Hemodialysis Outflow Vein Stenosis

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Introduction

Every year, there are approximately 100,000 new patients beginning hemodialysis, and the current prevalence of patients in the United States on chronic hemodialysis is near 450,000 [1]. Most of these patients are dialyzed through an autogenous arteriovenous fistula (AVF) or prosthetic graft (AVG). The durability of any type of surgical access is relatively short, with the half-life for AVGs being approximately 1 year and those of AVFs only marginally better. Maintaining patent dialysis access for end-stage renal disease (ESRD) patients is a critical aspect to decrease morbidity and mortality for this population. Thus, understanding the mechanisms of failure and specific treatments based on the anatomic location can have an enormous positive impact on controlling access complications and improving outcomes.

The mechanisms of failure of any hemodialysis access are the result of changes, usually stenosis, at the different levels of the arteriovenous circuit and can be categorized based on the anatomic location of the stenotic area. The most common problem involves the development of a stenosis at the venous anastomosis of an AVG or in the venous outflow of any access. Some studies have shown central vein stenosis in up to 15–20 % of all patients undergoing dialysis and in up to 30 % in those with a history of prior catheter placement [2, 3].

Hemodialysis access failures affect the quality of life of ESRD patients due to the increased morbidity associated with higher numbers of hospital readmissions, invasive diagnostic studies, and open and endovascular reinterventions. The goal of this chapter is to understand the pathophysiology and management of stenosis within the hemodialysis circuit in order to better preserve functional arteriovenous access.

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Pathophysiology

Neointimal hyperplasia is the eventual cause of essentially all stenosis. Several studies have shown that neointimal hyperplasia is strongly influenced by the turbulent flow associated with the creation of an arteriovenous anastomosis. The development of neointimal hyperplasia varies in location based on the type of conduit. The majority of AVGs fail due to stenosis at the venous anastomosis, but also local tissue ingrowth in prosthetic accesses simulates neointimal hyperplasia. On the other hand, AVFs tend to present with neointimal hyperplasia throughout the entire length of the autogenous conduit as a result of repetitive puncture for cannulation.

A very common location for stenosis is within the central venous outflow tract (e.g., subclavian vein), especially in the setting of previous prolonged or repeated central venous catheterization [3–5]. The underlying pathophysiology of central venous stenosis in dialysis patients is multifactorial, and complex central venous stenosis can be present even without a previous history of indwelling central catheters [6]. Approximately 60–80 % of patients are dialyzed at some point through a central venous catheter [2]. These catheters cause intraluminal trauma which induces endothelial denudation, subsequent endothelial pericyte proliferation, increased levels of tissue factor, and, ultimately, upregulation of cytokines and growth factors that favor neointimal hyperplasia [7, 8]. In addition to the intrinsic problem (i.e., venous neointimal hyperplasia), there is an extrinsic compression involved in the pathophysiology of stenosis at the costoclavicular junction (CCJ) due to anatomic factors similar to those involved in venous thoracic outlet syndrome (VTOS) [6, 9]. The subclavian vein crosses the costoclavicular junction extending from the lateral border of the first rib to the medial end of the clavicle. This segment of vein suffers external compression by excessive bulk of the anterior scalene muscle (which lies behind the subclavian vein) as well as by tethering by the subclavius muscle underlying the clavicle and the costoclavicular ligament. All these structures

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reduce the space surrounding the central veins at the CCJ in the anterior portion of the thoracic outlet (Figs. 30.1 and 30.2). The combination of high venous flow and associated turbulence resulting from the arteriovenous access most likely exacerbates the chronic inflammatory reaction at this anatomic segment of the subclavian vein leading to stenosis and eventual occlusion [9].

Clinical Presentation

The hemodynamic result of chronic venous outflow stenosis at any level is increased pressure within the AVG or AVF, which translates clinically into venous hypertension. This presents with increasing extremity edema and extensive prominent collateral veins, pain, prolonged bleeding both during and after decannulation, and/or inability to complete efficient dialysis sessions secondary to excessive recirculation (i.e., endless loop of treatment of the same blood already filtered through the dialysis machine with little net clearance effect).

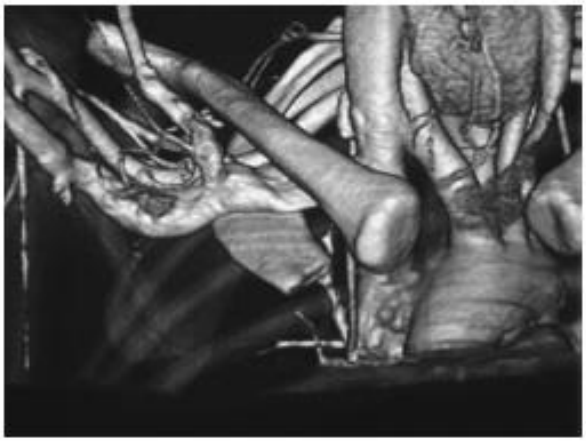

Fig. 30.2 Computed tomography scan of the right shoulder, viewed from an anterior projection, with soft tissues such as the subclavius muscle subtracted out. The right arm is elevated. Note compression of the subclavian vein as it passes between the clavicle and the first rib (Courtesy: Wallace Foster, MD, Brisbane, Australia; Reprinted from Glass et al. [25], with permission)

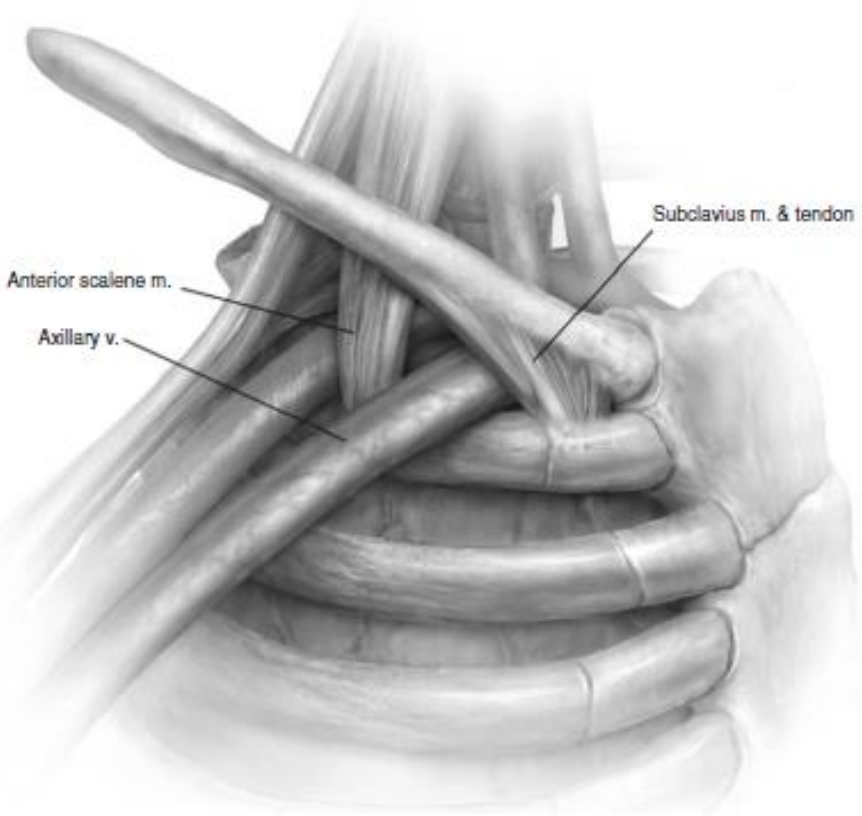

Fig. 30.1 Basic anatomy of the thoracic outlet. The axillosubclavian vein passes anteriorly, passing by the junction of the first rib and clavicle. This "space" is open superiorly, but the vein is tethered in this location by surrounding tissue. The two bones and the subclavius muscle and tendon chronically and repetitively exert pressure on it. In patients with high flow (i.e., with an ipsilateral arteriovenous fistula), this area can quickly become stenotic (Reprinted from Illig and Doyle [27], with permission)

Diagnosis

Digital subtraction fistulagraphy is the critical step in the diagnosis of patients with suspected outflow stenosis. Although invasive, a fistulagram allows identification of the anatomic location of the problem and offers the opportunity to perform therapeutic intervention in the same setting. Imaging can very easily identify stenosis in the body of the vein, the venous anastomosis of an AVG, and anywhere along the outflow tract into the atrium. Imaging of the arterial anastomosis requires occlusion of the fistula central to the injection site or injection via a catheter placed within the inflow artery itself, often with the tube angled properly to "unfold" the anastomosis. Although contrast venography is sufficient to diagnose costoclavicular junction lesions in the majority of patients, a central lesion that is present might not be identified with venography in up to 10% of cases. Intravascular ultrasound can be used in patients with classic clinical presentation without evidence of focal lesions on the fistulagram, especially in the setting of extensive collaterals on venography. Some studies suggest intravascular ultrasound should be used as standard adjunct in the diagnosis of central lesions in dialysis access patients due to its increased sensitivity [9].

Duplex ultrasound could help to confirm physical exam findings by detecting abnormalities in access flow at the level of the extremity, but the presence of the clavicle and ribs limits its utility to assess the full extent of the venous outflow tract. In terms of surveillance, studies have failed to prove any benefits of the use of duplex ultrasound to improve graft survival [10].

Management: Anatomic-Based Approach

The ultimate goal when treating a venous outflow stenosis is resolution of access function. Some signs and symptoms, such as pain and swelling, may take hours to days to resolve following the intervention. However, most problems should be expected to improve immediately following a successful procedure, including conversion of pulsatile flow to a palpable thrill in the vascular access, increased flow volumes on duplex imaging, decreased pressure gradient across the site of stenosis, and decrease filling of collateral veins on venography [6].

The options available to manage vascular access outflow stenosis or occlusion are based on the location and nature of the lesion. Once the anatomic problem is identified on the fistulagram, a definite treatment plan can be delineated. For treatment planning, it is useful to divide therapy into three separate anatomic areas where problems are commonly encountered: first, peripheral to the CCJ, which includes the arterial anastomosis, the body of the access, the venous anastomosis for an AVG, and the peripheral outflow veins (basilic and brachial veins and the cephalic arch) (Fig. 30.3); second, the veins central to the CCJ (the innominate veins and the superior vena cava (SVC)) (Fig. 30.4); and third, the subclavian vein at the CCJ (Fig. 30.5) [9].

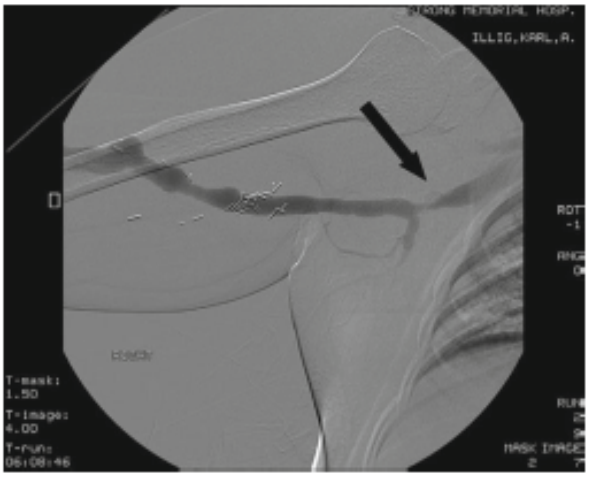

Fig. 30.3 Stenosis affecting the anatomic region proximal to the costoclavicular junction (CCJ): fistulagram showing smooth stenosis in the axillary vein in the axilla (*arrow*). This responded well to balloon angioplasty (Reprinted from Illig [9], with permission)

Outflow Stenosis/Occlusion Peripheral to the Costoclavicular Junction

The areas affected obviously differ somewhat according to whether an AVG or AVF is present. All of these lesions, however, are similar in the sense that they are only surrounded by soft tissue, making endovascular intervention attractive. Lesion location in failing AVGs can be classified into four categories: the arterial anastomosis, within the graft, the venous anastomosis, and the venous outflow tract (from the arteriovenous anastomosis to the cephalic arch). In AVFs, there are only the arterial anastomosis, body of the vein (loosely defined as the accessible segment), and outflow tract to the CCJ.

Surgical techniques were originally used to manage venous anastomotic stenosis, including placement of an interposition graft or enlargement of the anastomosis by means of patch angioplasty. Both techniques have been shown to be equivalent in terms of outcomes [11]. The main

disadvantage of using an interposition graft is the increased risk of infection (and perhaps decreased patency) due to substitution of autogenous vein with a prosthetic graft [12], although obviously autologous vein can in theory solve this problem. A patch angioplasty simply enlarges the area of stenosis without addressing the fundamental issue (i.e., neointimal hyperplasia), increasing the risk of restenosis, although this may then occur at a different and less critical location within the anastomosis.

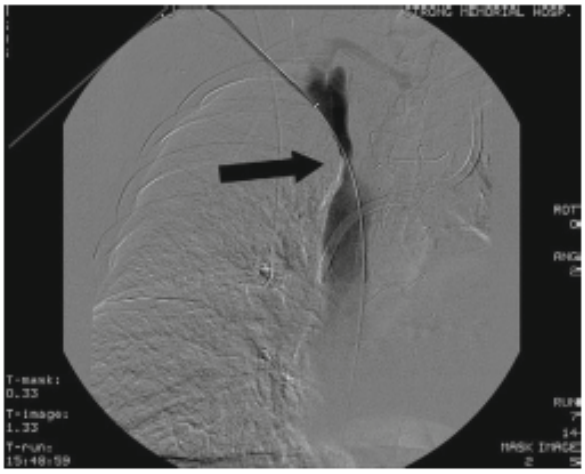

Fig. 30.4 Stenosis affecting central veins distal to costoclavicular junction (CCJ). Fistulagram of a patient with smooth stenosis of the superior vena cava (*arrow*). Note that this dialysis catheter, inserted from the left, does not seem to be involved with this lesion in any way. This responded well to placement of a 14-mm self-expanding stent that was angioplastied with a 12-mm balloon (Reprinted from Illig [9], with permission)

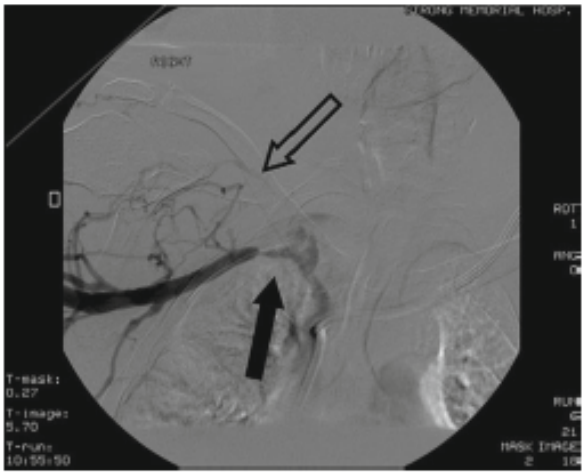

Fig. 30.5 Stenosis affecting central veins at the costoclavicular junction (CCJ). Fistulogram showing a high-grade stenosis at the CCJ with relatively normal vessels proximally and distally. Note the rather long, complex stenosis beginning at the CCJ with fairly normal vein peripherally (*solid arrow*) and extensive collateralization that is pathognomonic for this lesion (*open arrow*) (Reprinted from Illig [9], with permission)

Fully occluded outflow veins in this region require individualized treatment. Endovascular options are usually limited due to the chronicity of these lesions and the inability to cross them with a wire. In this situation, open surgical repair is usually required, with the goal being to establish adequate venous outflow. The open surgical approach depends on the extent and location of the occlusion and the status of the superficial and central veins. The most commonly used options include extensive mobilization and reimplantation of the distal segment of the AVF to a vein with patent outflow (e.g., distal cephalic vein-axillary vein), basilic or brachial vein translocation (e.g., distal cephalic vein-basilic vein), or the use of an interposition graft (autogenous or prosthetic) to bypass the lesion [9]. The patent outflow vein (i.e., cephalic) does not always need to be brought down to reach the deep system; the deep vein itself can be transected without significant clinical sequelae and brought up to meet the cephalic vein "halfway," thus preserving length for cannulation.

Most stenoses involving this anatomic segment respond well to endovascular techniques. In order of intervention, balloon angioplasty, cutting balloons for resistant lesions, or bare metal stents can all be used. Any percutaneous intervention should begin with imaging of the complete circuit to include the entire conduit from the arterial anastomosis to the central venous outflow. Endovascular percutaneous transluminal angioplasty (PTA) is the most common endovascular intervention for stenosis in this region. It is important to consider the pathophysiologic importance of neointimal hyperplasia as a cause of failure in this anatomic segment. The time and pressure required to treat the areas of stenosis can be increased due to neointimal hyperplasia. The result of these higher pressures is uncontrolled trauma to the vein, which can restimulate the neointimal hyperplasia process, leading to recurrent stenosis. Based on that assumption, multiple studies suggest that the best option may be initial use of a cutting balloon followed by PTA performed at a lower pressure [13–16]. Another important factor is the increased risk of extravasation following PTA as a result of tearing of the fibrotic neointimal hyperplasia, as opposed to the tendency to dissect in the setting of an atherosclerotic plaque.

Even though PTA has replaced surgical revision for hemodialysis access-related venous stenoses and occlusions [18], primary patency rates remain poor as a result of restenosis due to neointimal hyperplasia [17]. Even after placement of a bare metal stent, neointimal hyperplasia is still the major reason for restenosis [18]. However, when compared to angioplasty alone, stenting exhibits similar or improved patency rates. Stents are also useful for salvaging failed angioplasty procedures and thereby maintaining

patency of the hemodialysis graft. Some studies have suggested that primary patency following stenting was significantly better than the primary patency of the entire vascular access [19].

The type of stent used has been a subject of study. Covered stents have been used to prevent recurrent stenosis, probably by preventing the ingrowth of hyperplastic tissue, and thus, avoid the early failures seen with bare metal stents. This is particularly true for treating stenoses at the venous anastomosis of prosthetic AV accesses, where covered stents have been shown to have a patency advantage over bare metal stents [20].

The terminal portion of the cephalic vein, where it dives perpendicularly in the deltopectoral groove to join the axillary or subclavian vein, is labeled the cephalic arch. For unknown reasons, this is a segment particularly prone to stenosis. It is usually treated with conventional angioplasty, although high rates of restenosis are seen, and thus in and of itself is an area of research interest [17, 20]. The cephalic arch represents the outflow for any cephalic-based access (although radiocephalic AVFs usually include the deep system as outflow). Most recent studies have shown that management with bare metal stents results in unsatisfactory patency rates due to the rapid development of in-stent stenosis [21]. Some recent data support the use of covered stent grafts as an alternative to bare metal stents in recurrent cephalic arch stenosis after conventional PTA [20]. It should be strongly emphasized that any stent, whether covered or not, should protrude only minimally (or not at all) into the deep system, as this increases the risk of thrombosis of the deep as well as cephalic veins, which can lead to significant superior vena cava syndrome.

A significant clinical clue that such intervention has been hemodynamically successful is the elimination of previously present collateral veins. Such veins indicate obstruction somewhere between their origin and endpoint, no matter what is seen on the venogram. Intravascular ultrasound can be used as an adjunct in this setting to better characterize a poorly visualized stenosis, as well as to assess residual luminal diameter if collaterals are still present post-intervention. Most interventions will accomplish a relatively good result in the short term. Restenosis is common and an aggressive surveillance protocol is likely justified, although data are sparse [9].

Outflow Stenosis/Occlusion Affecting Central Veins Distal to the Costoclavicular Junction

This anatomic group includes the innominate veins and the SVC and is also usually treated with endovascular intervention (see Chap. 31, Central Venous Stenosis and Occlusion, for a full discussion).

Outflow Stenosis/Occlusion at the Costoclavicular Junction

Endovascular procedures, mainly PTA with or without stent placement, have been the most common method to manage central venous stenosis in dialysis patients with reasonable short-term results [22, 23]. Stenosis in this area seems to be much more common than would be expected. It was previously thought that the presence of subclavian dialysis catheters was the culprit, but the incidence does not seem to have decreased in the era when these are no longer used. We hypothesize that because this area is somewhat stressed in all patients, the addition of high flow after access placement causes localized turbulence in this area especially. This turbulence acts as a potent stimulus for neointimal hyperplasia, which creates an increasing fixed stenosis, worsening the turbulence and hence neointimal hyperplasia, and so on.

Recent data as well as decades' worth of experience with venous thoracic outlet syndrome suggest that, when treated with endoluminal interventions, lesions at the CCJ have poor outcomes compared to lesions surrounded by soft tissue only because of this bony impingement. Furthermore, the use of stents for treatment of lesions at the CCJ increases the risk of stent fracture and subsequent venous occlusion due to the "nutcracker" effect of the clavicle and first rib [24–27] (Figs. 30.2 and 30.6). These observations have led to changes in the management of access-related venous stenosis at the CCJ: surgical decompression by means of first rib resection or claviculectomy, with concomitant endovascular intervention, if needed [25].

The recommended algorithm starts with the diagnosis of a stenosis at the CCJ via venography/fistulogram (staged or intraoperative) (Figs. 30.5 and 30.7), followed by surgical decompression by means of infraclavicular first rib excision (i.e., removal of the anterior half of the first rib from posterior to the anterior scalene insertion site all the way to the

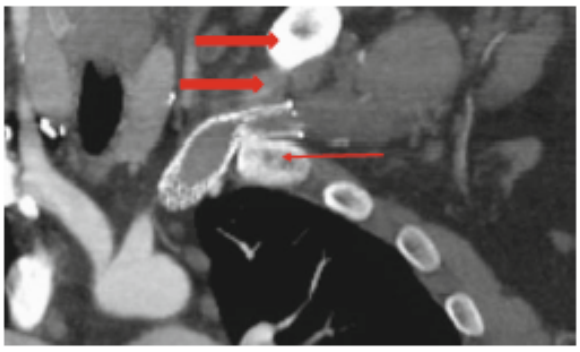

Fig. 30.6 Example of a stent crushed by the first rib (*thin arrow*) and clavicle/subclavius muscle (*thick arrows*). The CT was obtained 1 year following stenting (Courtesy Sherene Shalhub, MD)

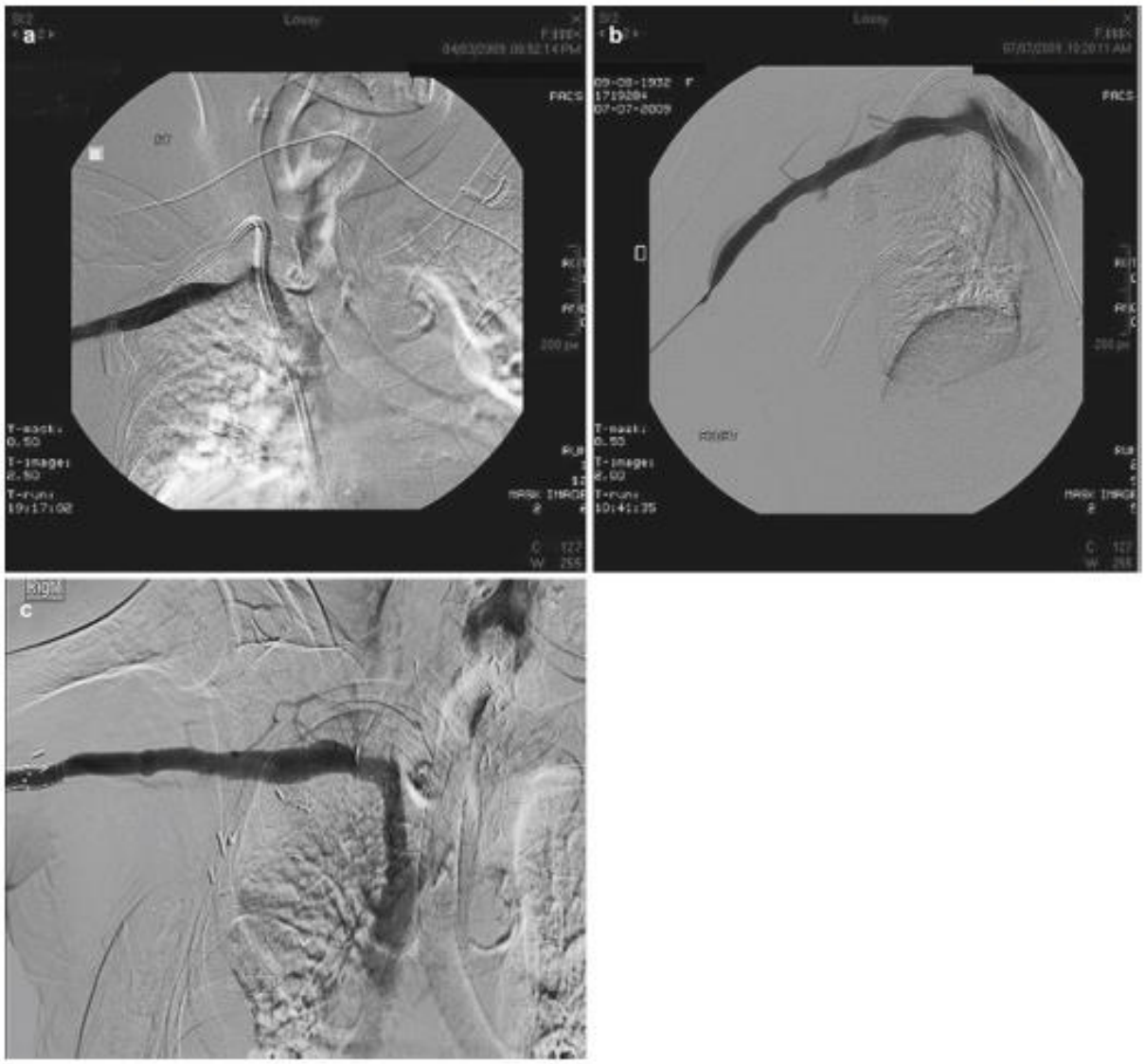

Fig. 30.7 Venography demonstrating right subclavian vein stenosis at the costoclavicular junction (**a**) before surgical decompression, (**b**) intraoperative immediately after surgical decompression with first rib resection, (**c**) demonstrating patent right subclavian vein 5 months after decompression with first rib resection (Reprinted from Glass et al. [25], with permission)

sternum), extensive mobilization of the vein, and thorough external venolysis to resect the dense cicatrix surrounding the vein. In order to ensure complete venous decompression, the tendino-cartilaginous tissue comprising the subclavius tendon and costoclavicular ligament must be completely removed and the vein completely dissected free from the overlying tissues. Claviculectomy is rarely required except for cases where extensive central outflow reconstruction extending to the innominate or SVC is expected [25].

Following rib resection, completion venography is performed to determine the degree of residual stenosis and choose endovascular vs. open repair before wound closure. The preferred option, if able to cross the lesion with a wire, would be venoplasty with or without stent placement (Fig. 30.7). An acceptable open surgical option to enhance the vessel diameter in this region after failed endovascular intervention is vein patch angioplasty (ideally using greater saphenous vein). Care should be taken to ensure that the patch extends beyond the site of the stricture both proximally and distally into the normal innominate vein medially, as well as into the normal axillary vein distally [28, 29]. Longer stenotic segments or

subclavian venous occlusions at the CCJ generally require direct reconstruction of the vein, jugular transposition, or other open surgical alternatives including extra-anatomic bypass to the internal jugular vein, subclavian vein to right atrial bypass [30, 31], and superior vena cava or innominate reconstruction using a vein or prosthetic graft for more proximal obstructions [32]. Finally, a rarely used approach in this setting includes extra-anatomic bypass from the axillary/subclavian vein to the ipsilateral internal jugular or contralateral axillary, assuming both axillary and jugular veins are patent [9].

We have used this approach since approximately 2009. In a series of cases performed at the University of South Florida, 24 patients with either failing access or need for access in the setting of CCJ lesions were so treated. Mortality was zero and morbidity low, and at 1 year 85 % of fistulas were still being used [24]. Our overall experience now includes approximately 60 patients. We have extended our indications to include the presence of a stent in situ (based on the venous TOS experience) (Fig. 30.6) and have experienced fistula salvage in approximately 90 % of patients.

Conclusions

Venous outflow stenosis or occlusion is the most common cause for access failure and is a multifactorial process that can be difficult to treat. Management of threatened hemodialysis access should be individualized based on the nature and location of the lesion. Venous lesions in the arm or chest (where the veins are surrounded by soft tissue only) can usually be treated very effectively with conventional endovascular approaches, and surgical options are excellent in the arm due to the ease of exposure. Lesions at the costoclavicular junction, however, must be addressed differently. The subclavian vein at this location is prone to injury by the bony and ligamentous structures that surround it, and for the same reason endovascular intervention, even stenting, is unusually prone to failure. Unless surgical decompression of the vein with first rib resection and venolysis is added to the algorithm, these patients very often undergo early ligation of their access, removing this arm from future consideration and likely shortening their lifespan.

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