Any overview of the treatment of venous disease should begin with a brief examination of its history. The first documented record of the treatment of venous disease comes to us from the writing on the treatment of varicose veins found in the Ebers papyrus circa 1500 BC.1 In the 2 millennia since the first description of vascular ligation from the Alexandrian School of Medicine in Egypt, circa 270 BC, knowledge of venous disease has seen steady advancement carried forward by the work of Leonardo DaVinci, William Harvey, Virchow, and Trendelenburg. From the first rudimentary attempts at venous thrombectomy in the early 1920s to the evolution of percutaneous and mechanical thrombectomy and endovascular stents in the 21st century to treat complex venous disease, there also exists a shared evolutionary pathway between knowledge of the disease and its treatment. It is the aim of this review to provide a comprehensive summary of the state of the art of venous disease treatment at the turn of the new century.

Endovascular Intervention

This review seeks to examine the endovascular approach to venous thromboembolic disease with a particular emphasis on current and evolving percutaneous treatment modalities available to the vascular interventionist and the evidence that currently exists substantiating their use.

Catheter-Directed Thrombolysis

Catheter-directed thrombolysis (CDT) has become a pivotal adjunctive therapy in the management of both acute and chronic thromboembolic venous disease. Direct infusion of the thrombolytic agent via specially designed, fenestrated catheters results in its effective delivery and leads to high local levels of drug within the thrombosed segment, thus increasing the likelihood of clot resolution and restoring vessel patency. This therapy is most likely to be successful when thrombus is acute (<14 days old) and much less effective when the clot is chronic (>4 weeks old).2 Such accelerated pharmacological thrombolysis may be performed even with a reduced dose of lytic agent associated with a lower overall duration of infusion. Various lytic agents can be chosen based on their individual biological half life, fibrin affinity and specificity, time to clot lysis, and respective dosing. These include alteplase, tenecteplase, reteplase, streptokinase, and urokinase. None however has specific Food and Drug Administration approval for use in deep vein thrombosis (DVT). No large-scale randomized trials of CDT therapy in the treatment of venous thromboembolic disease have been performed. The results of single arm studies compared with historical controls suggest that CDT could improve venous patency and preserve valvular function when compared with standard anticoagulation alone. Findings from the National Venous Thrombolysis Registry, the largest published experience with CDT to date, strongly point to a relationship between the degree of lysis and vessel patency. In this prospective, multicenter study, the use of CDT with the agent urokinase was evaluated in 303 limbs of 287 patients. The majority of patients (66%) had acute DVT, 16% had chronic DVT, and 19% had an acute superimposed on chronic condition. Most patients had iliofemoral DVT, and a minority (25%) had isolated femoropopliteal DVT. Contrast venography revealed that complete lysis (also denoted grade III lysis) occurred in only 31% of cases and that partial lysis (>50% clot resolution denoted Grade II lysis) occurred in 52%. Results were best for patients with acute iliofemoral DVT (65% clot lysis). In patients with complete clot lysis, venous patency was preserved in 78% at one year, whereas in those with partial (<50%) lysis, venous patency was only achieved in 37%. Venous patency was associated with improved valvular function in that 72% of patients in this study who had optimal clot lysis, maintained normal valve function, whereas 62% of patients with incomplete lysis demonstrated valvular incompetence. Most importantly, in the subgroup of patients with first time acute iliofemoral DVT, who had initial successful thrombolysis, 96% of the veins remained patent at one year. Major bleeding occurred in 11% of patients and was most common at venous access sites. The devastating complication of intracranial hemorrhage occurred in 0.2% and pulmonary embolism (PE) in 1% of patients. Thirteen percentage of the complications were retroperitoneal bleeds, but the mortality rate for the entire study cohort was 0.4%.3 These results have been corroborated by more recent studies of CDT for DVT, which have shown a reduction in major bleeding events by half, likely because of more careful patient selection and familiarity with management and dosing of lytic agents.4

These studies indicate that CDT for DVT achieves more rapid lysis, reduces the incidence of long-term sequelae of DVT, improves quality of life, preserves valvular competence and more completely restores vessel patency as compared with standard anticoagulation or systemic thrombolytic therapy, although at the expense of a higher rate of hemorrhagic complications (see Table 1 summary of CDT trials).5

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Further discussion of the value of CDT in venous thromboembolic disease will have to await the results of a new large-scale randomized trial that is currently in its interim phases. ATTRACT (Acute Venous Thrombosis: Thrombus Removal With Adjunctive Catheter-Directed Thrombolysis) is a multicenter, randomized trial that will definitively determine whether current state of the art lytic treatment (pharmacomechanical CDT) prevents post-thrombotic syndrome in patients with DVT. It represents the first National Institutes of Health’s National Heart, Lung, and Blood Institute (NHLBI)-funded multicenter, randomized trial of any interventional therapy for deep vein thrombosis. The trial will assess the presence and severity of post-thrombotic syndrome, quality of life, relief of symptoms, safety, and cost. At present, CDT should be reserved for exceptional circumstances, such as patients with limb-threatening ischemia caused by phlegmasia cerulea dolens and in young patients with extensive iliofemoral/inferior vena caval (IVC) DVT where the risk benefit ratio is deemed favorable. Other potential candidates for therapy include patients with multisegmental DVT, those with expected long-term survival, and individuals who remain symptomatic despite therapeutic anticoagulation. Guidelines for thrombolysis of deep vein thrombosis have been recently delineated by the American College of Chest physicians specifically outlining the role of adjunctive therapy with pharmacological thrombolysis.

- The routine use of systemic lytic therapy is not recommended in patients with DVT or PE (Grade 1 A).
- The routine use of CDT is not recommended in patients with DVT (Grade 1 C).
- In selected DVT patients with extensive acute proximal DVT (eg, iliofemoral/IVC, symptoms <14 days, good functional status, life expectancy >1 year) who have a low risk of bleeding, CDT may be used to reduce symptoms and patient morbidity if appropriate expertise and resources are available. (Grade 2 B).
- After successful CDT in patients with acute DVT, correction of underlying venous lesions by using balloon angioplasty and stents is recommended (Grade 2 C).
- Pharmacomechanical thrombolysis (eg, inclusion of thrombus fragmentation and aspiration) in preference to CDT alone to shorten treatment time if appropriate expertise and resources are available (Grade 2 C).
- After successful CDT in patients with acute DVT, the same intensity and duration of anticoagulation treatment as for comparable patients who do not undergo CDT is recommended (Grade 1 C).

Infusion catheters typically consist of multiple fenestrated catheters with an occluding wire that allows inspissation of the lytic agent directly into the clot, over a period of time, ranging from 4 to 48 hours. The EKOS Endovawe (EKOS Corporation, Bothell, WA) is a specialized infusion catheter that uses high frequency low power ultrasound to accelerate clot resolution, by increasing the surface area of fibrin and number of plasminogen receptor sites exposed to the lytic agent. Catheters of this type allow the operator to establish more rapid lysis, and to decrease both the dose of the lytic agent, and catheter dwell times, potentially reducing complications and decreasing length of hospital stay.

### Percutaneous Mechanical Thrombectomy

Percutaneous mechanical thrombectomy (PMT) has evolved concurrently with CDT in the management of complex subsets of veno-occlusive disease. The attraction of this modality centers on its ability to fragment, ablate, or extract thrombus to expedite lysis. Usually, complete thrombus removal requires the combined use of both CDT and PMT, but the advantages offered by PMT in the immediate treatment of an acutely ischemic limb, such as when faced with phlegmasia cerulea dolens, trump those of CDT, especially when rapid restoration of flow is required.

These devices generally work by simple aspiration, microfragmentation, and thrombo-aspiration (Venturi effect). Several of these catheters have the ability to coadminister with thrombolytic agents to facilitate clot extraction. There are however no randomized trials to date comparing any of the different

### Table 1. Summary of Catheter-Directed Thrombolysis Trials

<table>
<thead>
<tr>
<th>Study (year)</th>
<th>Design</th>
<th>Limbs Treated</th>
<th>Pathology</th>
<th>Arms</th>
<th>Agent</th>
<th>Short-Term Patency</th>
<th>Long-Term Patency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bjarnason et al (1997)</td>
<td>Institution series</td>
<td>87</td>
<td>Acute iliofemoral DVT</td>
<td>CDT (87)+PTA±stent±PMT</td>
<td>Urokinase</td>
<td>Immediate: 69 (79%), iliac, 86%; femoral, 63%</td>
<td>1 y: iliac, 63% primary, 78% secondary</td>
</tr>
<tr>
<td>Mewissen et al (1999)</td>
<td>National registry data</td>
<td>303</td>
<td>Acute and chronic suprapopliteal</td>
<td>CDT</td>
<td>Urokinase</td>
<td>Immediate: grade III in 96 (31%), II in (17% 162 (52%), I in 54</td>
<td>1 y: 181 (60%)</td>
</tr>
<tr>
<td>Rao et al (2009)</td>
<td>Institution series</td>
<td>43</td>
<td>Symptomatic iliofemoral DVT (19, &gt;14 days)</td>
<td>CDT+PMT r-tPA</td>
<td>Immediate: grade III, III lysis in 41 (95%)</td>
<td>Not reported</td>
<td></td>
</tr>
<tr>
<td>Baekgaard et al (2010)</td>
<td>Institution series</td>
<td>103</td>
<td>DVT &lt;14 days, open distal popliteal vein</td>
<td>CDT+stockings (103)+stent (57) r-tPA</td>
<td>Immediate: 95/103 (92%)</td>
<td>6 y: 84 (82%) mean follow-up 50 mo</td>
<td></td>
</tr>
<tr>
<td>Enden et al (2012)</td>
<td>Randomized controlled trial</td>
<td>209</td>
<td>Acute iliofemoral DVT</td>
<td>CDT±angioplasty±stent vs anticoagulation alone r-tPA</td>
<td>44.4% with PTS in CDT group vs 55.6% in control group at 2 y follow-up</td>
<td></td>
<td></td>
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</tbody>
</table>

CDT indicates catheter-directed thrombolysis; DVT, deep vein thrombosis; PTA, percutaneous transluminal angioplasty; PTS, Post Thrombotic Syndrome; and r-tPA, recombinant tissue-type plasminogen activator. Adapted from Patterson et al with permission of the publisher. Copyright © 2010, Wolters Kluwer Health. Authorization for this adaptation has been obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.
modalities currently available for thrombus extraction. One of the most widely used devices is the AngioJet rheolytic thrombectomy system (Medrad Possis, Minneapolis, MN), which uses high velocity saline jets to fragment and aspirate thrombus via a Venturi effect. It is Food and Drug Administration approved for both arterial and venous interventions. In the power pulse spray mode, the device can deliver variable amounts of thrombolytic agent directly into the clot, allowing both rapid saturation of thrombus with drug, combined with thrombus aspiration. In this technique, the catheter outflow lumen is occluded and a dose of lytic agent (eg, 10–20 mg tissue-type plasminogen activator in 50 mL saline) is pulsed outward from the distal catheter tip directly into the thrombus.

It has the potential advantage of diminishing the number and size of particles, in addition to enhanced speed of clot lysis, whereas reducing the need for large quantities of thrombolytic agent. After lytic penetration is maximized with a 20 to 30 minute dwell time, thrombectomy is then performed with the catheter in regular aspiration mode. Complications of the technique include hemolysis, and the theoretical risks of precipitating acute renal failure and anemia. The Trellis peripheral infusion system (Covidien, Dublin, Ireland) is an 8 French device that combines the triple modalities of thrombolytic infusion, aspiration thrombectomy, and embolic protection. This catheter has proximal and distal balloons with drug infusion holes located in between. The thrombotic segment is thus isolated after inflation of the distal balloon with subsequent proximal balloon inflation and lytic infusion through the side holes while catheter vibration facilitates lytic penetration into the thrombus. A smaller amount (eg, 4–10 mg of tissue-type plasminogen activator) of lytic agent can be used, and after 15 to 20 minutes of therapy, the proximal balloon is deflated with aspiration of thrombus from the distal port. This approach reduces the systemic absorption of the lytic agent such that this device has the potential to reduce both bleeding and distal embolization. Its use can potentially be expanded to include the treatment of patients who have traditional contraindications to lytic therapy. Experimental models suggest that the largest size and greatest number of resultant proximal emboli and PE occur with mechanical thrombectomy and fewer with power pulse spray thrombectomy when combined with lytic therapy.

CDT alone results in the fewest number of distal emboli, but at the expense of the slowest reperfusion rate. The geography of venous disease involvement (femoropopliteal, iliofemoral, caval, etc) often influences the therapeutic approach. Surgical therapy of venous thromboembolic disease, an important front line modality, varies in technique according to the particular venous segment being considered for treatment. Further consideration of interventional therapy for venous disease may best be approached by a detailed appreciation of the specific venous bed involved.

### Femoropopliteal DVT

The lure of CDT is especially attractive because of its minimally invasive nature and general safety and efficacy and has naturally fed the interventionist’s urge to extend the application of this therapy to the frequently encountered condition of acute femoropopliteal DVT. The well-established problematic natural history of iliofemoral DVT, with its strong predilection for the genesis of Post Thrombotic Syndrome (PTS), has encouraged the aggressive use of CDT. The more benign course of isolated femoropopliteal DVT makes it difficult to justify the risks of lytic therapy, which may outweigh its potential benefits in this particular venous segment. The current American College of Chest Physicians guidelines for thrombolytic therapy in venous disease reflect these concerns and appropriately state that CDT should be reserved only for those patients with extensive proximal acute iliocaval or iliofemoral DVT. Until the advent of further data from rigorously designed randomized trials, the routine use of CDT for isolated femoropopliteal DVT cannot be recommended, based on contemporaneously established guidelines.

### Iliofemoral DVT

Endovascular therapy with CDT and PMT has been shown to improve patency in patients with iliofemoral DVT. These modalities have revolutionized the treatment of venous thromboembolic disease, which affects >900,000 patients annually in the United States alone. Up to 300,000 people die of PE annually, and post-thrombotic syndrome is estimated to occur in 30% of DVT patients within 8 years. Persistent lower extremity edema, venous stasis ulceration, and venous claudication all can have serious deleterious affects on an individual’s quality of life. PTS occurs most commonly in patients with extensive multisegmental DVT, iliofemoral and occlusive IVC thrombus, as well as in patients with residual thrombus and recurrent disease. The majority of patients with PTS develop chronic venous insufficiency (90%), and 15% of these patients subsequently develop venous ulcerations. The ability of vascular specialists to move beyond the time honored standard of anticoagulation with heparin and warfarin, which (in the absence of data) may be still indicated for femoropopliteal DVT to recognize the need for more aggressive and definitive therapy to treat the larger thrombus burden prevalent in the iliofemoral segment versus the femoropopliteal segment, represents a milestone in the advancement of endovascular therapy. Endovascular PMT and CDT have replaced open surgical venous thrombectomy and temporary arteriovenous fistula as the primary interventional therapy for iliofemoral DVT. These techniques build on the 65% to 85% sustained patency rates of the older surgical techniques and offer patients a minimally invasive alternative to treat this disabling disease. Surgery is still considered an appropriate option for patients at high risk of bleeding on thrombolytic therapy. Indications for intervention include phlegmasia cerulea dolens and young patients with long life expectancy, associated with iliofemoral/IVC or multisegmental DVT. CDT and PMT are often used in concert; prophylactic IVC filters should be considered in cases where there is demonstrable free-floating iliocaval thrombus, and in those patients with compromised cardiopulmonary reserve. Ipsilateral antegrade popliteal vein access is preferred, so as to cause the least disruption to venous valvar architecture, and access is guided with the aid of venous ultrasound. Once the vein is rendered patent with CDT, PMT, or a combination of modalities, an underlying stenosis is readily amenable to balloon angioplasty, optimized with deployment of large self-expanding nitinol stents to obviate elastic recoil (Figure 1). Self-expanding stents are more resistant to extrinsic compression and, thus, can be extended into the region of the femoral vein below the inguinal ligament, if necessary, to ensure coverage of all segments with residual disease. Duplex
ultrasound imaging is recommended postprocedure as a baseline and at 6 and 12 months intervals to survey for stent patency and restenotic disease. The reported one-year patency rate with this strategy is 79% in selected series. Long-term follow-up results however are not yet available. Chronic obstructive lesions involving the iliac vein present a unique treatment challenge to the vascular interventionist. Left iliac vein compression from the right common iliac artery (May-Thurner, Cockett or iliac vein compression syndrome) or nonocclusive iliac vein lesion is estimated to comprise 49% to 62% of cases of left lower extremity disease. Although there is some degree of iliac vein compression present as a normal anatomic variant in otherwise healthy patients (>50% compression in up to 25% of patients), those who experience DVT frequently have anatomically abnormal veins with spur formation and, as such, are at high risk of developing recurrent DVT and PTS. Patients with chronic iliac vein obstruction fare well with stenting of the involved segment (Figure 2); this is especially true in nonocclusive iliac vein disease. Stented veins in patients with nonocclusive disease have a 1 year primary, assisted-primary, and cumulative secondary patency rates of 79%, 100%, and 100%, as compared with individuals with thrombotic occlusive disease with rates of 57%, 80%, and 86% at 60 months, respectively. Stent restenosis or thrombosis was rare in this series and was higher in thrombosed (10%) versus nonoccluded veins (1%). Complete coverage of the lesion often necessitates deploying the proximal stent into the IVC and at times extending distally into the common femoral vein. Adequate lesion coverage, often guided by intravascular ultrasound, seemed to provide the best long-term results.

Although IVC stent placement raises the possibility of thrombosis of the contralateral iliac vein, this phenomenon occurs only rarely (<1%) and seems to be related to recurrent thrombosis from underlying prothrombotic risk factors.

### IVC Obstruction

Thrombotic occlusion of the IVC usually occurs as a consequence of propagation from iliofemoral DVT, or IVC filter thrombosis (Figures 3 and 4), and can be associated with hypercoagulable states or abdomino-pelvic malignancies. Other causative factors include abdominal aortic aneurysms, congenital anomalies of the IVC, retroperitoneal fibrosis, and pregnancy. Furthermore although rare, IVC obstruction may result from extrinsic compression (eg, right common iliac artery, large renal and hepatic cysts or masses, hydronephrosis, and after liver transplantation from vascular anastomoses). This syndrome is also associated with the risk of PE, venous gangrene, and renal vein thrombosis, and has a variable presentation. Up to 10% of patients with chronic IVC obstruction experience no symptoms. Unilateral limb swelling occurs in about two thirds of cases. The presence of collateral pathways may mitigate the onset of classic symptoms such as bilateral limb edema and accounts for the variable clinical presentation of this syndrome. The development of symptoms is often associated with occlusion of the common iliac vein, which compromises an important collateral pathway from this vein to the IVC via the thoracolumbar vein.

Standard surgical therapy for IVC thrombosis/occlusion involves surgical thrombectomy, often with adjunctive temporary distal arteriovenous fistula creation. Endovascular therapy offers significantly less morbidity and mortality than surgery. In the largest reported series of endovascular therapy for IVC occlusion, 82% of the lesions in a cohort of 120 patients were infrarenal, with suprarenal involvement in 18% of cases. There was concurrent iliac vein occlusion in 93% of cases. IVC lesions comprised total occlusions in 14% of cases and partial occlusions (>60% stenosis) in 86%. Technical success with recanalization rates was 100%
for partial obstructions and 66% for complete occlusions. Cumulative primary and assisted-primary patency rates were 58% and 82%, respectively, at 2 years. The initial revascularization strategy uses CDT if clot is present, followed by PMT as needed. The femoral vein can be accessed directly or via ultrasound guidance at the groin; large caliber (9–14F) sheaths are usually required. Underlying lesions are identified and should undergo high-pressure angioplasty and stenting. The advantage of self-expanding venous stents include the ability to oversize them so as to allow proper fixation and reduce the risk of stent migration in these highly compliant vessels. Wallstents (Boston Scientific, Natick, MA) are often used in these vascular segments because of their recognized wide clinical experience and availability in large sizes suitable to accommodate this type of intervention. Sizes most often used are 14 mm (iliac) to 24 mm (IVC) in diameter, matched to the vessel diameter as determined by intravascular ultrasound. Generous overlap of stents 3 to 4 mm is necessary to mitigate against the loss of apposition to adjacent stent. Closure devices are rarely indicated when access is obtained via the femoral or popliteal vein.

**Axillosubclavian Vein Thrombosis**

Axillosubclavian venous thrombosis (ASVT) or upper extremity DVT is an often neglected cause of venous thrombosis. It is rare accounting for 2% to 4% of all DVT.\(^9\) It has traditionally been regarded to have a more benign clinical course as compared with lower extremity DVT. This preconception is misguided because PE can occur in up to 11% to 36% of patients with ASVT, and disabling post-thrombotic syndrome in up to 13% of patients.

A useful classification is to categorize its pathogenesis into primary and secondary forms because symptom severity and treatment strategies do differ between the 2 groups. Secondary ASVT occurs because of the presence of indwelling vascular devices such as pacemakers and implantable cardiac defibrillator leads, central venous and tunneled catheters, sometimes in concert with underlying thrombophilia or other significant comorbidities. Symptoms are frequently mild but can range from severe to asymptomatic. Most patients can be managed with a short 3-month course of anticoagulation, with or without catheter removal. However, the ideal solution is removal of the catheter, if feasible, followed by ≥4 weeks of anticoagulation, for a total duration of 3 months. If the functioning catheter is of medical necessity, anticoagulation is continued while the catheter remains in place. This conservative strategy is supplanted by CDT therapy when symptoms become severe or when preservation of vascular access is deemed to be paramount.

Primary ASVT (Paget–Schroetter Syndrome), although much less common than secondary ASVT, tends to affect young, otherwise healthy individuals, and can lead to chronic debilitating symptoms. Repetitive activity of the upper extremity in the setting of an underlying abnormality of the thoracic outlet predisposes susceptible individuals to axillosubclavian vein thrombosis. The subclavian vein is usually compressed between the first rib and a hypertrophied scalene muscle and subclavius tendon. This syndrome is also characterized by the development of perivenous fibrous and venous web formation in chronic cases. Common symptoms include arm pain, fatigue, and swelling after a history of trauma or strenuous use of the involved extremity. Prominent superficial veins around the shoulder (Urschel’s sign) may characterize the formation of collaterals on the anterior chest wall. Medical therapy with anticoagulation often fails these patients, who may subsequently develop chronic disabling symptoms. Post-thrombotic syndrome can occur in up to 13% of patients.\(^20\) The severity of symptoms correlates closely with the degree of obstruction.
Re-establishing venous patency becomes of paramount importance in such cases, and although studies have demonstrated the beneficial effects of rapid recanalization, the optimal revascularization strategy has not been subject to a randomized multicenter trial.23

One popular strategy is the aggressive use of CDT to re-establish flow expeditiously (Figure 5), followed by in-hospital surgical decompression with first rib resection, subclavious muscle, scalenectomy, and vein patch plasty of the stenotic segment of the vein either via transaxillary or supra/infravacular approach. Percutaneous transluminal angioplasty and provisional venous stenting may be required for persistent symptoms or when residual stenosis is observed after surgery to prevent rethrombosis of the diseased vein. Because the abnormality is frequently bilateral in up to 61% of patients, evaluation of the contralateral limb is also recommended on an elective basis. Contrast venography is the key diagnostic procedure in these cases, and images of the symptomatic extremity should be obtained in both neutral position and during thoracic outlet maneuvers. Elective repair of an involved but asymptomatic limb should be considered in patients with occupational risks for thrombosis, and in those cases where compression of the vein involves the dominant arm.22

First-rib resection for ASVT is an effective treatment. In Machleder’s initial series of 50 consecutive patients, 43 patients underwent thrombolytic or anticoagulant therapy followed by long-term warfarin treatment. Thirty-six patients (72%) had first-rib resection, and 9 patients had post–surgical balloon venoplasty to correct residual disease. Pain-free status was achieved in 93% of patients with a patent vein. No episodes of recurrent thrombosis after surgical correction were observed for a mean follow-up period of 3.1 years.

Urschel and Patel, in their much larger series of 626 patients with Paget–Schroetter Syndrome,23 reported on 506 patients who underwent prompt surgical first-rib resection after initially receiving thrombolytic therapy within 6 weeks of symptom onset. Of these, 486 patients had complete or nearly complete resolution of pain symptoms and were subsequently able to return to work. A late therapy group of 42 limbs were not treated until 6 weeks after venous occlusion. All received thrombolytic therapy, although none of the occlusions could be completely opened, all were treated with surgery. Twenty-four limbs subsequently recanalized or developed collateral circulation of sufficient extent as to be able to report good results after rib resection, whereas 9 limbs had fair results. Only 5 patients in this group manifested signs of severe PTS.

Catheter-based treatment of ASVT begins with basilic vein access, followed by CDT therapy. Adjunctive mechanical thrombectomy may be combined with CDT as required. Repeat venography to reassess the status of the vein is usually performed within 4 to 24 hours of commencing lytic therapy. Early in-hospital, first-rib resection is then aggressively pursued. A follow-up venogram is then advisable 4 weeks after surgery with adjunctive percutaneous transluminal angioplasty and stenting if residual disease is present and active symptoms are present. At this time, venography of the contralateral limb with the extremity in neutral and with active thoracic outlet syndrome maneuvers may also be performed to exclude asymptomatic disease. Figure 6 shows the treatment algorithm for management of Paget–Schroetter Syndrome.

**Superior Vena Cava Syndrome**

Obstruction of the superior vena cava (SVC) results in venous hypertension of the head, neck, upper thorax, and extremities, in varying severity. SVC syndrome is the symptom complex resulting from obstruction of blood flow through the SVC. There are an estimated 19,000 cases annually in the United States alone, with a rising incidence that has been attributed to the increasing use of indwelling central venous catheters. The pathogenesis of SVC syndrome is multifactorial (Table 2), but intrathoracic malignancy accounts for 60% to 85% of cases.24 Malignant obstruction of the SVC is either from extrinsic compression by tumor or by direct tumor invasion. Indwelling catheter-induced stenosis, thrombosis, and radiation fibrosis are contributing adjunctive factors. The emerging use of pacemaker-defibrillators and multiple transvenous leads and long-term indwelling catheters has also contributed to the genesis of the syndrome and are among its more common causes. However, rarer pathogeneses such as fibrosing mediastinitis and granulomatous disease, such as tuberculosis, and syphilitic aortic aneurysm causing secondary compression also need to be considered in the differential diagnosis.

The more common symptoms of SVC syndrome include dyspnea, cough, chest discomfort, dysphagia, hoarseness, and head fullness related to facial plethora. Headaches, delirium, and coma suggest the presence of associated cerebral edema, which is seen in <10% of cases. Signs of SVC syndrome include facial

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**Figure 5.** A. Venogram of right arm via basilic vein access depicting acute thrombus involving axillary and subclavian vein. B. Postlysis (4 hours tissue-type plasminogen activator) venography showing patency of axillary and SCV, albeit with residual stenosis at proximal SCV (pre-first rib resection).
and upper extremity edema, and jugular venous distension, all of which may be exacerbated by lying supine or bending forward. Prominent superficial venous collaterals may develop across the anterior chest wall. Airway compromise from laryngeal edema is rare. The severity of obstruction is dependent on the rapidity of onset of symptoms and the anatomic relationship of the occlusion to the origin of the azygous vein. Most symptoms take several weeks to evolve, and the clinical severity of symptoms is often mitigated by the recruitment of collateral venous pathways, which may take weeks to be become established. A level of obstruction below the azygous vein usually tends to cause more severe symptomatology because important collateral pathways include the azygous, internal mammary, paraspinal, lateral thoracic, and esophageal venous systems. There are 4 patterns of venous collateral return in SVC syndrome:

- Type I: Partial SVC obstruction with antegrade azygous vein flow.
- Type II: Near complete SVC obstruction with antegrade azygous vein flow.
- Type III: Complete SVC obstruction with flow reversal in azygous vein.
- Type IV: Complete SVC and azygous vein obstruction with prominent chest wall and mammary venous collaterals.25

Contrast-enhanced chest computed tomographic scan is usually sufficient to establish the diagnosis. This examination also allows assessment of the level and extent of the occlusion and the status of the collateral pathways. Computed tomographic scanning can also detect associated thoracic malignancy and alternative, coexistent diagnoses such as pericardial effusion and pulmonary embolus. Magnetic resonance venography is a reasonable alternative in patients without renal dysfunction but with allergy to iodinated contrast.26 The use of duplex ultrasound is confined to the assessment of associated thrombosis of the upper extremity veins and the axillosubclavian venous segment. This modality is of great value in planning for endovascular procedures but cannot reliably determine patency of the SVC. Venographic confirmation of SVC occlusion is best done at the time of endovascular intervention.

In addition to head elevation and administration of diuretics to reduce central venous hypertension, a concomitant search for causes and exclusion of coexistent SVC thrombosis is mandatory because venous thrombosis requires consideration of CDT, and the presence of malignancy raises the question of life expectancy. All of these factors ultimately impact and influence subsequent management and treatment options. Mild cases of SVC syndrome are often self-limited with oftentimes spontaneous resolution of symptoms, which are largely improved with the development of venous collaterals. Anticoagulation is recommended to prevent thrombus formation or subsequent propagation, preserve collateral patency, and reduce the risk of PE. Glucocorticoid therapy is indicated in the cases of steroid responsive malignancies such as lymphoma or in patients with laryngeal edema and impending airway compromise. Revascularization is indicated in the presence of significant symptoms. The presence of malignancy has a significant impact on treatment strategy. In SVC syndrome associated with a chest malignancy, the life expectancy is usually ≈6 months, and palliation of symptoms is the main goal of therapy. Long-term patency is less of an issue. In benign disease, which is often associated with younger patients, durability of the recanalization procedure and maintenance of central venous access assumes greater importance.

There are no randomized trials comparing surgical and endovenous therapy in the treatment of SVC syndrome.

Table 2. Causes of SVC Syndrome

<table>
<thead>
<tr>
<th>Malignancy</th>
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<tbody>
<tr>
<td>Bronchogenic carcinoma</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
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<table>
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<tr>
<th>Benign causes</th>
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<tr>
<td>Indwelling central venous catheters</td>
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<tr>
<td>Pacemakers/implantable cardiac defibrillators</td>
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<tr>
<td>Granulomatous infection (eg, tuberculosis)</td>
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<td>Mediastinal fibrosis and sclerosing mediastinal fibrosis</td>
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<tr>
<td>Histoplasmosis</td>
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<tr>
<td>Thoracic aortic aneurysm–related compression (eg, syphilis)</td>
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<td>Postsurgical (eg, cardiac-lung transplant or ventriculocavitary shunt)</td>
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<tr>
<td>Postradiation</td>
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SVC indicates superior vena cava.
Surgical options include venous bypass grafting from the jugular or innominate vein to the right atrial appendage or SVC. Autologous vein (spiral saphenous or femoral) is the conduit of choice, but polytetrafluoroethylene (PTFE) or human allograft can be used if autologous vein is unavailable. Surgical patency rates for benign disease range between 61% and 83%. Five-year primary, assisted-primary, and secondary patency rates of 45%, 68%, and 75%, respectively, have been reported.27,28 Results for endovascular intervention in benign SVC syndrome are less clear and remain to be determined. Limited data show a high technical success rate of 88% with primary patency rates of 44%, and primary assisted-patency and secondary patency rates of 96%, at 3 years. Maintenance of long-term assisted patency required multiple reinterventions during the 36-month period.29,30

SVC stenting for malignancy disease carries an excellent technical success rate of 95% to 100% and primary and secondary patency rates of 85% and 93%, respectively, at 3 months.31 Clinical relief of symptoms is usually almost immediate within hours to days after successful SVC recanalization. The endovascular approach to SVC occlusion begins with selection of the appropriate access point. Bilateral upper extremity venography is useful in delineating the extent of the disease and presence of thrombus. Focal SVC stenosis can be approached via either cephalic, basilica, or femoral veins, but more extensive occlusive disease involving the brachiocephalic or axillousubclavian venous systems usually requires basilic, internal jugular, femoral, or a combination of veins for access to facilitate comprehensive revascularization. CDT therapy is generally undertaken in the presence of significant thrombus, careful screening for contraindications is required and intracerebral metastatic disease if malignant SVC syndrome is the diagnosis. Residual stenoses and thrombus are treated with balloon angioplasty, using large caliber (8 to 16 mm) balloons. Stent placement is required in most cases because these lesions tend to be fibrotic, or in the case of extrinsic compression, prone to significant recoil. Large caliber stents are necessary, and stents are usually oversized by ~10% to 20% compared with the normal reference vein. This oversizing reduces the potential risk of stent migration. Focal lesions are amenable to balloon-expandable stents, for example, Palmaz/Genesis (Cordis Corporation, Warren, NJ) given the high radial force and precision in positioning offered by these stents, which offsets their relatively short lengths and inflexibility. Large diameter self-expanding stents, such as the Wallstent and the Gianturco Z-stent (Cook Medical, Bloomington, MN), which are flexible, may be required in a large SVC. However, these stents have less radial strength and are prone to tissue and tumor prolapse through the wide gaps in the struts predisposing to restenosis. Nitinol stents, although supportive because of the intrinsic strength of their alloy, are limited by their available maximal diameters of 14 mm, which are too small to accommodate most SVC diameters. If indwelling catheters or recently placed pacemakers are thought to be at risk for malfunction and can be safely removed, they should be repositioned after stenting is completed (Figure 7). If pacing lead extraction is not feasible, stenting across pacemaker leads seems to be safe without adverse consequences.32 Obstruction at the confluence of the brachiocephalic veins with the SVC poses a special problem for the interventionist. In older patients, or patients with reduced life expectancy, recanalization of one side is usually sufficient to improve symptoms because collaterals provide

Figure 7. A, Subtotal occlusion of superior vena cava (SVC) in woman with metastatic lung cancer and permanent pacemaker via right SCV. B, Contrast venography from the contralateral side displays the innominate vein and subtotal occlusion of the SVC. C, Balloon dilation of SVC with 12 mm high-pressure catheter, note the deflection of pacemaker wires. D, Final venacavogram poststenting (Genesis) of SVC after pulling pacer wires out of position and reimplanting after successful stent deployment.

Figure 8. A, Venacavogram with occlusion of superior vena cava (SVC) and bilateral innominate venous stents in young male with implantable cardiac defibrillator-induced SVC thrombosis. B, Venography after reconstruction of innominate vein confluence with kissing stents and SVC stenting.
adequate drainage from the contralateral side. In younger patients, with expected long-term survival, where maintenance of vascular access is of importance, bilateral arm or femoral vein access and kissing stents implantation should be considered (Figure 8). There is no consensus as to the type of and duration of anticoagulant therapy postprocedure. In the absence of SVC thrombosis, antiplatelet therapy with aspirin and clopidogrel until stent endothelialization occurs is sufficient. A low threshold for anticoagulation should be maintained in patients with severe SVC obstruction or history of malignancy, where increased thrombogenicity is a factor. Patients should be followed postprocedure with serial upper extremity duplex ultrasonography to assess flow and vessel patency. Contrast venography or computed tomography venography is usually performed at 3 to 6 months postprocedure in selected cases or as appropriate when the clinical scenario suggests instant restenosis or thrombosis. Complications of SVC interventions are infrequent, occurring in 3.2% to 7.8% of cases. These range from minor complications, such as access site hematoma, epistaxis, and chest pain, to major ones, such as pulmonary embolus, cardiac tamponade, stent migration, and thoracic hemorrhage. Thrush pulmonary edema from the sudden restoration of robust venous return to an underfilled right heart has also been reported albeit rare.

Despite these issues, endovascular intervention for SVC syndrome is an appropriate primary intervention because it is less invasive than surgery with lower morbidity. In benign SVC syndrome, its efficacy and midterm patency rival that of surgery. However, long-term patency is as yet unknown. Surgery is appropriate in patients with benign SVC syndrome who are not suitable or who fail endovascular therapy. Endovascular therapy is appropriate first-line therapy for patients with malignant SVC syndrome. Endovascular therapy is associated with high assisted-primary and secondary patency rates in these patients, although multiple interventions are often required.

Conclusions

The interventional therapy of venous thromboembolic disease has steadily migrated from primary surgical treatment toward more minimally invasive techniques such as CDT and mechanical thrombectomy. Although there is currently a paucity of data from well-validated large randomized trials to firmly establish the efficacy of percutaneous therapy, its ease of use and generally widespread applicability to a range of patient subsets has earned this modality a well-favored place in interventional practice. The emergence of exciting new catheter-based technology that shortens lytic exposure, thereby increasing safety while enhancing good technical outcomes, has consolidated its position as the therapy of choice to treat this problematic disease. It is hoped that further clinical research will help validate the use of early and aggressive treatment of this relatively common undertreated condition.

Disclosures

None.

References


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