Surgical intervention is not required for all patients with subclavian vein thrombosis

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Purpose: The role of thoracic outlet decompression in the treatment of primary axillary-subclavian vein thrombosis remains controversial. The timing and indications for surgery are not well defined, and thoracic outlet procedures may be associated with infrequent, but significant, morbidity. We examined the outcomes of patients treated with or without surgery after the results of initial thrombolytic therapy and a short period of outpatient anticoagulation.

Methods: Patients suspected of having a primary deep venous thrombosis underwent an urgent color-flow venous duplex ultrasound scan, followed by a venogram and catheter-directed thrombolysis. They were then converted from heparin to outpatient warfarin. Patients who remained asymptomatic received anticoagulants for 3 months. Patients who, at 4 weeks, had persistent symptoms of venous hypertension and positional obstruction of the subclavian vein, venous collaterals, or both demonstrated by means of venogram underwent thoracic outlet decompression and postoperative anticoagulation for 1 month.

Results: Twenty-two patients were treated between June 1996 and June 1999. Of the 18 patients who received catheter-directed thrombolysis, complete patency was achieved in eight patients (44%), and partial patency was achieved in the remaining 10 patients (56%). Nine of 22 patients (41%) did not require surgery, and the remaining 13 patients underwent thoracic outlet decompression through a supraclavicular approach with scalenectomy, first-rib resection, and venolysis. Recurrent thrombosis developed in only one patient during the immediate period of anticoagulation. Eleven of 13 patients (85%) treated with surgery and eight of nine patients (89%) treated without surgery sustained durable relief of their symptoms and a return to their baseline level of physical activity. All patients who underwent surgery maintained their venous patency on follow-up duplex scanning imaging.

Conclusion: Not all patients with primary axillary-subclavian vein thrombosis require surgical intervention. A period of observation while patients are receiving oral anticoagulation for at least 1 month allows the selection of patients who will do well with nonoperative therapy. Patients with persistent symptoms and venous obstruction should be offered thoracic outlet decompression. Chronic anticoagulation is not required in these patients. (J Vasc Surg 2000;32:57-67.)

Primary axillary-subclavian vein thrombosis or Paget-Schroetter syndrome is a serious problem, the short- and long-term sequelae of which have only recently been appreciated. The pathophysiology of this syndrome remains poorly understood, and the treatment is varied and controversial. Untreated, symptomatic patients will sustain chronic disability from venous obstruction, with arm swelling, pain, and early exercise fatigue. This may lead to significant loss of occupational productivity and quality of life,[1] especially because most cases involve the patient's dominant arm.[2,3] However, surgical intervention is not without potential for serious complications, including brachial palsy, chronic postoperative pain syndromes, chylothorax, and phrenic nerve palsy.

The diagnosis of Paget-Schroetter syndrome is suspected in the setting of an acute onset of symp-

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Competition of interest: nil.

Presented at the Fourteenth Annual Meeting of the Western Vascular Society, Squaw Creek, Calif, Sep 19-22, 1999.

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0741-5214/2000/$12.00 + 0 24/6/107313
doi:10.1067/mva.2000.107313

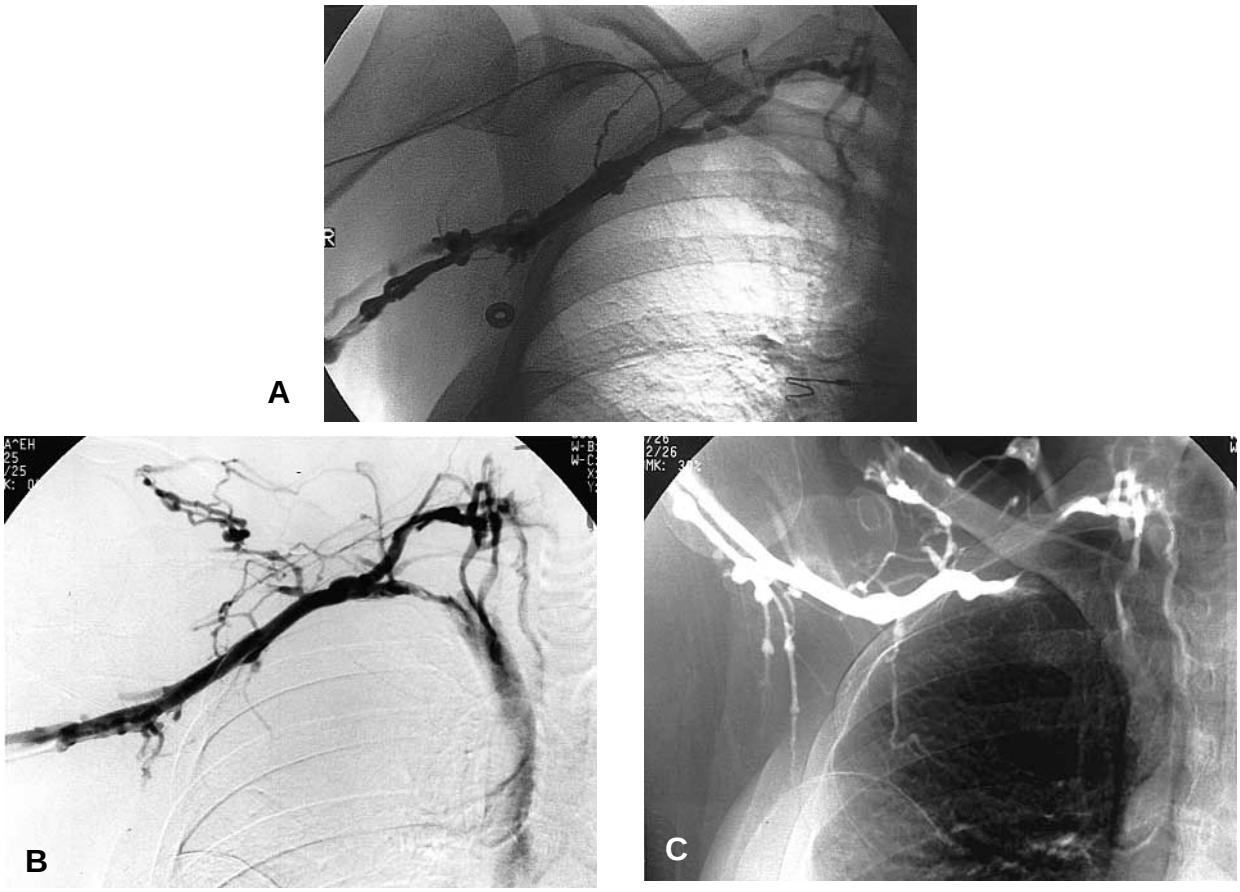

Fig 1. Right upper-extremity contrast venogram. A, Initial venogram demonstrating a completely thrombosed right axillary-subclavian vein. B, Complete recanalization with abundant venous collateralization. C, Positional venography with the arm abducted and externally rotated showing the occlusion of the veins with the maneuver.

tomatic upper-extremity swelling, usually with an antecedent episode of repetitive or sustained ipsilateral abduction and external rotation in an otherwise healthy individual.[4] It is distinguished from secondary causes of axillary-subclavian thrombosis that occur in the presence of predisposing mechanical or physiologic factors, such as direct trauma, indwelling catheter, or hypercoagulable state.

Successful treatment requires prompt diagnosis and thrombolysis. Once the diagnosis is suspected, a duplex ultrasound scan of the effected extremity is obtained for noninvasive evaluation of deep venous thrombosis. This is followed by a dedicated contrast venogram. Specific catheter-directed thrombolysis and intravenous heparin are started, and after thrombolysis, the patients are converted to oral anticoagulation with warfarin.[3,5]

Controversy exists regarding the indications for and the timing of surgical thoracic outlet decompression and other adjunctive vascular and endovascular procedures in the treatment of this syndrome. This study was designed to evaluate the efficacy of a treatment algorithm for the management of primary subclavian vein thrombosis, in which the decision regarding the necessity for surgical intervention was deferred for approximately 1 month to determine the patient's response to conservative therapy (Fig 2). The decision to study this algorithm was based on three factors: the findings in an earlier study from our institution documented that not all patients with primary subclavian vein thrombosis required surgical intervention for relief of their symptoms[6]; our service had been seeing more patients referred because of serious complications after thoracic outlet decompression; and our experience that a delay in surgical intervention allows resolution of the inflammation

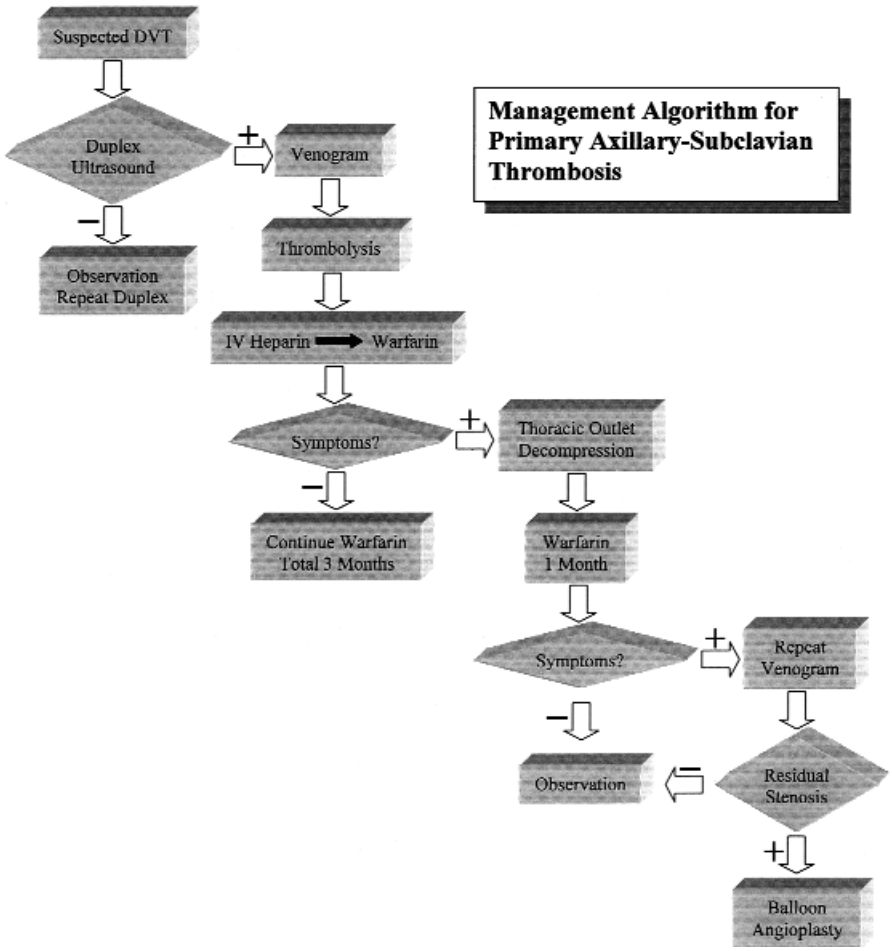

Fig 2. Diagram of the treatment algorithm.

associated with vein thrombosis and thus makes the dissection around the subclavian vein easier and safer.

PATIENTS AND METHODS

From June 1996 to June 1999, patients in whom primary axillary-subclavian vein thrombosis was diagnosed were enrolled in an algorithm of selective surgical therapy (Fig 2). Follow-up examinations of these patients were completed through November 1999. The clinical diagnosis of venous thrombosis was made by means of the initial history and a physical examination demonstrating ipsilateral arm swelling and pain, usually with an antecedent episode of physical exertion involving the affected extremity, and the absence of other mechanical or physiologic risk factors, including intravenous catheters and radiation phlebitis. When initially seen at the authors' institution, the patients immediately underwent color-flow venous duplex ultrasound scanning before any anticoagulation. When a deep venous thrombosis was demonstrated by means of the study, the patient was admitted for an urgent contrast venogram with full visualization of the venous system, from the level of the proximal forearm to the innominate-superior vena caval confluence. Special attention was given to the region of the shoulder girdle, and the images were obtained with the arm in a neutral position and in the abduction and external rotation.

Catheter-directed thrombolysis was started, with the periodic advancement of the multi-sidehole infusion catheters, as needed. Urokinase (Abbokinase, Abbott Laboratories, Abbott Park, Ill) was used as a means of initially lacing the clot and then was infused at a dose of 120,000 to 180,000 IU / h. Infusions lasted from 24 to 72 hours, depending on the success of the degree of thrombolysis that was demonstrated by means of the venogram. Concurrent heparin infusion

Table I. Summary of results

	Surgical	*Nonsurgical*
Total	13	9
Sex (male / female)	7 / 6	6 / 3
Side (right / left)	9 / 4	6 / 3
Lytic therapy	11 (85%)	7 (78%)
Angioplasty	8 of 11	4 of 7
Postlysis result (complete / partial)	4 / 7	4 / 3
Symptoms at last follow-up	10 minimal / 3 moderate*	9 minimal†
ASCV patency by means of duplex at last follow-up	13 (100%)	9 (100%)

*Includes one patient whose symptoms improved from a preoperative severe level to postoperative moderate level. The other two patients' symptoms did not significantly improve postoperatively, compared with preoperative levels.
†Includes one patient who had persistent moderate symptoms despite lack of objective findings but who, at last follow-up, at 18 months from the initial event, had significant improvement.
ASCV, Axillary-subclavian vein.

was administered through the sidearm of the infusion sheath at rates from 500 to 1200 U / h to obtain an activated partial thromboplastin time of 60 to 80 seconds. The success of thrombolysis was assessed by means of serial venograms at 6- to 12-hour intervals. Thrombolysis was stopped when any one or more of these conditions were met: no interval change in the angiographic appearance of the vein in two sequential venograms, bleeding complications, biochemical evidence of disseminated intravascular coagulopathy, or 72 hours of continuous infusion reached. In one patient, recombinant tissue-type plasminogen activator (rt-PA, Activase, Genentech, San Francisco, Calif) was used for thrombolysis because of the unavailability of urokinase. The dose was 2 mg / h continuous infusion. The remaining aspects of this thrombolysis treatment protocol were unchanged from those of the protocol with urokinase (Fig 1).

At the conclusion of thrombolysis, the patency of the vein was assessed with a completion venogram and read as either occluded, partially obstructed (> 50%), or patent. Positional venography was performed with the abduction and external rotation of the ipsilateral arm. Any positional impingement of the main subclavian-axillary vein or collaterals was noted. The patient was transitioned from intravenous heparin to warfarin and was discharged receiving oral anticoagulation when the prothrombin time-international normalized ratio was therapeutic. The dose of warfarin was regulated on an outpatient basis to maintain an international normalized ratio of 2.0 to 3.0 by a dedicated anticoagulation clinic. Before discharge, clinical improvement was assessed by means of an interview and physical examination and characterized as minimal, moderate, or severe. Patients were instructed to engage in the normal activities of daily living, but to avoid strenuous or repetitive exercises involving the ipsilateral arm.

All patients were observed in our vascular clinic. At each clinic visit, an assessment was made as to the patient's level of activity and disability, if any. A color-flow venous duplex scanning study was performed at each clinic visit to determine the status of the deep venous and collateral circulation. The patients were maintained on warfarin and were reexamined as outpatients after 1 month. They were interviewed about any symptoms at rest and with exercise and examined for swelling and the presence of dilated superficial veins in the arm and shoulder areas. When the patient was asymptomatic with minimal physical findings, the patient was maintained on warfarin for 2 more months. At the end of this time, the anticoagulation was discontinued, and the patients were allowed to resume all their normal activities, including vigorous athletic activities. These patients were observed as outpatients toward the end of their warfarin course, then at 6 months, and yearly thereafter. Follow-up for the patients who did not undergo surgery ranged from 5 to 40 months and averaged 25.8 months (Table II).

For failures of nonoperative therapy, the patient was advised to undergo surgical decompression of the thoracic outlet and venolysis. Specific indications for surgery were first and most important, the persistence or recurrence of symptoms of venous hypertension; second, positional occlusion of venous collaterals with concomitant axillary-subclavian vein thrombosis on repeat venography; and third, other evidence of failure of anticoagulation, such as thrombus extension or pulmonary embolus.

Our surgical approach involved a single supraclavicular incision. The anterior scalene muscle was exposed in the usual manner, and the phrenic nerve

was always identified and carefully isolated. The anterior scalene muscle was exposed from the superior extent of our incision to its costal insertion. This entire section of the muscle was excised, as opposed to undergoing a simple division, to prevent a reinsertion through scarring. The subclavian artery and the brachial plexus were mobilized, and the middle scalene muscle was divided at its insertion into the first rib and resected back to the level of the long thoracic nerve. The first rib was skeletonized from the surrounding structures, especially medially, deep to the subclavian vein, and resected. Any protruding bony spurs were resected, and all fibrous bands impinging on the subclavian vein were divided. Care was taken not to divide any major collateral veins during the dissection. Finally, a complete, circumferential subclavian venolysis was performed. The subclavian vein was dissected free from all soft tissues from the lateral border of the clavicle to the subclavian-jugular confluence. No attempt was made to perform any venous reconstruction. After surgery, the patient underwent anticoagulation for at least 1 month. When the patient had persistent symptoms, a second venogram was performed. Balloon angioplasty without a stent placement was reserved for any hemodynamically significant residual stenoses after surgical decompression (Fig 2).[7,8]

Patients who underwent thoracic outlet decompression were observed after 1 month and then every 6 months. The follow-up period for these patients ranged from 11 to 36 months and averaged 22.3 months. As with the conservatively treated patients, an assessment was made about the patient's level of activity and any disability. Color-flow venous studies were performed at each clinic visit.

RESULTS

Between June 1996 and June 1999, 22 patients with primary axillary-subclavian vein thrombosis were examined and treated at our hospital. The mean age of the patients was 28.8 years (range, 18-47 years). There were 13 male and nine female patients. Fifteen right extremities and seven left extremities were involved. No instance of bilateral involvement was encountered. In 17 of 22 patients, a distinct antecedent history of strenuous or repetitive activity could be elicited before the onset of symptoms. Of these 17 patients, five patients were engaged in professional or collegiate varsity-level sports, and the remainder of the patients were engaged in recreational or occupational activity, such as weightlifting, swimming, carrying heavy objects, or stocking shelves above the shoulder level.

Table II. Nonoperative group

Patient number	*Months follow-up*	*Major athlete*	*Collateral obstruction on venogram*
1	40	Yes	No
4	36	Yes	Yes
5	34	No	Yes
6	33	No	No
12	26	No	No
15	24	No	Yes
17	19	No	No
20	15	No	No
22	5	No	Yes

Treatment was initiated at referral institutions in 13 patients. The average duration between the initial diagnosis and the time of examination at our institution was less than 1 month and ranged from 1 week to 6 months. The remaining nine patients were either primarily seen at this institution or transferred shortly after diagnosis from referral institutions, before the initiation of therapy. The diagnosis in 13 of the 22 patients was initially made with a color-flow duplex venous ultrasound scan. The use of the color-flow duplex ultrasound was dependent on the availability of the study at the time of presentation and the degree of clinical suspicion of the primary physician. Four of the 13 patients initially seen at the referral institutions underwent systemic anticoagulation with intravenous heparin and started on warfarin, but did not undergo a diagnostic venogram at the time of initial presentation. However, all patients eventually underwent a satisfactory contrast venogram before beginning a definitive treatment plan at our institution.

Eighteen of the 22 patients underwent thrombolysis. Sixteen patients underwent urokinase/rt-PA treatment alone, one patient underwent combined mechanical (percutaneous) thrombectomy and pharmacologic thrombolysis, and one patient underwent mechanical thrombectomy alone. The remaining four patients demonstrated a patent, recanalized but stenotic axillary-subclavian vein and collateralization that did not require thrombolysis. Of the 18 patients that underwent thrombolytic therapy, initial complete venographic evidence of clot lysis was achieved in eight patients, and partial (more than 50%) lysis was achieved in 10 patients. In the latter group, the initiation of thrombolytic therapy was delayed in three of the 10 patients between 4 and 6 weeks from the onset of symptoms; the remaining 15 patients who had thrombolytic therapy were all treated within 2 weeks of presentation. In two of the

eight completely lysed cases, rethrombosis occurred, in one patient after the discontinuation of warfarin therapy more than 1 year after the initial event and in one patient within 2 weeks of thrombolysis, despite adequate oral anticoagulation. The former patient was initially treated elsewhere and would have been offered thoracic outlet decompression earlier had she been treated at our institution.

Thirteen of the 22 patients had documented occlusion or marked stenosis of the axillary-subclavian venous system or regional collaterals. In the remaining nine patients, a nonocclusive contrast-filling defect at the costoclavicular junction was demonstrated, even with the arm at rest. In more than half of the cases (12 of 22), balloon angioplasty of these venographic lesions was attempted, and in one of these cases (from a referral institution), a stent was placed. None of the 12 angioplasties resulted in any significant venographic improvement, and in the case of the stent placement, a fracture of the stent at the site of the previous stenosis was demonstrated by means of a subsequent venogram.

All patients (except one patient who never underwent anticoagulation because of late presentation and near resolution of her initial symptoms) were given a trial of outpatient anticoagulation. Those patients who were nonoperatively treated (nine of 22) underwent anticoagulation for an average of 3.6 months (range, 2-7 months). Eight of the nine nonoperatively treated patients had minimal symptoms at the conclusion of their anticoagulation. The other patient had moderate, subjective symptoms of early arm fatigue with exercise, despite a widely patent axillary-subclavian vein demonstrated by means of serial venous duplex imaging, a lack of positional occlusion by means of venography, and a lack of physical findings by means of gross examination. Of the 13 patients who underwent surgery, five had minimal, six had moderate, and two had severe symptoms. Only one patient had an adverse event during the initial observation period after thrombolysis, with an acute, symptomatic rethrombosis. He underwent an urgent second lysis and promptly underwent surgery during the same admission. Four of the five patients with minimal symptoms, who underwent surgery, were involved in competitive sports (two in baseball, one in swimming, one in weightlifting).The fifth patient was concerned about a possible recurrence because of his active lifestyle, and he elected to undergo surgery rather than an extended period of anticoagulation. Of the five major collegiate or professional athletes in this series, three were treated surgically (one collegiate and two professional baseball players), and two were successfully treated conservatively (one collegiate football player and one collegiate swimmer).

Eleven of the 13 patients who underwent thoracic outlet decompression sustained either marked or partial resolution of their initial symptoms at their last follow-up examination. The remaining two patients had moderate symptoms that were relatively unchanged postoperatively. With the exception of one patient (who is also one of the two patients whose symptoms were unchanged), all the patients underwent anticoagulation for less than 1 month. Five postoperative complications occurred in five patients. They included two cases of pneumothoraces (one required a chest tube for 2 days), one case of chylothorax requiring a single thoracentesis, and two cases of asymptomatic transient phrenic nerve palsy. The average postoperative length of stay was 2.7 days (range, 2-4 days). A summary of the results of surgical versus nonsurgical patients is shown in Table I.

During the follow-up period, all 13 patients maintained patency of their axillary-subclavian veins on duplex imaging. No patient in this series required postoperative balloon angioplasty. Those patients who were treated conservatively continued to do well, without the need for further intervention.

DISCUSSION

Although the clinical significance of primary axillary-subclavian vein thrombosis has been increasingly recognized in the last decade, the appropriate scope and timing of treatments have remained intensely controversial.[3] The sheer number of treatment algorithms and surgical approaches to thoracic outlet decompression point to our limited understanding of the pathophysiology and natural history of this disorder. The optimal treatment will likely involve an interdisciplinary approach, with vascular surgery and interventional radiology.

The purpose of this study was to examine the outcomes of patients with primary axillary-subclavian vein thrombosis who were treated with a selective and delayed surgical treatment of their thoracic outlet syndrome, according to a defined treatment algorithm (Fig 2). This approach contrasts with some of the previously published literature, which supports the prompt surgical decompression of all patients who have this problem.[7] We began our current protocol in 1996. Since that time, we have treated 22 patients. Like others who have reported in this area, we found that Paget-Schroetter syndrome is frequently a condition of young patients.[9] There is no particular

predilection in either sex, but there was a preponderance of the right arm (68%) over the left-upper extremity.[2] This may simply reflect the right-handed dominance of the general population and the observation made by others that the thrombosis often occurs on the side of the dominant extremity.[8,9] A history of antecedent strenuous or repetitive activities in more than 75% of the patients in this study confirms the use of the term "effort vein thrombosis."

More than half of our patients were initially treated elsewhere and were referred to us after a variable period. Although points of controversy remain regarding the use of adjunctive interventions after thrombolysis, our understanding of the syndrome during the past decade has brought near universal acceptance of thrombolysis and anticoagulation as the initial form of therapy. Early confirmation of axillary-subclavian vein thrombosis is essential for increasing the success of thrombolysis. In this regard, early color-flow venous duplex scanning can be a safe and effective means of confirming the diagnosis so that prompt referral for venography and catheter-directed thrombolysis can occur. In our series, nearly 60% of patients had a rapid confirmation of the diagnosis with color-flow venous duplex imaging.

In this study, 82% of the patients underwent thrombolysis. Previous investigators have noted a decreased success of lysis with an increasing duration of time from the apparent onset of symptoms to the initiation of lytic therapy. These studies note that after 2 weeks, the efficacy of catheter-directed thrombolytic therapy significantly diminishes.[10] Although this study did not specifically address the issue of thrombus age, the overall success of the initial thrombolytic therapy in this series did not appear to have been biased by any excessive delays in the initiation of lytic therapy, whether the treatment was administered at our institution or elsewhere.

Positional venography has greatly contributed to our understanding of the complex anatomy of the venous thoracic outlet syndrome.[3,7,11] Although it may be a sufficient enough means of demonstrating a simple stenosis of the subclavian vein in the region of the costoclavicular junction to recommend surgical decompression, a more compelling argument comes with a functional demonstration of the loss of collateral flow during provocative shoulder-arm maneuvers. Diminished venous flow was documented with such maneuvers in more than half of our patients. Previous treatment algorithms have included this finding alone as an indication for surgery.[7,12] We believe that although this may serve as corroborative evidence, it does not suffice as the sole indication for surgery. In fact, 44% of our conservatively treated patients had an obstruction of their collateral circulation by means of venography but remained asymptomatic and, therefore, did not undergo surgery (Table II).

Post-thrombolytic balloon angioplasty of stenotic lesions without surgical decompression and venolysis has been largely unsuccessful and is not recommended.[6,13,14] The experience of this study confirms this view. Lesions frequently seen by means of completion venography after successful thrombolysis represent extrinsic compression from fixed, musculoskeletal structures of the thoracic outlet and cannot be corrected with adjunctive stenting. As we and other authors have noted, the result is a fracture of the stent.[15] Most stents are not designed to withstand the repetitive crushing strain between two bony structures, and currently, no stent has the radial strength to maintain a distraction of an area such as the costoclavicular space.

Nearly all the patients (21 of 22) underwent oral anticoagulation for variable periods. Conventional management of lower-extremity deep venous thrombosis involves anticoagulation for 3 to 6 months. This practice has been, to a large part, carried over to the initial conservative treatment of upper-extremity venous thromboses. The trend has been, however, toward shortening the duration of oral anticoagulation in cases of primary axillary-subclavian vein thrombosis. Some investigators have noted that this initial period of anticoagulation places the patient at an increased risk of rethrombosis.[16] In our series, this occurred in only one case, which was immediately treated with a second course of thrombolysis, without any long-term sequelae. Furthermore, prompt surgery shortly after thrombolysis could decrease the total duration of anticoagulation to as little as 1 month postoperatively. We agree that, although this would eliminate the inconvenience of interval anticoagulation and a second admission for heparin transition before surgery, this approach de facto commits all patients to surgery, which, we would submit, is not always necessary. Furthermore, surgical dissection can be more difficult with the acute inflammation surrounding a recently thrombosed vein.[8,14] Close follow-up and gradual return to full physical activity allowed a significant percentage of patients (more than 40%) to achieve a baseline, premorbid status without the need for surgery or prolonged anticoagulation beyond the usual period.

In this series, nearly 60% of the patients (13 of 22) eventually underwent surgery. More than half of these patients (seven of 13) came to surgery before completion of their outpatient anticoagulation course. This

demonstrates the need for close observation, including serial color-flow venous duplex ultrasound scanning.

In most cases, there was minimal perivenous inflammation, which facilitated a safe venolysis. As previously noted, this may be a result of allowing at least 1 month of oral anticoagulation before surgery so that the acute thrombophlebitis has had a chance to become quiescent. None of the patients required surgical venous reconstruction or open thrombectomy. This partially reflects our experience from a previously published series, in which half of all direct venous reconstructions had failed on follow-up examination.[6] Furthermore, we believe that a complete decompression of the thoracic outlet and of the collateral circulation is perhaps more critical than reestablishing flow in the axillary-subclavian vein per se in preventing the recurrent symptoms of venous obstruction.[7,18]

We favor the supraclavicular approach over a transaxillary, paraclavicular, or other combined approaches to the thoracic outlet, because it allows two surgeons to work together over a wider operative field and offers a clear exposure of the three key structures that contribute to the axillary-subclavian thrombosis: the first rib, the anterior scalene muscle, and the subclavian vein. We have not found it necessary to make any counterincisions or secondary exposures, although, as other authors have noted, this may be required in some patients.[11,13] Furthermore, although some investigators have advocated a selective removal of one or two structures on the basis of intraoperative findings,[13] we favor a complete resection of the first rib and the scalene muscles. This ensures the elimination of all possible anatomic causes of subclavian vein compression during the initial operation, with minimal risk and morbidity. If a patient were to have recurrent symptoms, a reoperation to remove a residual structure would be much more hazardous.

In summary, we draw these conclusions based on our experience of a selective surgical approach to the treatment of primary axillary-subclavian thrombosis. First, not all patients with axillary-subclavian vein thrombosis require surgery. A period of close follow-up while patients undergo oral anticoagulation is warranted to select patients who will do well with conservative treatment alone, especially given the potentially serious neurovascular complications of operative intervention. Second, mainly symptoms and confirmatory positional venography should guide surgical therapy. In those cases that do come to surgery, a supraclavicular approach with resection of the first rib, scalene muscles, and venolysis is safe and effective, and adjunctive venous reconstruction is not routinely necessary. Finally, although there may be a role for postoperative endovascular therapy in a very small subset of patient with refractory symptoms, there is currently no role for preoperative endovascular treatment beyond thrombolysis.

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Submitted Sep 28, 1999; accepted Dec 3, 1999.

DISCUSSION

Dr Eric S. Weinstein (Englewood, Colo). I would like to congratulate Dr Lee for an excellent presentation of this interesting paper and thank the authors for providing me with a copy of the manuscript in a timely fashion to review prior to the meeting.

A selective approach to surgical therapy in cases of neurogenic thoracic outlet syndrome has been shown to improve overall outcome for patients with this condition. According to these authors, the same may be true for patients with venous thoracic outlet compression syndromes. Based upon their preliminary studies, the Stanford group's treatment algorithm for patients with effort thrombosis was prospectively evaluated to examine the outcomes of patients treated with or without surgery following initial thrombolytic therapy and a short period of outpatient anticoagulation and observation. Their conclusion that "not all patients with primary axillary-subclavian vein thrombosis requires surgical intervention" is provocative.

I have several comments and questions for the authors. The first relates to the inclusion criteria for patients in this review. The purpose of the study, as stated in the manuscript, was to evaluate both operative and nonoperative management following thrombolytic therapy and develop selection criteria for surgery for patients with this syndrome. However four out of 22 patients presented with recanalized axillo-subclavian veins and thus did not undergo lytic therapy. In my opinion these patients may have already self-selected the appropriate treatment and cannot truly be considered to be in the acute phase of their illness. In addition their surgical therapy may be different from those presenting acutely (ie, jugular vein turndown vs rib resection). They therefore warrant a separate consideration. Why did the authors feel it appropriate to include these patients among the 18 who presented with acute thrombosis requiring intraclot lysis?

My second question addresses the activity level of the nonoperatively managed group. For all patients in the series, the initial 4 weeks of anticoagulation is accompanied by a gradual return to nonstrenuous activity. Patients who where asymptomatic or only mildly impaired were managed with an additional 2 months of anticoagulation. Did these patients return to their previous activity levels that precipitated the thrombosis or did they require permanent modification of their activities to remain asymptomatic? It has been our experience that many of our patients who were either professional or amateur athletes or whose occupation required repetitive arm activity above their shoulders were adamant in their desires to return to their previous activity level and were able to do so following surgical treatment.

My third question has to do with those patients in your series with incomplete clot lysis and / or residual subclavian vein stenosis of more than 50% following urokinase treatment. I wholeheartedly agree with the authors that balloon angioplasty has no role in the treatment of this disease prior to rib resection. We have seen several cases of acute thrombosis secondary to an ill-conceived angioplasty in this setting. However, I am also concerned about treating a > 90% residual vein stenosis with anticoagulation alone. In such situations we have kept these patients on a heparin drip and operated the next day performing first-rib resection, venolysis, and, in selected cases, venous reconstruction, with excellent results. My question for the authors is in cases where there is a critical (> 80%) residual stenosis following lysis, do you still advocate conversion to outpatient anticoagulation or do you recommend early surgical intervention in the severely symptomatic patient? Although the author saw only one case of early rethrombosis, how many of their patients had > 80% residual vein stenosis following lysis?

Finally, my last comments and questions focus on the surgical approach. We feel that the supraclavicular approach is the procedure of choice for those patients with neurogenic TOS; however it has some significant limitations in cases of venous thrombosis.

First, the supraclavicular incision places the major collaterals from the subclavian to the jugular vein at risk. These can be more easily avoided with a transaxillary or infraclavicular approach. Second, in our experience, the structures that produce the venous constriction (namely the hypertrophied subclavius muscle and more important the costoclavicular ligament) are more easily and completely accessed via these alternative approaches in order to perform a complete venolysis. In addition, we have found it often necessary to remove the very proximal rib and cartilage to the sternochondral junction in order to completely free up the proximal vein and prevent recurrent symptoms. In our experience, this cannot be safely reached via the supraclavicular incision alone. In Denver, our approach has been to perform transaxillary first-rib resection for cases in which there is minimal or no fixed stenosis of the subclavian vein following lysis. An infraclavicular approach is utilized when we feel that there is a possibility that a venous reconstruction may be necessary. We are presently compiling our data on approximately two dozen patients treated in this manner in which it was necessary to perform endovenectomy and vein patch angioplasty in six patients with a markedly stenotic subclavian vein following lysis and rib resection. The authors in this series had no patients who required venous reconstruction and advocated possible delayed angioplasty for residual thrombosis following rib resection secondary to a relatively high rate of rethrombosis following venous reconstruction in their previous experience. We have not seen this in our recent series, and I wonder if this may have been a result of residual ligament or rib remnant secondary to their operative approach.

Although we are less enamored with the results of balloon angioplasty in these cases, I would stress the word *delayed* in the authors' recommendations for treatment of

residual vein stenosis. The Albany group has recommended immediate angioplasty following rib resection. We have seen one case of a ruptured subclavian vein and nearly exsanguinating hemorrhage when this was performed and do not share their enthusiasm for early treatment.

Again, I would like to congratulate the authors on an excellent presentation and thank the society for the opportunity to discuss this fine paper.

Dr W. Anthony Lee. Thank you, Dr Weinstein. I would like to first say that we recognize the limitations of our study with its relatively small numbers and short follow-up. To that end we would welcome an opportunity to present a follow-up report in the future to the society regarding these patients and additional patients that will be accrued.

Dr Weinstein first asked about our inclusion criteria, more specifically regarding our inclusion of the four patients who presented from outside institutions without undergoing a venogram and thrombolysis. It is true that they do represent a subset of patients who presented in a different manner compared with the 18 other patients. However, we felt their primary pathophysiology and pathology did fall under the label of primary axillary subclavian vein thrombosis and that they were appropriate to be included.

In addition, the lack of an acute thrombosis at the time of their presentation at our institution on a venogram precluded them from undergoing thrombolysis.

In regard to your second question concerning gradual increase of patient activity and how these patients were advised, our recommendation was to gradually increase their activity and not to engage in strenuous or repetitive activity immediately. How exactly they interpreted that advice I cannot specifically comment.

In regard to the small subset of young individuals who were either very physically active or involved in professional or collegiate level varsity sports, in many ways they had the most to lose and in some ways the most to gain from a successful outcome, whether it be conservative or surgical management.

In these patients, despite still being on the team, either from their coaches or fear of incurring additional injury, they have voluntarily reduced the intensity of their activities compared with their premorbid levels.

Regarding cases of incomplete lysis, we agree that there is no role for preoperative balloon angioplasty of these lesions. I cannot tell you exactly how many of these patients out of the 10 that achieved only partial lysis fell into the category of 80% to 90%. Whether these people should also be considered for conservative treatment, yes, I believe we should.

I think what we are starting to appreciate from this series and treating these people over time is that, in fact, the venous collaterals may be more physiologically important than the named subclavian or axillary vein itself and that even with visualization of 80% to 90% or near occlusive stenosis, these people should be given a chance to declare themselves.

Lastly, in terms of technical aspects of the operation, indeed much has been written about various approaches, namely, transaxillary and also the so-called paraclavicular approaches where combined supraclavicular and infraclavicular approaches are used. We can imagine where there may be circumstances where other surgical approaches may seem more appropriate.

However, I believe that most of these arguments have to do with local expertise, and in our hands the supraclavicular approach has afforded us extremely good visualization and an opportunity for two surgeons to work together with a clear view of the field. We have been able to reach the most medial aspects of the first rib and subclavian vein without much difficulty.

Dr Robert Rutherford (Denver, Colo). One cannot really argue with your title that says not *all* patients require operation. Certainly those with a normal venogram after lysis and a negative positional venogram one would certainly observe. On the other hand, I am not sure I can agree that if you get away without surgery in nine out of 22 that you can claim after a short follow-up, they did not *require* surgery.

What I understood from your presentation was that, after about a month on anticoagulants, these patients, as you say, "declare themselves," and that you made your selection mainly on the basis of symptoms, that is, the patients' symptoms with return to activity.

On the other hand, five of the nine patients you operated on had minimal symptoms but were athletes. So there is more to your selection process.

So I would like to know a little more about your selection process. I think it is possible to select patients you do not operate on, but were you not influenced at all by other considerations, particularly the venographic findings; by the residual intrinsic lesions; or by extrinsic compression on positional venography? Was the decision really entirely made on the basis of symptoms?

Dr Lee. Thank you for your questions. I would like to respond to that by saying that indeed our primary indication is the presence of symptoms. We have found that in a majority of these individuals with hyperabduction and external rotation you can obtain some level of venous occlusion or obstruction. However, on top of that, we have added an additional condition that not only should they occlude the main named vessels, but also the collaterals as demonstrated in one of our slides.

I think the real answer behind this controversy remains what is the true pathophysiology behind primary axillary subclavian thrombosis? Review of the literature seems to show conflicting understanding of the problem. I think the future may bear out that the presence of collaterals may be more important than initially suspected.

In regard to your point about our surgical therapy for five of those patients who had preoperatively minimal symptoms, these involved primarily athletes and those who were very physically active. They had minimal symptoms insofar as being able to participate in many of their nonathletic activities. However, they expressed strong concern about possible recurrence. They also showed some aversion

to the prospect of any increased duration of anticoagulation that was other than absolutely necessary. Given the prospect of a shorter period of anticoagulation, even at the risk of surgery, they wished to undergo surgery.

Dr Julie A. Freischlag (Los Angeles, Calif). I rise to sort of tell you we do it different. It has taken three of us to take over Dr Machleder's incredible practice at UCLA, and we do see a lot of effort thrombosis. I have been quite frustrated that the majority are treated initially somewhere else, and in your series see that you are seeing the same thing: that 60% to 70% of these patients we see after someone has tried to lyse and balloon them. It is usually 4 to 6 weeks later.

I like operating on this group of patients because they get better, and I think that is the difference I like about the effort thrombosis patients. Unlike neurogenic patients, that even if you select them carefully, there is always a ringer that you did not make better or that is going to call you and be in your office frequently.

The effort thrombosis patients tend to be very active individuals who want to go have a life, and therefore, they go do that. And, therefore, I rise to say that I love operating on these patients, and there are very few of them I would elect not to operate on.

I find that they tend to be gladiators. They are very active. They are weight lifters. They are surfers. Actually, I have two surfers wearing their ribs around their neck now in San Luis Obispo. I think they are a group of patients that actually would do well perhaps without surgery because they are going to go ahead anyway, but I think you can make them better.

My frustration with them coming late is that we do see patients with an occluded vein when they come that you think you could have treated. My one question to you is what do you do with someone who is occluded and has only collaterals?

I do agree with you the collaterals are important, and I have operated on a handful of patients who have primary thrombosis of the vein and only patent collaterals. We resect the rib, and we are unable to open up the main vein, but they are better, and I think you can make a difference.

We have gotten more aggressive in doing this faster. Dr Machleder initially wrote about waiting 3 months. We have gone to 1 month, and Dr Gelabert is actually doing similar to what Dr Weinstein mentioned. Some patients, if we do get to see them first, and we do lyse open their vein and will resect the rib during the same hospitalization.

However, I have had one patient develop hemorrhage following a vein angioplasty in hospital 2 days following the rib resection. The bleeding was from the bed of the rib, and this patient required a thoracotomy with a hemothorax. Therefore, I think I too would delay the angioplasty a couple weeks later after the rib resection.

I enjoyed your comments. We still do this procedure transaxillary. Certainly across the nation there are good results with both types of surgical approaches with this disease.

Dr Lee. Dr Freischlag, thank you very much for your comments. I believe that some thromboses are silent. However, if we do encounter a patient who does come back with a recurrent thrombosis after what we felt was a period of adequate anticoagulation, those patients would be restudied, they would be reimaged, and relysis would be attempted, and given this recurrent episode, they would be strongly considered and recommended for surgical therapy.

Dr Cornelius Olcott IV. Well, I told Anthony this was going to raise some shackles in this organization, and I feel I am kind of compelled to get him off the hook a little bit.

The surgeons that have discussed this paper are all excellent surgeons. However, I am sure they have seen patients that have been operated on and have had bad results because of brachial plexopathies, subclavian artery injuries, and persistent lymphatic leaks, etc.

Because of some of the bad results that we have seen, thankfully not in our institution, we have pursued this conservative approach, operating on only those patients with persistent symptoms of venous hypertension.

We are not trying to tell you on the basis of relatively short follow-up that this is the ultimate answer, but I believe we can say on the basis of this study that a conservative approach should be considered. There is little downside, and some patients are spared surgical intervention.

Also, a little delay we believe helps because the subclavian vein is not as inflamed, thus making the surgery technically easier. Thank you.