A comprehensive review of Paget-Schroetter syndrome

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Venous thoracic outlet syndrome progressing to the point of axilosubclavian vein thrombosis, variously referred to as Paget-Schroetter syndrome or effort thrombosis, is a classic example of an entity which if treated correctly has minimal long-term sequelae but if ignored is associated with significant long-term morbidity. The subclavian vein is highly vulnerable to injury as it passes by the junction of the first rib and clavicle in the anterior-most part of the thoracic outlet. In addition to extrinsic compression, repetitive forces in this area frequently lead to fixed intrinsic damage and extrinsic scar tissue formation. Once primary thrombosis is recognized, catheter-directed thrombolytic therapy is usually successful if initiated within ten to 14 days of clot formation, but often unmasks an underlying lesion. The vast majority of investigators believe that decompression of the venous thoracic outlet, usually by means of first rib excision, partial anterior scalenectomy, resection of the costoclavicular ligament, and thorough external venolysis, is necessary, although opinion is less uniform as to the need for and method of treatment of the venous lesion itself. Using this algorithm, long-term success rates of 95 to 100% have been reported by many investigators. This review, in addition to discussing the overall treatment algorithm in more detail, attempts to point out controversies that still exist and research directions, both clinical and basic, that need to be pursued. Prospective randomized trials addressing this entity are surprisingly lacking, and although there is consensus based on experience, it may be necessary to step back and rigorously explore several aspects of this entity. (J Vasc Surg 2010;51:1538-47.)

Paget-Schroetter syndrome, also referred to as "effort thrombosis," refers to primary thrombosis of the subclavian vein at the costoclavicular junction. Sir James Paget[1] was the first to describe a case of "gouty phlebitis" of the upper extremity in 1875, which turned out to be spontaneous thrombosis of the subclavian vein, and von Schroetter[2] postulated in 1884 that this entity resulted from direct damage to the vein caused by stretching that occurred from muscular strain. The English surgeon, Hughes,[3] termed the condition Paget-von Schroetter syndrome in 1949, and it has been known by variations of this eponym ever since.

A surprising amount of confusion surrounds thoracic outlet syndrome (TOS) in general, due in part to the mistaken assumption that this is all one entity. There are two different and distinct anatomic spaces to consider – the brachial plexus and subclavian artery pass through the triangle formed by the scalenus anticus and medius muscles and the first rib, whereas the subclavian vein re-enters the chest more anteriorally, passing adjacent to the junction of the clavicle and first rib which is further reinforced by the subclavius muscle and tendon (Fig 1). In order of incidence, neurogenic (NTOS), venous (VTOS), and arterial (ATOS) thoracic outlet syndromes are three distinct entities and should be conceptualized, discussed, analyzed, and treated as such. VTOS is further divided into three different categories: intermittent/positional venous obstruction, secondary subclavian vein thrombosis (in the setting of catheters or pacemaker leads), and primary "effort thrombosis" (Fig 2). The last entity, primary effort thrombosis, is the topic of the current review.

Essentially, no prospective randomized trials concerning the treatment of effort thrombosis exist; most of what we do today is guided by single series reports, retrospective reviews, expert opinion, book chapter, and general review articles (for example, Swinton et al[4] [1968] for an early overview, Shebel and Marin[5] [2006] for a very readable review presented to vascular nurses, and Landry and Liem[6] [2007] for a recent endovascular update). At this point in time, we feel that certain areas are well-established by consensus, but point out that prospective randomized trials are sorely needed. This review will discuss the evolution of treatment for this entity over the past half century (from heparinization alone to catheter-based thrombolysis followed by thoracic outlet decompression), review current management schemes, and attempt to summarize modern consensus opinion. We will also provide a list of needed data – what needs to be done to better guide our care of these patients?

EPIDEMIOLOGY, ANATOMY, AND PATHOPHYSIOLOGY

Primary effort thrombosis seems to be a relatively rare condition. The incidence has been extrapolated from a Swedish experience to be about 2.03 per 100,000 people per year,[7] whereas even as a regional referral center, we have seen only 1.0 patients per 100,000 population per year over the past 5 years. If the true incidence is between one and

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Competition of interest: none.

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The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a competition of interest.

0741-5214/$36.00

doi:10.1016/j.jvs.2009.12.022

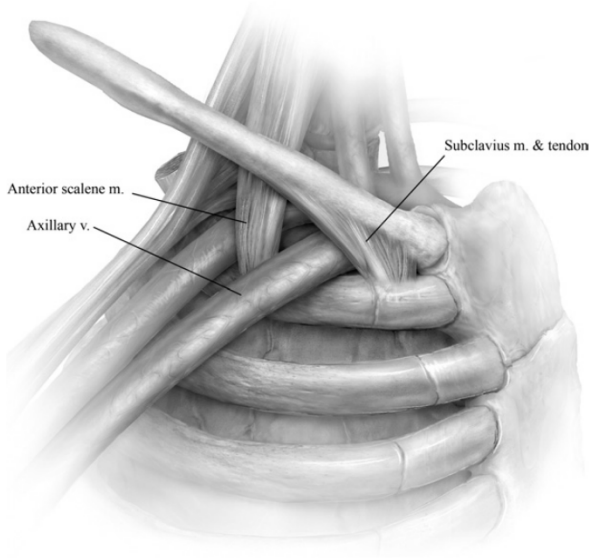

Fig 1. Basic anatomy of the thoracic outlet. The subclavian/axillary vein is located anteriorally, and passes *in front* of the anterior scalene muscle (shown detached from its origination on the spine). Note the position of the vein between the first rib and clavicle, the position of the subclavius tendon, and the potential for "nutcracker-like" compression by the two bones, even with only minimal movement. *m,* Muscle; *v,* vein.

two per 100,000 people per year, the yearly incidence in the United States would be 3000 to 6000 cases yearly. Upper extremity effort thrombosis accounts for approximately 1% to 4% of all episodes of venous thrombosis,[8,9] which yields a slightly higher estimate. Like many "rare" problems, its incidence is likely under-recognized by nonspecialists.

Mean age at presentation is the early 30s, and the male to female ratio is approximately 2:1. It is more common on the right, likely because of the incidence of right-hand dominance, and 60% to 80% of patients report a history of vigorous exercise or activity involving the upper extremities.[7,10-12] A recent review of one major league and one division I baseball team over an 11-year period revealed 4 such cases, which yields a rate of 1 case every 5 years per high-level baseball club, for example.[13]

The relative rate of primary effort thrombosis vs secondary thrombosis is difficult to identify, as no comprehensive studies have been performed. Two surveys of all episodes of upper extremity thrombosis at each of two institutions suggest that the ratio is close to 40%,[11,14] although both series are small.

Anatomy and pathophysiology. VTOS is a disorder of the anterior part of the thoracic outlet region, where the subclavian vein passes by the intersection of the clavicle and first rib (Fig 1). Whereas the posterior/cephalad portion of this area is open (the anterior scalene, lying posterior to the vein, does not communicate with the clavicle), a hypertrophied anterior scalene can compress the vein from behind.

In addition, the subclavius muscle itself underlying the clavicle and providing "bulk" at the costoclavicular junction can further compress this area. Although the first rib and clavicle don't move very much, they do so with extreme force and leverage – and the vein is located precisely at the point of maximal compression. It is unclear whether an anatomically smaller costoclavicular space, resulting from either hypertrophied muscle (scalenus anterior or subclavius) or abnormal bone morphology (clavicle or first rib) is required or whether this condition can simply occur without a defined abnormality.

Adams et al[15] demonstrated that even in normal patients the subclavian vein can easily be compressed within the costoclavicular space (Fig 3). Regardless of which anatomic structure is thought to be abnormal, the subclavian vein is compressed with arm abduction by any one structure alone or in combination.[16-19]

In our experience, when vigorous activity cannot be elicited, maneuvers where the arm is frequently overhead (auto repair, painting, recreational badminton, and weight training) is often present, and we have seen several recent cases in teenaged baseball pitchers and teenaged swimmers. A history of clavicle fracture is not uncommon, although the presence of a cervical rib (a relatively posterior structure) is not felt to be a risk factor for VTOS. Forty percent of patients recall an activity that involves repetitive or prolonged hyperabduction or external rotation of the shoulder joint,[20,21] and at times no factor other than increased muscle bulk can be elicited.

It is unclear whether thrombosis results from a single insult or is the result of the cumulative effects of chronic injury to this area. It is thought that chronic compression and trauma eventually produce external inflammation, which in turn leads to fibrosis, relative fixation to the surrounding anatomic structures, and perhaps intimal hypertrophy.[22] It is clearly seen at operation that the loose connective tissue which normally surrounds the vein is replaced by dense collagen scar. This scar-entrapped vein becomes less mobile as it traverses the costoclavicular space and, therefore, becomes at increased risk for further injury. Because the vein is no longer able to freely move in this area, it is stretched and torn whenever the diameter of the costoclavicular space is changed.

Some patients are thought to have intermittent venous outflow obstruction caused by compression in this area without objective evidence of actual injury to the vein. These patients will have venograms that are normal at rest but abnormal (varying degrees of extrinsic compression with "new" venous collaterals) with the arm abducted (Fig 3, *A*, *B*). The natural history of these patients is unclear, but they are thought to be at risk for later thrombosis and are often electively treated. Alternatively, a subclinical syndrome may develop wherein there is recurrent partial thrombosis followed by recanalization,[15,23] with or without symptoms. Each time the vein is partially thrombosed and recanalized, the sequence of local inflammation and further scar formation progressively add to the intrinsic venous defects; the presence of collagen webs and fibroelastic strictures

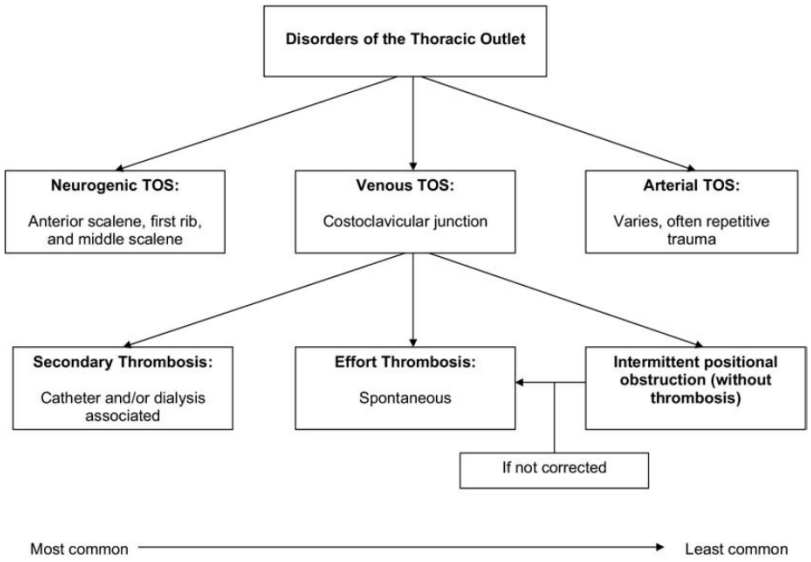

Fig 2. Basic classification of thoracic outlet syndrome. Intermittent positional venous obstruction is felt to be a precursor of effort thrombosis if not recognized and treated. The exact incidences of these conditions is unknown, but their relative frequencies are shown, most common to least common, reading left to right. *TOS,* Thoracic outlet syndrome.

within such a vein, even if not thrombosed at the time of exploration, is not uncommon.

Whatever the mechanism, when the vein fully occludes symptoms are almost always present and, if thrombosis is sudden and complete, severe. Multiple collateral pathways exist, termed by Adams et al[19] "first-rib bypass collaterals," most notably connecting cephalic vein and profunda branches with the transverse cervical, scapular, and external and internal jugular veins. These collateral pathways, in addition to providing drainage from the arm, are extremely valuable diagnostic venographic clues that a hemodynamic obstruction exists even if not well seen itself, but are not usually adequate to provide full drainage and obviate symptoms. Typically the early thrombus is soft and easily treated, whereas chronically (over weeks) it becomes organized, adherent, and fibrotic. In extreme cases, the vein can fibrose to a solid lumenless cord. Although a report from Sweden published in 1988[7] suggested that hypercoagulable states are relatively infrequently seen, a more recent investigation suggested that the rate of any hypercoagulable condition may be as high as 67%.[24]

CLINICAL PRESENTATION

Patients with intermittent positional venous obstruction will present with episodic arm discoloration and swelling, usually elicited by either exercise or arm elevation. By contrast, those with true effort thrombosis will almost always be persistently and, if acutely thrombosed, severely symptomatic. Clinical presentation is classic, with the patient complaining of a blue, swollen, heavy, painful arm. Patients typically present with sudden onset of an aching discomfort with a feeling of heaviness, swelling, and frequently a reddish-blue discoloration of the affected upper extremity. Sixty to 80% of patients report a history of vigorous exercise or activity involving the upper extremities, and approximately 85% of patients will have symptoms within 24 hours of the inciting event. A prominent venous pattern consisting of dilated superficial collateral veins over the upper arm, base of the neck, and anterior chest wall develops in many patients, especially if occlusion is chronic.[5,8,10,12,25,26]

The diagnosis is usually straightforward. A duplex ultrasound scan is diagnostic, with high accuracy in experienced hands. In a recent randomized trial, for example, a duplex scan was found to have a sensitivity of 78% to 100% and a specificity of 82% to 100%.[27] At times, positional stress can help, but in true effort thrombosis by definition the vein is thrombosed at rest, so examining the arm in a neutral position is usually adequate. As seen during any duplex venographic evaluation for clot, a fresh thrombus, although echolucent, will be apparent by lack of compressibility and absence of flow, whereas a more chronic clot will be more fibrotic and echogenic. An experienced technician can often also visualize the prominent collateral venous pathways that develop. Potential drawbacks include the inability to adequately visualize the central portions of the subclavian and innominate veins and difficulty in differentiating a central vein from a large collateral. In a recent imaging consensus statement published by the American College of Radiology,[28] an ultrasound scan was felt to be the best first approach for direct evaluation of arm veins, whereas venography, for example, was recommended if noninvasive studies are inconclusive (or intervention is planned).

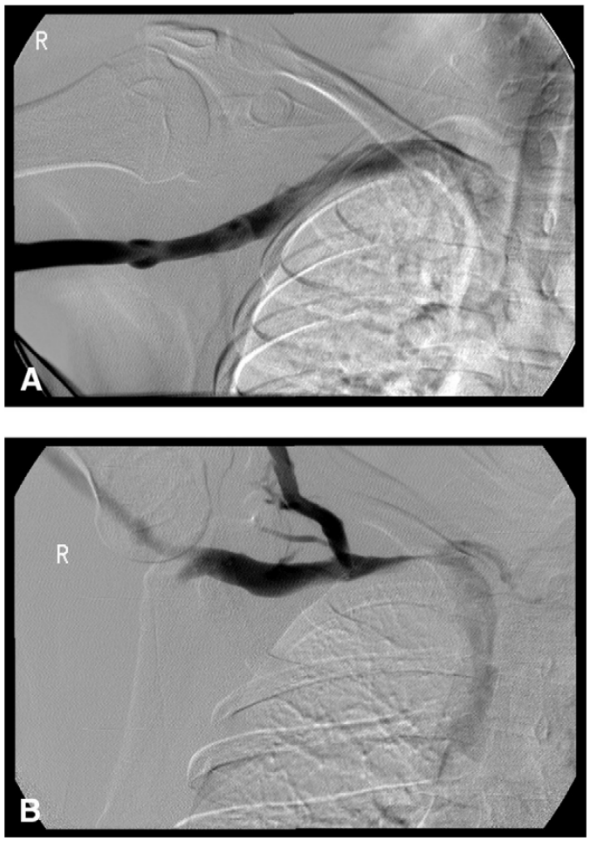

Fig 3. Effect of arm position on the axillary/subclavian vein at the costoclavicular junction. **A,** Arm outstretched but less than 90 degrees. Note the absence of obstruction and the absence of collaterals. **B,** Arm abducted well over 90 degrees. Note the smooth extrinsic compression at the costoclavicular junction and the visualization of the external jugular vein and surrounding collaterals.

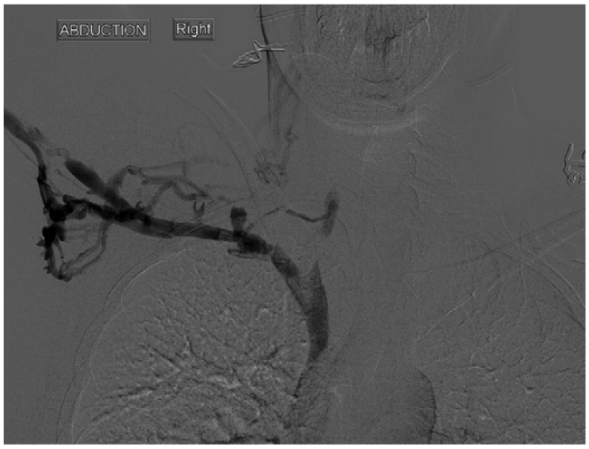

Fig 4. Venogram in a patient after thrombolysis with significant residual obstruction. Note that although the obstruction itself is poorly visualized, extensive venous collaterals are present. These are pathognomonic for a hemodynamically significant obstruction to outflow.

Axial imaging (CT and MR) have been disappointing when used in the evaluation of TOS in general, probably because no gross or categoric structural abnormality usually exists. MR and CT are increasingly useful to examine the central veins,[28] but no investigator has been able to identify bony and/or soft tissue abnormalities that affect treatment in this situation. We have recently experimented with CT and MR "venograms" to assess central venous inflow in difficult dialysis access patients, but have been discouraged by the inability to visualize the venous structures at the costoclavicular junction with adequate resolution. In addition, because history, physical examination, and duplex ultrasound scans are so reliable and venography essentially always follows this diagnosis, the benefit of further axial imaging is unclear.

Venography is both diagnostic and often therapeutic. Diagnostic venography can be performed via relatively distal access of a peripheral vein, although if visualization is suboptimal or if intervention is planned, ultrasound scan-guided access to the deep system (true brachial veins) at the antecubital fossa or distal upper arm is needed. As pointed out by Green and Rosen,[29] the diagnosis can be missed if the upper arm cephalic vein is used for contrast injection. The diagnosis should be immediately obvious by noting occlusion of the subclavian vein at the costoclavicular junction (at times with more distal extension of thrombus) and by the presence of collaterals, which will not be visualized if axial flow is normal. If the vein seems open but collaterals are present, some degree of obstruction must exist (Fig 4), and if the vein is open and no collaterals are seen the arm must be abducted to well over 90 degrees with a normal venogram before VTOS is ruled out. If the deep system is nonvisualized and the venogram is otherwise normal, the study should be repeated with a tourniquet in place to occlude the superficial venous system (although it should be pointed out that the problem lies central to the normal confluence of the cephalic vein into the axillary-subclavian system).

TREATMENT

The treatment of effort thrombosis has been the subject of a surprising volume of literature over the past half century, perhaps in disproportionate volume to its incidence. The central issues are whether this should be treated at all, the best method of treatment of the thrombus itself, timing and method of "permanent" correction of the underlying defect, and how to treat and follow these patients in the long term.

Natural history and anticoagulation alone. It was recognized as early as a 1949 report[30] that leaving this condition untreated results in significant morbidity in the majority of patients, and once anticoagulation became available this became the earliest standard of care. Results with anticoagulation alone, however, are quite poor. For example, acute pulmonary embolism occurs in 6% to 15% of

such cases.[31-33] Adams and DeWeese[12] found that untreated effort thrombosis causes residual upper extremity venous obstruction in up to 78% of cases, whereas persistent symptoms and permanent disability are present in 41% to 91% and 39% to 68% of such patients, respectively.[11,12,21,30-32,34] Heron et al[35] reported "negligible" symptoms at follow-up in only 25 of 54 patients (46%) so treated, whereas in a more modern review Urschel et al[20] reported "excellent or good" long-term results in only 10 of 35 patients (29%) treated with anticoagulation (with first rib resection reserved for persistent problems) alone.

Thrombolytic therapy. Because of the disappointing long-term outcomes after anticoagulation alone, catheter-directed thrombolysis has become the standard first step in all patients with acute effort thrombosis unless significant contraindications are present. Apparently, first performed in the late 1970s, the first reports of such were published in the early to mid 1980s by Zimmerman et al,[36] Becker et al,[37] Taylor et al,[38] Druy et al,[39] and Perler and Mitchell,[40] with encouraging, albeit uncontrolled results.

Machleder, in a seminal 1993 paper, described the results of a structured algorithm introduced at UCLA in 1985, which consisted of thrombolysis and selective first rib resection after approximately 3 months' delay to "avoid rethrombosis." Although 50 patients were treated by this protocol, only 43 had thrombolysis and 36 thoracic outlet decompression. A total of 93% of patients who were left with an open vein were free of symptoms at follow-up, whereas only 64% of those whose veins could not be reopened were free of symptoms.[41]

Catheter-directed thrombolysis is successful in 62% to 84% of cases,[14,42] although this rate is much higher the fresher the clot, nearing 100% if initiated within a few days of symptom onset. In three recent reports, no patient with symptoms persisting for longer than 10 days had successful lysis,[36,43,44] whereas the success rate in patients at the University of Rochester with symptoms of less than 14 days' duration has been 84% over the past decade.[42] In a large experience from Baylor, only 50% of occluded veins could be partially opened if treated more than 6 weeks after symptom onset; none were completely recanalized.[20] A greater clot burden also correlates negatively with success; Molina[45] and Green and Rosen[22] report 25% and 22% success rates in "long segment" occlusions, respectively.

After thrombolysis, a significant number of patients are shown to have intrinsic venous defects[45,46] caused by scarring due to persistent injury and essentially all will have extrinsic compression at the costoclavicular junction. If surgical decompression is not performed, rethrombosis within 30 days has been reported to occur in as many as a third of patients.[20,39,47,48] Angioplasty and even stenting of these patients is tempting, but the costoclavicular junction is unyielding, and angioplasty before decompression fails at high rates.[41,49-51] It has been suggested (but not proved) that predecompression angioplasty may even directly worsen venous patency by further damaging the endothelium.[52,53] Stenting of the vein running through the nondecompressed costoclavicular junction has been shown to be complicated by stent fracture in some, deformation in nearly all, and rethrombosis rates as high as 40%.[49] Stents in this location, whether fractured or not, obviously complicate subsequent repair, and for this reason as well should be avoided at all costs. It is essential to remember that the force of the costoclavicular junction far overwhelms the strongest stent.

Correcting the problem. Thrombosis is only the acute symptom of the underlying chronic problem, which is extrinsic compression and internal damage to the vein at the costoclavicular junction. Thrombolysis treats the immediate complication, but clot will recur and symptoms persist in as many as a third of patients whose underlying anatomic problem is not corrected.[20,39,47,48] It is generally accepted that surgical decompression of the costoclavicular junction should follow thrombolysis, but recommendations, dogma, and beliefs vary widely according to whether lysis is complete, whether intrinsic venous defects persist, and the degree of residual symptoms. In addition, significant differences exist regarding both methods and timing of decompression, and a respected minority view, discussed below, holds that decompression may not be necessary at all.

Transaxillary first rib resection, first reported by Roos in 1965,[54] is the most common method of doing so. The major advantage of this method is that it offers excellent exposure of the anterior portion of the first rib where the pathology exists with excellent cosmesis. It is technically challenging, however, and complications, which can include hemopneumothorax and long thoracic nerve injury, are not trivial; a "complication" unusual to this procedure in inexperienced hands is removal of the second rib instead of the first by mistake. Results are generally favorable: Urschel and colleagues in sequential evaluations of their experience report "good to excellent long-term results" in 85% to 95% of their patients so treated.[55] We and others[56,57] emphasize two technical points: the subclavius tendon at the costoclavicular junction and muscle separating the vein from the clavicle should be aggressively debulked, and second, the fibrotic tissue surrounding the vein should be resected after the bone and muscles are out. The vein can safely be circumferentially freed to the level of the jugular vein in most cases. It should be noted that although this venolysis has not been extensively emphasized in the literature most clinicians with large VTOS practices feel this is an intrinsic part of the repair.

Decompression of the costoclavicular junction can also be performed by various combinations of supra-, para-, and infraclavicular first rib resection[52,58-60] (advantages: best visualization of critical structures and access for reconstruction; disadvantages: two incisions may be required for full removal of the anterior part of the first rib), sternal disarticulation with first rib resection[61,62] (advantage: excellent visualization of the costoclavicular junction; disadvantage: healing is not assured and morbidity if so significant), and medial claviculectomy[63] (advantage: most complete exposure of the vein; disadvantage: cosmetics and perceived mechanical drawbacks of claviculectomy). Whatever ap-

proach is used, it is absolutely critical to emphasize that the anterior first rib and/or medial clavicle must be addressed and the vein freed from surrounding fibrotic tissue and mobilized.

It should be noted that a significant dissenting opinion exists regarding the necessity to decompress the bony thoracic outlet at all. Kaj Johansen describes a series of 50 patients with primary effort thrombosis undergoing thrombolysis who were then anticoagulated and observed, but did not undergo surgery. At a mean follow-up of 57 months, 82% were entirely asymptomatic, and another 10% had only mild symptoms.[64] He argues that decompression is based on relatively old data (1980s-2000) in patients not undergoing thrombolysis, and quotes symptom-free rates of 83% to 90% (with one outlying study reporting 96%).[65,66] A recent study from Stanford, however, showed a 23% recurrence rate in patients initially managed nonoperatively,[51] and his own series demonstrated an 18% occlusion rate with another 24% of patients having stenoses greater than 50%.[64] These results must be compared to those of Urschel and Razzuk,[20] who showed (in 2000) a 95% rate of excellent or good outcomes in 199 patients treated with thrombolysis and first rib resection over a 20-year period and Molina et al,[67] who showed (in 2007) a 100% patency and 0% rate of significant symptoms at 5 years after thrombolysis and first rib resection for acute effort thrombosis. It is fair to say that the data suggest that a prospective randomized trial to address this issue is not unreasonable, but modern results of thrombolysis followed by surgical first rib resection in the proper hands are superb.

Timing of decompression. Although substantial consensus exists that the costoclavicular junction must be decompressed to prevent recurrence, less agreement as to timing of this decompression is present. Based initially on theoretical concerns and examination of venous endothelium and function after thrombosis[53] and the perceived risks of operation soon after thrombolysis, the UCLA group led by Herb Machleder established the precedent of waiting 3 months for decompression.[41,68] Results in a rather heterogeneous group of patients were good, with 83% of patients undergoing both lysis and thoracic outlet decompression being free of symptoms in their 1993 report.[41] In a 2005 series of 71 patients undergoing staged decompression after thrombolysis at the University of Michigan, 90% returned to work.[69]

The problem with this strategy is that rethrombosis can occur in 10% or more of patients in the interval[41] and that this strategy delays definitive correction of the problem and return to premorbid status with interval disability.[70] Multiple series and descriptions now exist of patients undergoing immediate thoracic outlet decompression after thrombolysis which demonstrate excellent results and reasonably low complication rates.[20,42,52,58,60,70-72]

Urschel and colleagues[71] working at the University of Texas Southwestern/Baylor were early proponents of operative decompression immediately after thrombolysis. In a 1991 review of their experience with 67 patients treated over 25 years, they reported that the last 33 patients were treated with "early" first rib resection after thrombolysis, with good results.[71] They updated their experience in 2000, describing extremities treated with thrombolysis followed by "prompt" first rib resection (defined as "generally the next day" in the discussion). In the 199 extremities treated within 6 weeks of the onset of symptoms, 189 (95%) had excellent or good results whereas only two had poor results, and no recurrences were observed.[20] Azakie et al[58] and Lee et al[52] noted similar good results in smaller groups of patients, and the latter specifically stressed that early decompression had both medical and employment advantages. In 2007, Molina et al[67] described immediate subclavicular first rib decompression after thrombolysis in 97 patients with only one bleeding complication.

Results were persuasive enough that by the late 1990s the UCLA group shifted to this policy of early thoracic outlet decompression, reporting their early experience with this new protocol in 2000. Although comparing only 9 patients in each group, the "early" group (mean delay 3 days, though ranging up to 15) had the same blood loss and overall outcome than the "staged" group (mean, 87 days; range, 42-125). No patient had a surgical complication or required transfusion, and all patients had "resolution of symptoms" and returned to work or avocation.[70] At present, it is fair to say that although prospective comparison will be needed to definitively answer this question, immediate decompression after thrombolysis has been shown to be safe with regard to historic complication rates and very effective overall, and probably returns the patient to their premorbid status earlier.

Treatment of residual intrinsic defects. In many cases, significant intrinsic defects are seen in the vein after lysis of all possible thrombus and full surgical venolysis. Assuming the extrinsic problem is addressed by costoclavicular decompression, several schools of thought regarding treatment of intrinsic residual venous defects exist. First is to leave this alone (and anticoagulated). Proponents of this approach stress the high failure rates of angioplasty and stenting in the undecompressed venous thoracic outlet and the endothelial damage that even balloon angioplasty creates, and point out that many or most such lesions will remodel with time once bony decompression and venolysis has taken place.[56] Another approach is to perform delayed venography and balloon venoplasty after allowing several weeks for the endothelium to recover from the insult of thrombosis and thrombolysis, whereas a third is to perform immediate balloon venoplasty and even stenting at the time of bony decompression. Kreienberg et al[73] described the performance of balloon venoplasty alone in 9 patients and stenting in another 14 patients immediately after decompression. Interestingly, patency was 100% at 4 years in the 9 patients undergoing angioplasty alone, but only 64% at 3.5 years in the 14 who required stenting. Although they identified several factors worsening results of stenting apparently independent of the stent itself, this difference is interesting. At present, it seems fair to say that evidence does exist that stents in this situation, even if the costoclavicular joint has been decompressed, may have a worse

prognosis than balloon angioplasty alone, and that both postdecompression balloon angioplasty and observation alone for residual postlytic intrinsic defects both yield good long-term results.

The role of venous reconstruction. A third major question is when to reconstruct the vein in situations where significant intrinsic lesions persist. Thompson advocates a fairly aggressive approach to reconstruction, using it when external venolysis is unsuccessful,[60,74] often with a temporary arteriovenous (AV) fistula, as do Molina and others.[67,75] We advocate reserving reconstruction for those in whom significant hemodynamic effects persist, defined as persistent and significant symptomatology, despite bony decompression, external venolysis, and balloon angioplasty, and have observed a 94% patency rate in the most severe group of chronic occlusions treated with medial claviculectomy in combination with venous reconstruction.[42] Jugular vein turndown[76] is an excellent option in this situation, allowing removal of all diseased endothelium from the flow channel, but direct reconstruction as advocated by Thompson also shows durable results. We believe that jugular turndown and reconstruction are best performed with the direct vision allowed by claviculectomy,[63] but good results can be achieved leaving it in place in certain circumstances.[60,77] At present, all results of the various reconstructive procedures are anecdotal.

Total occlusion. Finally, there is a subset of patients who remain totally occluded after attempts at thrombolysis. We believe that such patients should be treated identically to those with residual defects; that is, based on symptom status. It has been shown that recanalization can occur in this situation. De Leon documented 4 patients with total occlusion who underwent thorough bony decompression who recanalized at a mean of 7 months after surgery with good symptom relief.[78] Once the venous thoracic outlet has been decompressed, symptom status should be assessed. If the patient is functional, observation and anticoagulation is probably best to allow recanalization or collateral maturation, although if symptoms are severe, reconstruction (usually by means of jugular vein turndown because the cord-like residual vein is not otherwise reconstructable) is carried out.

Postoperative care. All agree that these patients should be anticoagulated, although no data exist as to timing. Most agree, however, that as the extrinsic problem has been corrected and the incidence of hypercoagulable syndromes is low, anticoagulation can be temporary. We use a 6-month window based on the treatment of deep vein thrombosis (and because 2 of our patients whose Coumadin was stopped before this time rethrombosed), although many report limiting anticoagulation to 3 months. We perform examination and ultrasound at 1 and 6 months after surgery with yearly visits after, and instruct patients to contact us immediately if symptoms recur. The rate of contralateral effort thrombosis or venous symptomatology in these patients, although not zero, seems to be low based on clinical symptomatology, although rates of thrombosis and compression when studied venographically have been shown to be as high as 15% to 70%.[79,80] Recurrence rates are very poorly documented in the literature, but may be inferred to be low by the relative absence of such reports.

OUTCOME

As might be expected from a large number of relatively uncontrolled single-center series reporting on outcomes of patients treated in a variety of different ways over many years, outcome data are very difficult to describe. Based on the data presented and cited above, the authors would suggest that good results may be expected in only 50% to 66% of patients treated with anticoagulation alone (with or without rib resection), in 80% to 90% of patients treated with thrombolysis and delayed thoracic outlet decompression, and in 90% to 95% of patients diagnosed quickly and treated with thrombolysis and immediate decompression.

The one objective study of this issue was recently published by Chang et al,[81] who studied 26 patients seen at Johns Hopkins for venous TOS over a 3-year period using validated quality of life survey instruments. Only 77% of such patients returned to work, although another 2 returned to part-time employment and the statistical treatment of students and those unemployed before their illness was unclear. Patients with VTOS seemed to be fully recovered by 1 year after their operation.

SUGGESTED TREATMENT ALGORITHM

Fig 5 presents the treatment algorithm we suggest based on our observations and the existing literature, modified somewhat from Doyle et al.[42]

When a patient presents with effort thrombosis (or symptomatic partial intrinsic obstruction), the duration of symptoms (hence urgency of initiation of treatment) is the most critical factor. In all cases, diagnostic venography should be performed. If symptoms have been present for more than 14 days, wire passage can be attempted, but thrombolysis is unlikely to be successful. If symptoms have been present for less than 14 days, thrombolysis is more likely to be successful.

Even if the vein cannot be recanalized, decompression of the venous thoracic outlet should be performed. The method depends on whether ancillary reconstruction should be performed, which in turn depends on symptom status. If symptoms are mild, decompression alone is carried out by means of transaxillary first rib resection including aggressive external venolysis and debulking of the subclavius muscle and tendon. If symptoms are severe, reconstruction is warranted. We believe medial claviculectomy offers the widest exposure and most options in this situation, but others advocate clavicular preservation.

If thrombolysis can be initiated and is successful, subsequent treatment depends on the status of the vein. If normal (with the arm adducted), transaxillary first rib resection (with venolysis) is performed. No consensus currently exists for treatment of a residual defect. We believe that if symptoms are relatively mild, transaxillary first rib resection is adequate. If balloon angioplasty is to be considered, repeat venography is performed and an-

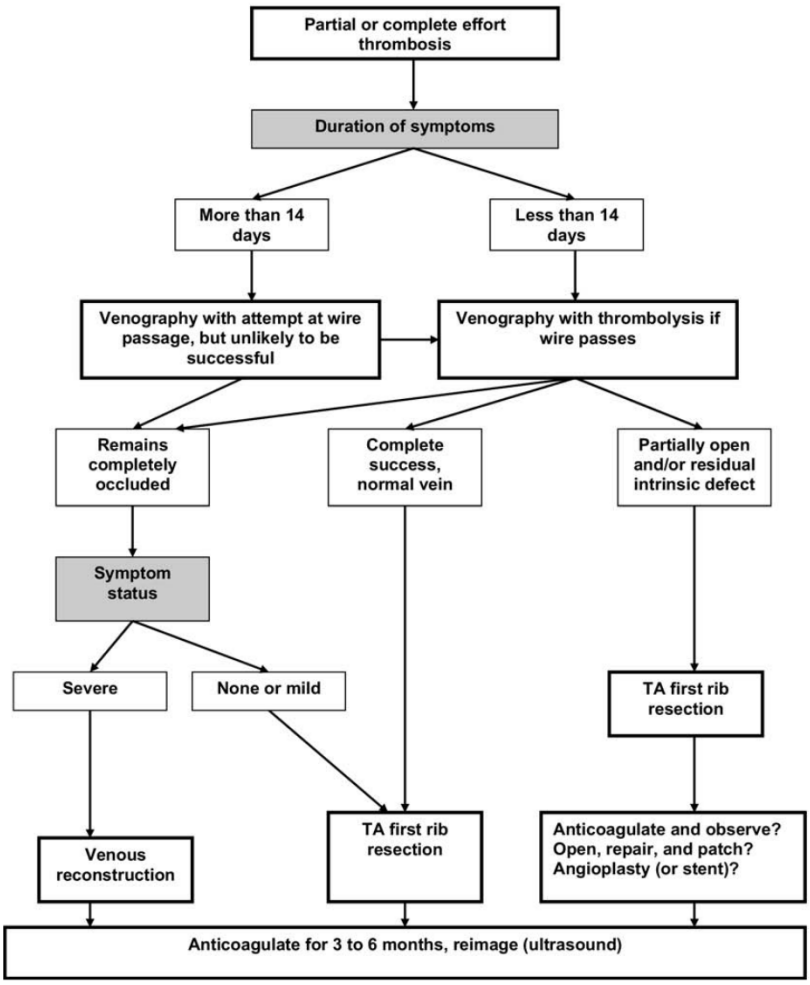

Fig 5. Algorithm for treatment of patients with partial or complete effort thrombosis. The best initial procedure (more accurately, the chances of success) is defined by the duration of symptoms, whereas the subsequent method of thoracic outlet decompression is defined by the status of the residual vein and residual symptoms. Timing of decompression is not defined in our protocol, although we believe decompression should immediately follow thrombolysis.

gioplasty used to treat a residual lesion. If symptoms are severe, claviculectomy and reconstruction should be considered.

All patients are anticoagulated for 3 to 6 months and followed clinically and by ultrasound scans with attention paid to the contralateral side as well. Angioplasty and stenting should never be used in the nondecompressed venous bony thoracic outlet, and at this point we believe that although angioplasty is safe once the rib or clavicle has been removed, stenting even in this situation should be used with caution.

SUMMARY

Although the basic algorithm is generally agreed upon, numerous questions remain and no randomized studies exist. A partial list of questions to answer would include:

- Definitive outcomes with and without thoracic outlet decompression after thrombolysis by means of a true prospective randomized trial.
- Definitive answer to the timing of decompression – acute or delayed?
- The role of angioplasty vs observation for residual defects after decompression.
- The role of stents in the decompressed thoracic outlet.
- Duration of postoperative anticoagulation.
- Results after claviculectomy: functional and cosmetic perception and reality.
- Natural history of the contralateral side.
- Long-term functional outcome – occupational and recreational.
- Best treatment of the vein that cannot be opened with thrombolysis.

- When venous reconstruction is needed, and the best method thereof.
- Cellular and molecular events at the diseased costoclavicular junction.
- More information on the role of hypercoagulable states in effort thrombosis.

In addition, the problem is common enough and data confusing and incomplete enough that a consensus statement from a relevant professional society would be extremely helpful.

The current standard of care in patients with effort thrombosis is catheter-directed thrombolysis followed by definitive decompression of the anterior part of the thoracic outlet (costoclavicular junction), although proof of effectiveness of such decompression is lacking. As Urschel et al[20] pointed out at the turn of the (21st) century, "In Paget-Schroetter syndrome, the earlier the diagnosis and treatment, the better the results." If patients are seen early after the onset of total thrombosis (within a week or 2), results of this algorithm are excellent, but this concept is surprisingly often violated, even in 2009. In addition to understanding how to treat this condition with the tools at our disposal, vascular surgeons also need to be aware of the need to educate those who see these patients first, including primary care physicians, emergency room personnel, military and student health clinic personnel, and the patients themselves. This is a problem of young, functional adults, and thus is it unusually critical that it be treated correctly.

AUTHOR CONTRIBUTIONS

Conception and design: KI, AD
Analysis and interpretation: KI, AD
Data collection: KI, AD
Writing the article: KI, AD
Critical revision of the article: KI
Final approval of the article: KI, AD
Statistical analysis: Not applicable
Obtained funding: Not applicable
Overall responsibility: KI

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Submitted Sep 23, 2009; accepted Dec 6, 2009.