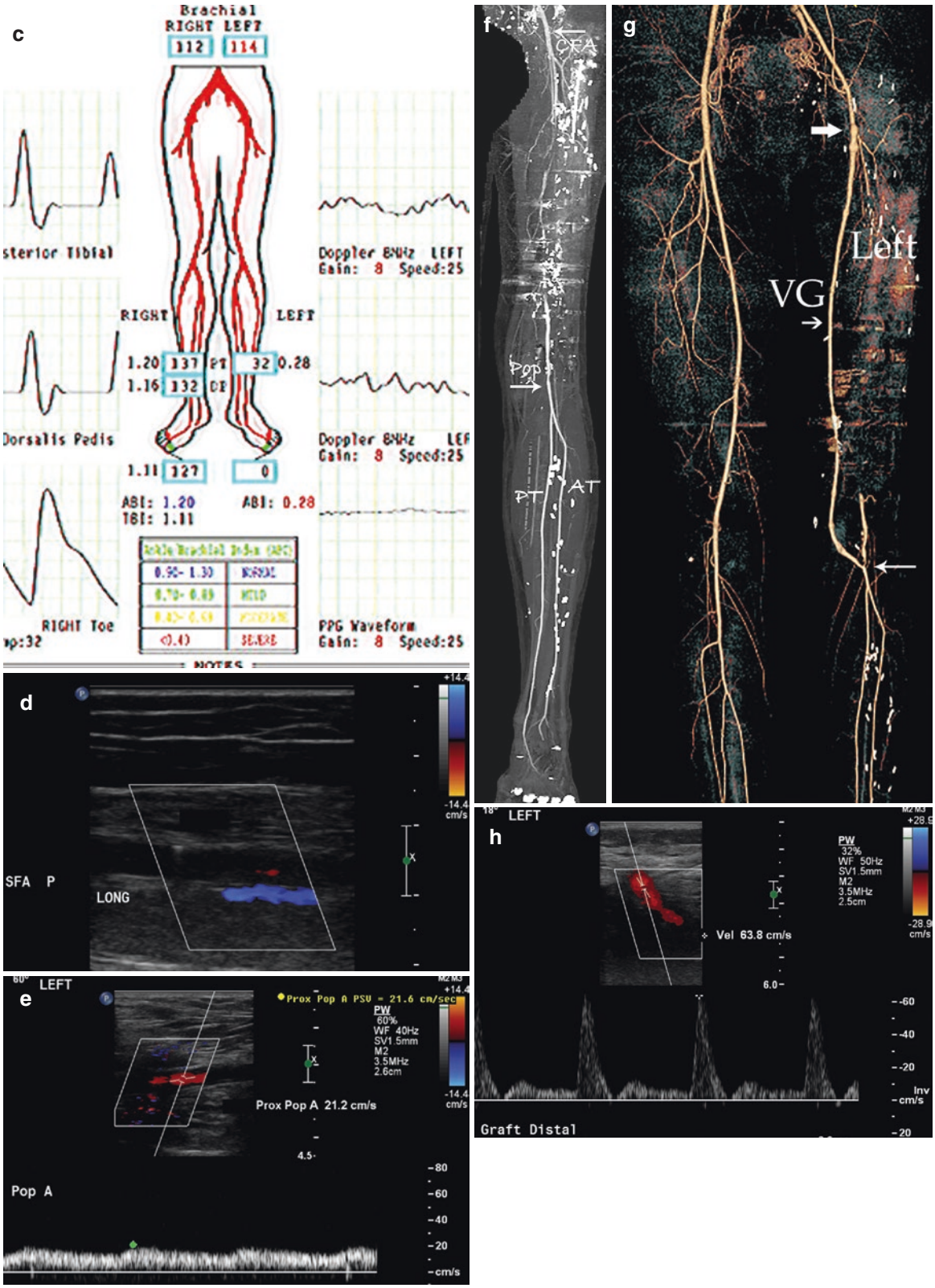


Fig. 9.8 (continued) (**c**) Left ABI is markedly reduced (0.28) indicating severe ischemia. (**d**) Colorflow image of the left superficial femoral artery (SFA) shows no flow in artery; flow is seen (*blue color*) in the adjacent left femoral vein. (**e**) Flow velocity by Doppler is markedly reduced in the reconstituted popliteal artery. (**f**) Reformatted CT angiogram shows chronic occlusion of the left SFA, reconstituted distal SFA and popliteal arteries, and patent AT and PT; numerous metal clips from prior surgeries are seen causing beam artifacts. (**g**) Post-operative reformatted CT angiogram shows satisfactory appearance of the left femoral popliteal artery bypass vein graft (VG). *Short arrow* points to the proximal anastomosis and *long arrow* to the distal anastomosis. (**h**) Colorflow ultrasound image shows satisfactory Doppler flow velocities at the distal femoral-popliteal anastomosis

Comments: Endovascular intervention was not considered in this case because of the long chronic occlusion of the superficial femoral artery and small distal target vessel. Surgical revascularization in the irradiated and scarred operative field was indeed very challenging in this case. Healthy soft tissue coverage of vascular graft is imperative in irradiated field to help promote wound healing and prevent complications. For this patient, we transposed the left sartorius muscle to provide coverage of the vein graft in the irradiated groin wound. We have kept the patient on aspirin and will continue to monitor her leg bypass graft with periodic duplex ultrasound.

Case # 9. Radiation-Induced Iliac Occlusive Disease Following Treatment for Cervical Cancer

A thirty-nine year-old woman had hysterectomy and pelvic node dissection and high dose radiation for uterine cervix squamous cell cancer in 2006. The patient developed recurrent right pelvic wall disease and had further surgical resection including right ureter reconstruction in 2008. Additional targeted Proton radiation therapy was given to the site of the recurrent disease. In 2013, the patient developed insidious ischemic rest pain and numbness in the right leg for about 1 month prior to seeking medical attention. Vascular work-up showed occlusion of the right common and external iliac arteries with reconstitution of the common femoral artery (Fig. 9.9a, b). The patient had no other cardiovascular risk factors. She is a lifelong non-smoker. Pharmaco-mechanical thrombectomy and catheter directed thrombolysis resulted in successful revascularization of the right leg (Fig. 9.9c–e). A focal stenotic plaque in the right external iliac artery was stented using self-expandable 6 mm stent. The patient was maintained on clopidogrel. One year later, the patient developed re-occlusion of the right common and external iliac arteries and stent, and had recurrent ischemic symptoms. Repeat endovascular intervention was again successful with pharmaco-mechanical thrombectomy, catheter directed thrombolysis, and additional stenting of the right external iliac (6 mm), and overlapping stenting of the common iliac artery (7 and 8 mm) using covered self-expandable stent-grafts (Fig. 9.9f–i). Following revascularization, the patient was kept on antiplatelet and anticoagulation. Unfortunately, the patient became symptomatic again about a year later with re-occlusion of overlapping right iliac stents. The decision was made to proceed with surgical revascularization. A cross-over left common femoral to right common femoral artery was constructed using an 8 mm PTFE graft. The patient did well after bypass surgery and was kept on aspirin therapy. Approximately 1 year after surgical revascularization, the patient developed acute ischemic symptoms again with thrombosis of the cross-over femoral bypass graft. Catheter directed thrombolysis restored patency to the bypass graft and normal flow to the right leg (Fig. 9.9j, k). The patient is currently doing well without symptoms at 13 months since the last intervention on aspirin and rivaroxaban.

Comments: Long-term radiation induced vasculopathy is an uncommon disease in cancer survivors. Endovascular treatment is usually preferred over surgical intervention for radiation-induced vasculopathy. However, in-stent restenosis remains an obstacle in the treatment of radiation-induced vasculopathy. Surgical bypass in irradiated field is technically challenging and is associated with higher morbidity than endovascular intervention. In our experience, surgical bypass for radiation-induced vasculopathy appears to require less repeated interventions when compared to endovascular treatment. In this patient, we identified acute dehydration as possible cause of the acute femoral graft thrombosis.

Case # 10. Axillary Artery Occlusion 8 Years After Radiation Treatment for Breast Cancer

A sixty-three year-old woman complained of finger discoloration, pain and numbness in the right hand for several months. Eight years prior to this presentation, the patient had modified radical right mastectomy and post-operative adjuvant high dose external beam radiation to the chest wall and axilla. Although, she had chronic right arm lymphedema, the patient denied prior symptoms of arm claudication. On exam, the patient had distal necrosis of the tip of the fifth finger (Fig. 9.10a). Duplex showed severe stenosis of the right axillary artery and reduced distal flow to the right hand (Fig. 9.10b, c). Selective angiography showed multiple stenoses of right axillary artery with two sites of near occlusion. We deployed two overlapping self-expandable 6 and 5 mm stents with great angiographic result (Fig. 9.10d, e). Revascularization was successful and relieved the patient's ischemic symptoms. The distal fifth finger wound healed without complication (Fig. 9.10f). Since the initial stent angioplasty, the patient has had four

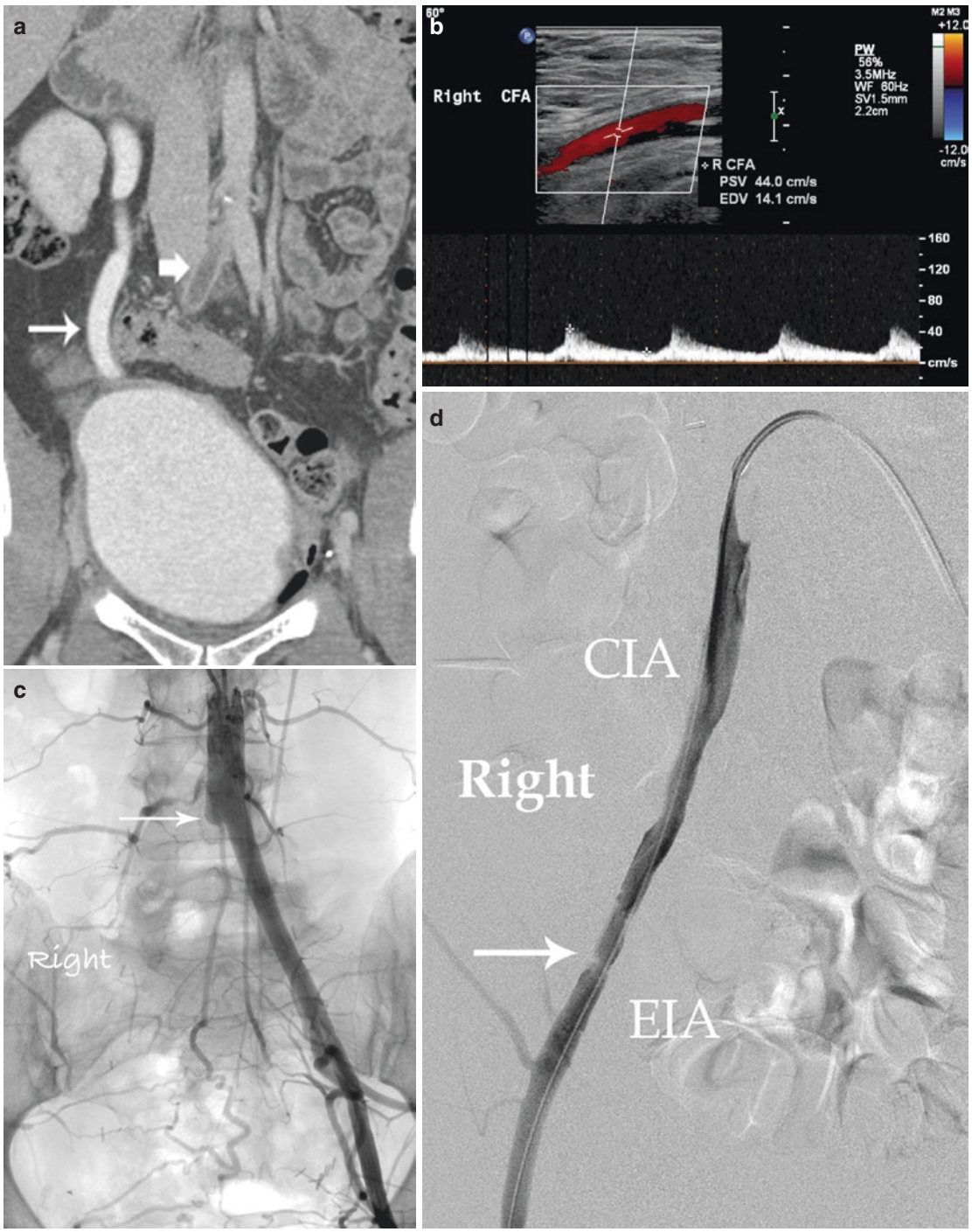


Fig. 9.9 Radiation-induced iliac occlusive disease following treatment for cervical cancer. (**a**) Coronal CT image shows thrombosed right common iliac artery (*short arrow*) and reconstructed right ureter (*long arrow*) to bladder junction. (**b**) Doppler flow velocity is reduced in the reconstituted right common femoral artery (CFA). (**c**) DSA image demonstrates flush occlusion of the right common iliac artery (*arrow*). Left common and external iliac arteries are normal and widely patent. (**d**) Following successful recanalization of the right common (CIA) and external iliac (EIA) arteries, a residual stenosis is seen (*arrow*) in the EIA.

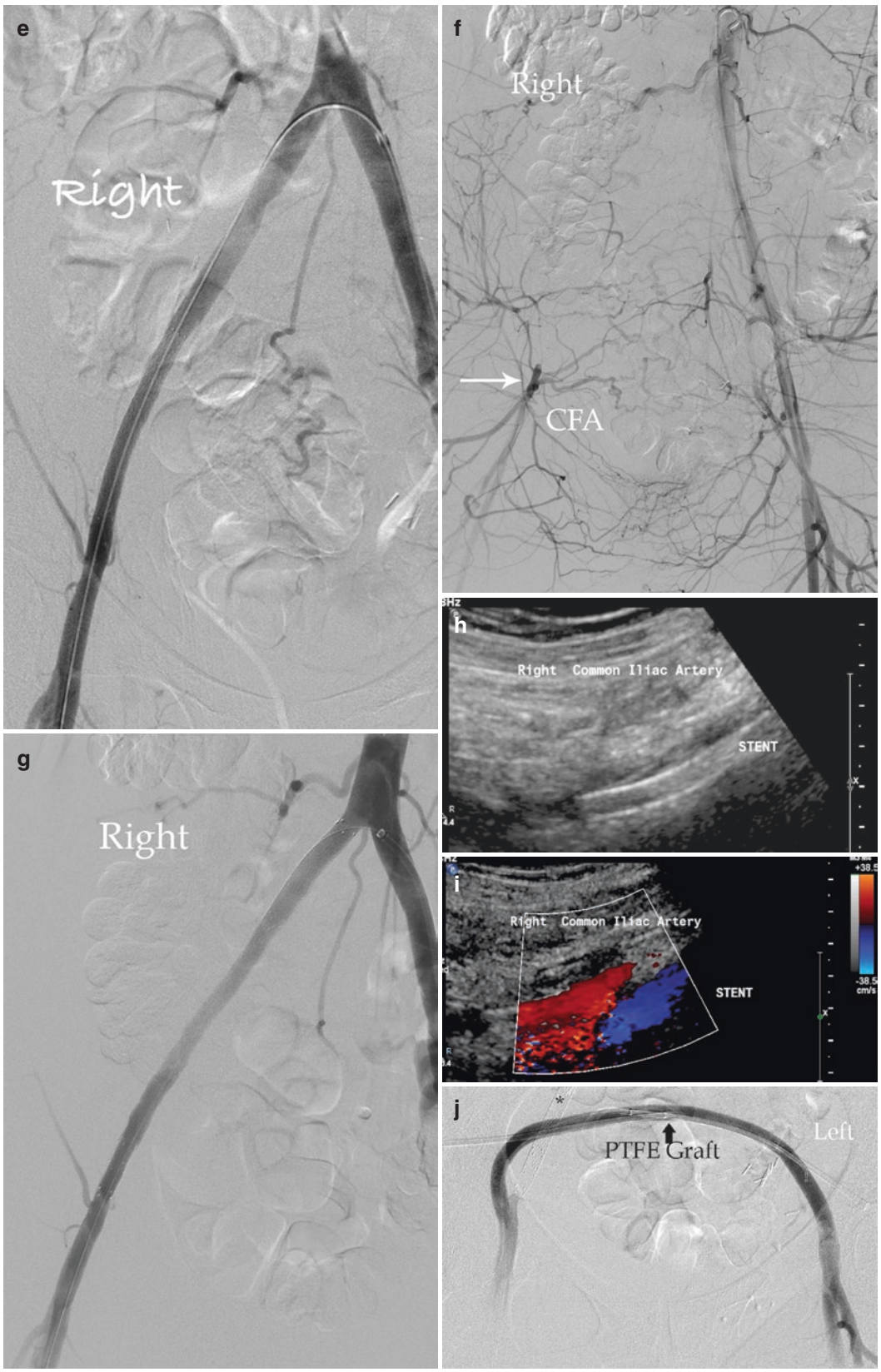


Fig. 9.9 (continued) (**e**) DSA image shows satisfactory result after stenting of the right EIA stenosis. (**f**) DSA image shows re-occlusion of the right CIA and EIA with reconstitution of the CFA (*arrow*). (**g**) Repeat endovascular intervention including pharmaco-mechanical thrombectomy, catheter directed thrombolysis and further stenting of the right CIA and EIA successfully restored flow as shown in this DSA image. (**h**) Gray-scale ultrasound image of right CIA stent demonstrates good apposition of stent to vessel wall. (**i**) Ultrasound color-flow image shows patency of right CIA stent. (**j**) DSA image shows patent cross-over synthetic femoro-femoral bypass graft after repeat endovascular intervention; vascular sheaths are still inside graft (*arrow*). *Asterisk* denotes the old occluded iliac artery stent.

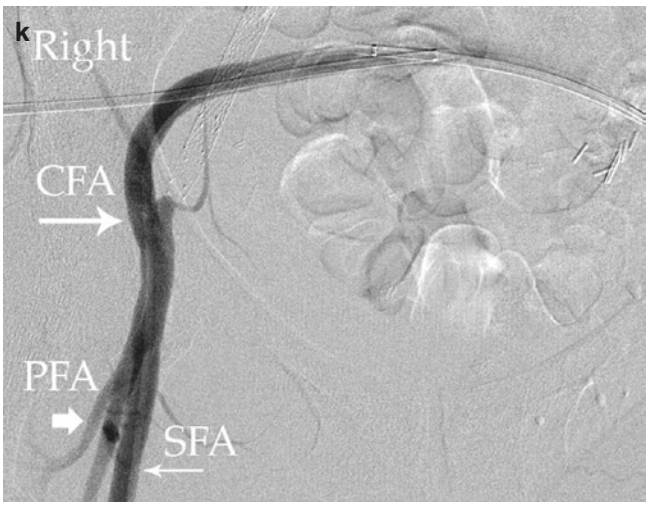


Fig. 9.9 (continued) (**k**) DSA image demonstrates widely patent right CFA anastomosis, profunda femoral (PFA) and superficial femoral (SFA) arteries

additional endovascular interventions and stenting within 16 months (Fig. 9.10g, h). In addition, at 17 months, the patient developed acute right axillary artery thrombosis, which was treated successfully by surgical thromboembolectomy. The patient is currently maintained on clopidogrel and anticoagulation.

Comments: As mentioned in the previous example, high rate of in-stent restenosis remains the Achilles heel of endovascular treatment for radiation-induced vasculopathy. In this patient, the restenotic lesions have occurred primarily at the very distal edge of the stent. Surgical revascularization in this patient would entail a long bypass from the subclavian artery to the brachial artery, traversing chronically edematous tissues in the previously irradiated field, which would be associated with increased risk of wound complication. Should the patient develop re-occlusion of the multiple-times stented axillary artery, surgical bypass will be indicated for limb-salvage.

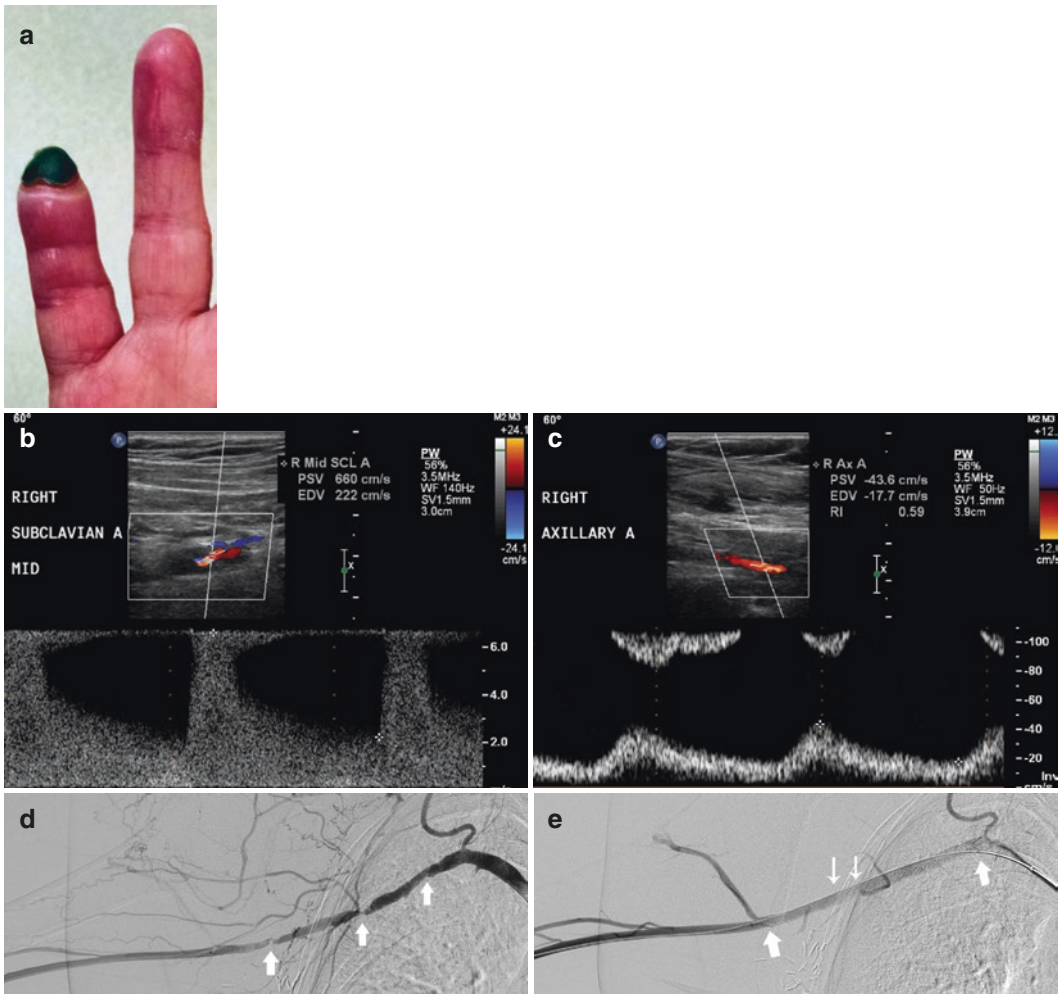


Fig. 9.10 Axillary artery occlusion 8 years after radiation treatment for breast cancer. (**a**) Photograph depicts dry necrosis of the distal tip of right fifth finger, consistent with chronic digital ischemia. (**b**) Ultrasound image of the right axillary artery shows markedly increased Doppler flow velocities indicating focal severe stenosis of the vessel. (**c**) Reduced monophasic Doppler flow velocities are shown in the right axillary artery distal to the stenotic lesion. (**d**) DSA image reveals multiple in tandem stenotic lesions (*arrows*) of the right axillary artery associated with prominent collateral vessels. (**e**) Post-stenting DSA image shows satisfactory appearance of stented axillary artery; *thick arrows* denote the proximal and distal edge of the overlapping self-expandable uncovered stents (6 and 5 mm diameters, respectively), and *thin arrows* point to the overlapping part of the stents.

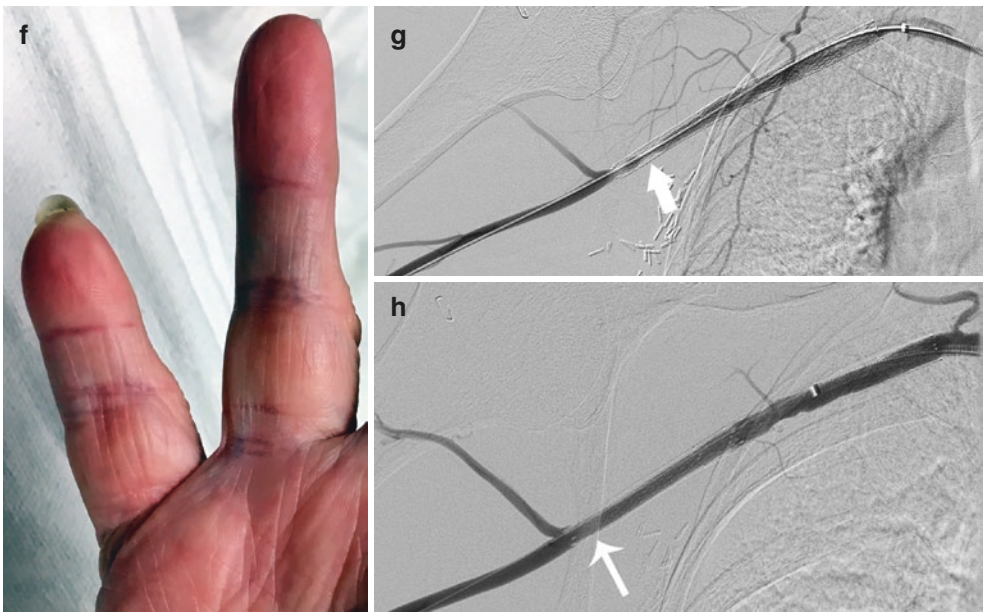


Fig. 9.10 (continued) (**f**) Photograph shows complete healing of the fifth digit after 3 months after successful revascularization. (**g**) DSA image demonstrates in-stent restenosis (*arrow*) in the distal stented axillary artery, 6 months after initial stenting procedure. (**h**) Completion DSA image shows satisfactory appearance after additional stenting using 5 mm self-expandable stent-graft (*arrow*) with overlap within the existing stent

Summary

Although peripheral artery disease is prevalent among elderly cancer patients, arterial complications are relatively uncommon in patients undergoing oncologic treatment. Endovascular or surgical revascularization is indicated for critical ischemia and can achieve high rate of limb-salvage in cancer patients. Survival outcome is generally related to the underlying cancer prognosis.

References

1. Levitan N, et al. Rates of initial and recurrent thromboembolic disease among patients with malignancy versus those without malignancy. Risk analysis using Medicare claims data. Medicine (Baltimore). 1999;78(5):285–91.
2. Sorensen HT, et al. Prognosis of cancers associated with venous thromboembolism. N Engl J Med. 2000;343(25):1846–50.
3. Prandoni P, Falanga A, Piccioli A. Cancer and venous thromboembolism. Lancet Oncol. 2005;6(6):401–10.
4. Herrmann J, et al. Vascular toxicities of cancer therapies: the old and the new--an evolving avenue. Circulation. 2016;133(13):1272–89.
5. Lenneman CG, Sawyer DB. Cardio-oncology: an update on cardiotoxicity of cancer-related treatment. Circ Res. 2016;118(6):1008–20.
6. Al-Kindi SG, Oliveira GH. Prevalence of preexisting cardiovascular disease in patients with different types of cancer: the unmet need for onco-cardiology. Mayo Clin Proc. 2016;91(1):81–3.
7. Di Nisio M, et al. Arterial thrombosis in ambulatory cancer patients treated with chemotherapy. Thromb Res. 2011;127(4):382–3.
8. Javid M, Magee TR, Galland RB. Arterial thrombosis associated with malignant disease. Eur J Vasc Endovasc Surg. 2008;35(1):84–7.
9. Bennett KM, et al. Outcomes of surgical revascularization for lower extremity arterial thromboembolism in patients with advanced malignancy. J Vasc Surg. 2014;60(4):987–92.
10. Morris-Stiff G, Lewis MH. Surgical treatment of acute limb ischaemia in the presence of malignancy. Int J Surg. 2010;8(3):233–5.
11. Tsang JS, et al. Acute limb ischemia in cancer patients: should we surgically intervene? Ann Vasc Surg. 2011;25(7):954–60.
12. Mouhayar E, et al. Outcome of acute limb ischemia in cancer patients. Vasc Med. 2014;19(2):112–7.
13. Allison MA, et al. Ethnic-specific prevalence of peripheral arterial disease in the United States. Am J Prev Med. 2007;32(4):328–33.
14. Peripheral Arterial Disease (PAD) Fact Sheet. http://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_pad.htm. 2016. 06/16/2016 [cited 2016 9/05/2016].
15. Hirsch AT, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. JAMA. 2001;286(11):1317–24.
16. McDermott MM, et al. Leg symptoms in peripheral arterial disease: associated clinical characteristics and functional impairment. JAMA. 2001;286(13):1599–606.
17. Diehm C, et al. Mortality and vascular morbidity in older adults with asymptomatic versus symptomatic peripheral artery disease. Circulation. 2009;120(21):2053–61.
18. Heart Protection Study Collaborative, G. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. Lancet. 2002;360(9326):7–22.
19. Poredos P, Jezovnik MK. Antiplatelet and antithrombotic treatment of patients with peripheral arterial disease. Int Angiol. 2010;29(1):20–6.
20. El Sakka K, et al. Association of malignant disease with critical leg ischaemia. Br J Surg. 2005;92(12):1498–501.
21. Norgren L, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). J Vasc Surg. 2007;45(Suppl S):S5–67.
22. Fowkes FG, et al. Comparison of global estimates of prevalence and risk factors for peripheral artery disease in 2000 and 2010: a systematic review and analysis. Lancet. 2013;382(9901):1329–40.

23. Fowler B, et al. Improving maximum walking distance in early peripheral arterial disease: randomised controlled trial. Aust J Physiother. 2002;48(4):269–75.
24. Hankey GJ, Norman PE, Eikelboom JW. Medical treatment of peripheral arterial disease. JAMA. 2006;295(5):547–53.
25. Rooke TW, et al. 2011 ACCF/AHA Focused Update of the Guideline for the Management of Patients With Peripheral Artery Disease (updating the 2005 guideline): a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2011;58(19):2020–45.
26. Klinkert P, et al. Vein versus polytetrafluoroethylene in above-knee femoropopliteal bypass grafting: five-year results of a randomized controlled trial. J Vasc Surg. 2003;37(1):149–55.
27. Indes JE, et al. Clinical outcomes of 5358 patients undergoing direct open bypass or endovascular treatment for aortoiliac occlusive disease: a systematic review and meta-analysis. J Endovasc Ther. 2013;20(4):443–55.
28. Conte MS, et al. Results of PREVENT III: a multicenter, randomized trial of edifoligide for the prevention of vein graft failure in lower extremity bypass surgery. J Vasc Surg. 2006;43(4):742–751; discussion 751.
29. Adam DJ, et al. Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. Lancet. 2005;366(9501):1925–34.
30. Aggarwal V, Waldo SW, Armstrong EJ. Endovascular revascularization for aortoiliac atherosclerotic disease. Vasc Health Risk Manag. 2016;12:117–27.
31. Dake MD, et al. Nitinol stents with polymer-free paclitaxel coating for lesions in the superficial femoral and popliteal arteries above the knee: twelve-month safety and effectiveness results from the Zilver PTX single-arm clinical study. J Endovasc Ther. 2011;18(5):613–23.
32. Tran K, et al. Real-world performance of paclitaxel drug-eluting bare metal stenting (Zilver PTX) for the treatment of femoropopliteal occlusive disease. Ann Vasc Surg. 2017;38:90–8.
33. Candy N, Ng E, Velu R. Paclitaxel-coated balloon reduces target lesion revascularization compared with standard balloon angioplasty. J Vasc Surg. 2017;65(2):558–70. e10
34. Laird JR, et al. Durability of treatment effect using a drug-coated balloon for femoropopliteal lesions: 24-month results of IN.PACT SFA. J Am Coll Cardiol. 2015;66(21):2329–38.
35. Duda SH, et al. Drug-eluting and bare nitinol stents for the treatment of atherosclerotic lesions in the superficial femoral artery: long-term results from the SIROCCO trial. J Endovasc Ther. 2006;13(6):701–10.
36. Hajibandeh S, et al. Covered vs uncovered stents for aortoiliac and femoropopliteal arterial disease: a systematic review and meta-analysis. J Endovasc Ther. 2016;23(3):442–52.
37. Mwipatayi BP, et al. Durability of the balloon-expandable covered versus bare-metal stents in the Covered versus Balloon Expandable Stent Trial (COBEST) for the treatment of aortoiliac occlusive disease. J Vasc Surg. 2016;64(1):83–94. e1
38. McQuade K, et al., Four-year randomized prospective comparison of percutaneous ePTFE/nitinol self-expanding stent graft versus prosthetic femoral-popliteal bypass in the treatment of superficial femoral artery occlusive disease. J Vasc Surg. 2010;52(3):584–90; discussion 590–1, 591 e1–591 e7.
39. Geraghty PJ, et al. Three-year results of the VIBRANT trial of VIABAHN endoprosthesis versus bare nitinol stent implantation for complex superficial femoral artery occlusive disease. J Vasc Surg. 2013;58(2):386–95. e4
40. Modrall JG, Sadjadi J. Early and late presentations of radiation arteritis. Semin Vasc Surg. 2003;16(3):209–14.
41. Baerlocher MO, et al. Primary stenting of bilateral radiation-induced external iliac stenoses. J Vasc Surg. 2004;40(5):1028–31.
42. Moutardier V, et al. Iliac atherosclerotic occlusive disease complicating radiation therapy for cervix cancer: a case series. Gynecol Oncol. 2002;84(3):456–9.
43. Haddad TC, Greeno EW. Chemotherapy-induced thrombosis. Thromb Res. 2006;118(5):555–68.
44. Fernandes DD, et al. Acute aortic thrombosis in patients receiving cisplatin-based chemotherapy. Curr Oncol. 2011;18(2):e97–100.
45. Schutz FA, et al. Bevacizumab increases the risk of arterial ischemia: a large study in cancer patients with a focus on different subgroup outcomes. Ann Oncol. 2011;22(6):1404–12.
46. Alhawiti N, et al. The tyrosine kinase inhibitor, nilotinib potentiates a prothrombotic state. Thromb Res. 2016;145:54–64.
47. Lang K, et al. Mortality and vascular events among elderly patients with chronic myeloid leukemia: a retrospective analysis of linked SEER-Medicare Data. Clin Lymphoma Myeloma Leuk. 2016;16(5):275–285.e1.