Review Article
Article de revue

Management of subclavian-axillary vein thrombosis: a review

Gary J. Hicken, MB ChB; F. Michael Ameli, MB ChB

Objective: To study, by literature review, the management of subclavian-axillary vein thrombosis (SAVT) and to make recommendations.

Data sources: The MEDLINE database and cross-referenced articles.

Study selection: Key words subclavian-axillary vein thrombosis, venous thrombosis, Paget–Schroetter syndrome, anticoagulation, and thrombolysis were used to extract articles related to SAVT.

Data extraction: Independent extraction of articles by 2 observers.

Data synthesis: Although numerous studies are available in the literature, they vary widely in their patient selection, treatment methods, follow-up and conclusions. As such, the management of patients with SAVT remains controversial.

Conclusions: Anticoagulation remains the initial treatment of choice for acute SAVT although there is definitely a role for thrombolysis and surgery in selected cases. Surgical intervention should be reserved for patients in whom there is a specific indication. Since chronic symptoms depend largely on the etiology of the disease, treatment should be tailored to address the causative factors. A multicentre, prospective study is necessary to evaluate the optimum management strategies for patients with SAVT.

Objectif : Étudier, en procédant à une recension des écrits, la prise en charge de la thrombose de la veine axillaire sous-clavière (TVAS) et formuler des recommandations.

Sources de données : La base de données MEDLINE et renvois à des articles.

Sélection d'études : On a utilisé les mots clés thrombose de la veine axillaire sous-clavière, thrombose veineuse, syndrome de Paget–Schroetter, anticoagulation, et thrombolyse pour extraire des articles portant sur la TVAS.

Extraction de données : Articles extraits par deux observateurs indépendants.

Synthèse des données : Même si de nombreuses études sont disponibles dans les publications, la sélection des patients, les méthodes de traitement, le suivi et les conclusions y varient considérablement. La prise en charge des patients victimes d'une TVAS suscitera toujours la controverse.

Conclusions : L'anticoagulation demeure le premier traitement de choix de la TVAS aiguë, même si la thrombolyse et l'intervention chirurgicale ont un rôle à jouer dans certains cas. Il faudrait réserver l'intervention chirurgicale pour les patients chez lesquels il y a une indication précise. Comme les symptômes chroniques dépendent beaucoup de l'étiologie de la maladie, le traitement devrait viser les facteurs étiologiques. Il faut procéder à une étude prospective multicentrique pour évaluer les stratégies optimales de prise en charge des patients victimes d'une TVAS.

Subclavian-axillary vein thrombosis (SAVT) was first described independently by Paget and Von Schroetter in the latter part of the nineteenth century. In 1949, Hughes[1] reviewed 320 cases of spontaneous upper limb venous thrombosis and named this condition Paget–Schroetter syndrome. Although the peer-review literature and standard surgical texts describe various treatment strategies for SAVT, there have been no ran-

From the Division of Vascular Surgery, The Wellesley Hospital, University of Toronto, Toronto, Ont.

Presented at the International Multidisciplinary Vascular Disease Symposium, Winnipeg, Man., May 15, 1996

Accepted for publication Feb. 17, 1997

Correspondence to: *Dr. F. Michael Ameli, Suite 212, E.K. Jones Building, 160 Wellesley St. E, Toronto ON M4Y 1J3; tel 416 926-7700; fax 416 926-7742*

domized, controlled trials comparing treatments, and the majority of published series are small, retrospective ones. As a result, there is no consensus on the optimum management strategy for this condition.

In response to this problem we reviewed the literature on the management of SAVT, focussing on the role of thrombolysis in the treatment of this condition.

Etiology and nomenclature

The descriptions "primary,"[2–5] "spontaneous,"[6–9] "idiopathic,"[10,11] "effort"[9,12–18] and "traumatic"[19] have all been used inconsistently to describe Paget–Schroetter syndrome. However, several etiologic factors or events associated with SAVT are now recognized:

- strenuous upper body activity, resting arm position and positional activities;
- an anatomic abnormality causing venous compression and possibly intimal damage to the vein[18] at the thoracic outlet (including abnormal anterior scalene, subclavius and pectoralis minor muscles, abnormal first rib or clavicle, congenital bands, scarring and congenital webs or malformed valves within the vein[3]);
- local conditions, including damage due to a tumour or radiotherapy;
- systemic disease, including malignant disease, cardiac failure and hematologic abnormalities;
- local intravascular trauma, chemical irritation or flow disruption, including catheterization, dialysis fistula formation and intravenous drug use and abuse;
- oral contraceptive use.

True Paget–Schroetter syndrome is "the more or less rapid onset of venous obstruction in an arm of an otherwise healthy person."[1] Sanders and Haug[20] pointed out that "most authors have regarded thoracic outlet syndrome-associated venous thrombosis as primary rather than secondary, because the anatomy is grossly normal and the mechanism speculative," and Lindblad, Tengborn and Bergqvist[21] reported that up to 39% of cases of SAVT were secondary to an identifiable cause. It has also been suggested that the pathogenesis of the thrombosis determines outcome and chronic morbidity.[22,23] It is important to distinguish primary and secondary SAVT (Table I[3,5,21,24–36]). Primary SAVT is idiopathic or related to physical activity or arm positioning with or without anatomic compression at the thoracic outlet ("true" Paget–Schroetter syndrome); secondary SAVT is related to such causes as cardiac failure, radiotherapy, instrumentation, catheterization, dialysis fistulae, intravenous drug abuse and tumour (including both local compression from a tumour mass and thrombosis secondary to the systemic hypercoagulable state often associated with neoplasia). Secondary causes can be further divided into those associated with local or systemic disease processes and those associated with catheterization and local irritants.

Since abnormalities in the coagulation and fibrinolytic systems can be associated with both primary and secondary causes of SAVT,[21] their presence should not be considered the main factor when classifying the thrombosis. Associations between SAVT and pregnancy[24] and SAVT and Raynaud disease[25] have also been described but are difficult to classify.

Incidence

Between 1966 and 1986 SAVT accounted for less than 2% of all cases of deep venous thromboses (DVT)[21,26] and only 11 of 100 000 hospital admissions.[26] However, more recently, the incidence has increased owing to greater use of central venous catheterization.[37–39] Lindblad[40] summarized the results of 10 series (456 patients) in which mural or occlusive thrombus was identified in an average of 18.9% of patients who had a central venous catheter.

Presentation

The characteristics of SAVT are swelling of the affected arm, venous engorgement, mild cyanosis and pain or discomfort.[41] Other symptoms, including parasthesias and pruritus, have also been described,[1] and palpable, tender veins may be present.[12,26]

Patients often present within 2 to 3 days of the onset of symptoms, but the delay to presentation may be months, especially if there is a history of previous episodes of similar symptoms, which may be due to intermittent extrinsic venous compression

Table I

Causes of Subclavian-Axillary Vein Thrombosis

Primary
Strenuous upper body activity[3]
Upper limb immobility[5]
Venous compression at the thoracic outlet[3]
Secondary
Systemic disease
Local tumour compression[24]
Local radiotherapy[25]
Systemic effects of malignancy[28]
Cardiac failure[21]
Shoulder trauma[26]
Amyloidosis[29]
Sarcoidosis[27]
Oral contraception[21]
Catheter and local irritant
Central venous catheterization[30–33]
Pacemaker wire[27]
Intravenous drug abuse[34]
Parenteral nutrition[35]
Dialysis fistula formation[36]

rather than thrombosis per se.[42,43] In fact, Dunant[17] reported that up to 80% of patients who present with SAVT have had previous symptoms of intermittent venous obstruction. Since the timing of presentation has implications for management,[26] patients who present within 7 days of the onset of symptoms should be considered to have acute SAVT, within 7 to 14 days subacute, and after more than 14 days chronic SAVT.[44]

SAVT occurs most commonly in young and middle-aged men,[3] although both sexes and all age groups may be affected, and appears more often in the right arm,[3,5] probably because this is the usual dominant limb and hence is involved most frequently in strenuous activity. The differential diagnosis includes superior vena caval occlusion, lymphedema,[45] inflammatory carcinoma of the breast, lymphangitis, cellulitis,[46] allergy, hematoma and gas gangrene.[47]

Investigation

After history-taking and clinical examination, the diagnosis of SAVT is confirmed by radiologic investigation, with venography being the technique of choice. Introduction of the contrast medium into the basilic vein is the optimum way to facilitate visualization of the deep venous system.[48] Venography will clarify the location and extent of the thrombus as well as the extent of the collateral circulation and, when performed with the arm in the neutral and military positions, will also identify extrinsic compression.[42] The disadvantages of venography are its invasive nature and potential to induce thrombosis, especially with repeated use,[5,26] although this is unusual with modern, less irritant contrast media.

Doppler ultrasonography is also a useful investigation in the diagnosis of SAVT. It is safe and reliable,[49] and its role in the repeated visualization of the upper limb veins has been emphasized,[50] especially in patients with long-term indwelling venous catheters.[51]

Doppler ultrasonography also has its limitations. Acoustic shadowing from the clavicle can cause a "blind spot," resulting in nonvisualization of a short segment of the subclavian vein.[52] Also, the presence of large collateral vessels can make interpretation of the scan difficult, leading to false-negative results.[46] Thus, Haire and associates[53] have suggested that although a positive Doppler ultrasound scan can preclude the need for venography, when there is a strong suggestion of SAVT but a negative scan, then venography is mandatory.

Plethysmography may be used to assess venous outflow.[44] Although Pollak and Walsh concluded that it had poor specificity for SAVT,[46] in a more recent study[55] it was found to be highly accurate in identifying upper extremity DVT. However, as with Doppler ultrasonography, a negative result still requires confirmation by venography.

Other forms of investigation have been described, including intravascular ultrasonography,[56] radionuclide venography,[16] magnetic resonance imaging (MRI)[52] and spiral computed tomography (CT);[57] however, venography remains the standard.

If there is no obvious cause for a case of primary thombosis, then further investigation into its etiology is mandatory. Investigations that should be considered are radiologic examination of the chest and thoracic outlet and CT of the thoracic cavity. It has also been recommended that the more common thrombotic disorders (including antithrombin III, protein C and S deficiencies) should be sought, especially in patients under 40 years old[58] and in those who are considered to be candidates for long-term anticoagulation.[59] Sundqvist and colleagues[60] found that 26 (49%) of 53 patients with confirmed SAVT had defective fibrinolytic capacity in excised sections of vein wall, and they recommended studies of fibrinolysis.

Management options

The 2 important elements of the management of SAVT are treatment of the acute thrombosis, and investigation and treatment of any underlying disease. Effective treatment aims to reduce both acute morbidity (pain, swelling, venous gangrene and pulmonary embolism) and chronic morbidity (pain, swelling and limitation of movement).

Conservative management

In years past, acute SAVT has been managed with bed rest, limb elevation and warming of the limb. However, the results of this strategy have been poor, with significant long-term morbidity.[5] Gloviczki, Kazmier and Hollier[61] found that anticoagulation was significantly better than conservative management at reducing chronic morbidity, and although Cohen and Dubin[62] suggested that there was no difference between conservative management and anticoagulation, only 12 patients were studied and the cause of the thrombosis differed in the 2 groups. Currently, there is little to recommend such a conservative approach, with anticoagulation being the minimum intervention required for these patients.

Anticoagulation

Anticoagulation is the initial treatment for patients with acute SAVT and remains the standard by which all other treatments are judged. An intravenous heparin infusion is started as soon as the diagnosis (or presumptive diagnosis) is made and is titrated to gain an ac-

tivated partial thromboplastin time of 2 to 3 times the control. The infusion is maintained for 5 to 7 days followed by conversion to anticoagulants taken orally, which are typically continued for about 3 months.[6,61,63] Anticoagulation will not recanalize the vein, but it will prevent clot propagation, especially along venous collaterals, and helps to protect against pulmonary embolism.

A number of authors have emphasized the high incidence of chronic symptoms of arm swelling, pain and discomfort that occur after anticoagulation.[2,64,65] However, Ameli and associates[63] have shown that anticoagulation is effective in controlling early morbidity and preventing long-term symptoms; this work is supported by other authors.[21,66,67]

Surgery

Although early surgical thrombectomy for SAVT has had its advocates,[15,68] this procedure done in isolation now has little to recommend it. An approach consisting of thrombectomy with simultaneous correction of any underlying anatomic abnormality allows restoration of venous patency and theoretically reduces the risk of pulmonary embolism and chronic symptoms. However, surgery has the disadvantage of requiring general anesthesia and carries the risk of pneumothorax or arterial and brachial plexus damage with the possibility of disrupting venous collaterals. There are, unfortunately, no large trials comparing patients who have received early surgery and those treated by less invasive methods, and the reports that have been published are often anecdotal. Thus, the role of surgery in the treatment of SAVT remains unclear.[41]

Balloon thrombectomy is also an option in these patients, but this procedure carries a risk of intimal damage and further thrombosis.[69] Venous bypass has been used with some success in patients with chronic symptomatic SAVT,[70–73] but this approach is not appropriate for acute thrombosis.

Thrombolysis

Why use thrombolysis?

Venous thrombosis can result in chronic venous occlusion. If recanalization occurs as a physiological phenomenon, it causes valvular damage leading to valvular insufficiency and may leave residual mural thrombus, which can organize, stenose the vessel and impair venous return, thus causing chronic symptoms in the arm. Acutely, venous gangrene has been reported but is rare; however, pulmonary embolization is more common than once thought. Visualization of a venous stenosis or an underlying compressive abnormality at the thoracic outlet may be impaired if clot remains in the vein, even if its propagation is reduced with the use of anticoagulants.

Considering these problems associated with SAVT, thrombolysis has theoretic advantages over both anticoagulation and surgery.

Venous patency, valvular integrity and chronic symptoms

Although heparin is protective against secondary thrombosis of collaterals and helps maintain venous return, some authors[38,74] have reported better long-term results in patients treated with thrombolysis than with anticoagulation. Thrombolysis has the potential to restore deep venous patency early,[75,76] especially in the upper limb,[77] and preserve valvular function.[78,79] In 14 studies of 69 patients undergoing thrombolytic therapy for SAVT, total or partial primary patency was seen in 61 (88%) of the patients.[6,7,9-11,27,64,69,74,80-84] This is an important finding because venous occlusion, whether complete or partial, compromises venous return and this, along with valvular destruction, may result in venous hypertension. However, this series of events has more impact in the lower limb, and the major postphlebitic changes often seen around the ankle are uncommon in the upper limb. There are 2 reasons for this. First, collateralization around the shoulder is very good, having 4 main pathways: shoulder to chest wall, shoulder to ipsilateral anterior neck, shoulder to ipsilateral posterior neck, and shoulder to contralateral neck.[85] A number of these collaterals, however, do traverse the costoclavicular space and are themselves prone to compression depending on the arm position. It has been shown that in the lower limb, major vein occlusion may be associated with a good clinical outcome as long as adequate venous collaterals are present.[86] This appears to be true of the upper limb as well. Campbell and associates[23] found that symptoms correlated better with venous outflow obstruction than with main channel patency per se, and Tilney, Griffiths and Edwards[47] correlated chronic symptoms in the arm with venous hypertension rather than venography findings.

Second, in contrast to the upper limb, the lower limb venous valves protect against the pressure effects on the ankles of a long column of blood, especially during exercise.[54] Although the role of venous valves in the upper limb is probably not as critical as in the lower limb, it remains important. Thus, treatment should aim to maintain the integrity of the valves where possible.

It should be noted that some data regarding venous patency and collateralization after thrombolysis has to be viewed with caution, as patients may not be reassessed if they have become asymptomatic after SAVT. Also, since a number of authors perform some

form of thoracic outlet decompression on all[65] or some[87] of their patients, patency rates cannot be directly related to the use of thrombolysis alone.

Acute symptoms and embolization

In a few patients with acute SAVT, phlegmasia cerulea dolens will progress to frank venous gangrene. This condition is rare but has important consequences. Smith and colleagues[88] described 3 patients with this complication, all of whom had an associated life-threatening systemic illness. One patient with bilateral SAVT was treated with streptokinase and showed definite improvement in both arms, suggesting that thrombolysis may have a role in this condition. However, all 3 patients eventually died of their systemic disease; hence, thrombolysis had no effect on the final outcome.

It was originally thought that SAVT-associated pulmonary embolism was rare, if indeed it existed at all.[1] However, this has been refuted by more recent work,[89–91] and a rate of 14% has been suggested.[3] The role of thrombolysis in the restoration of the pulmonary microcirculation after embolization has been stressed,[78,83] and is an action not observed with heparin. It is clear, therefore, that thrombolysis plays a dual role in patients with respect to pulomary embolism.

Visualization of compression

Venous patency immediately after thrombolysis averages 88%. The restoration of venous patency allows identification of intrinsic stenoses[10] and extrinsic compression.[14] By putting the arm through its range of movements, particularly hyperabduction,[12] visualization of any extrinsic compression is enhanced, allowing for the planning of further intervention, including surgery.

Method of administration

To achieve adequate lysis, the lytic agent has to be delivered effectively to the site of the clot. This can be done either by systemic infusion through a peripheral catheter placed in a vein in the dorsum of the hand or by local infusion directly into the clot through a long catheter introduced (usually) into the basilic vein. Both systemic[6] and local[7,8,80,81,87] infusions of the thrombolytic agent have been described but have not been directly compared using large enough numbers of patients to clarify any advantage of one over the other. In the analogous situation of peripheral arterial thrombosis, it is generally accepted that local infusion is the best method of delivering the agent directly to the thrombus in high concentration, although "burst therapy" utilizing intermittent peripheral infusions of the lytic agent for both arterial and venous thrombosis has been described with good results.[92] Comerota and Aldridge[79] suggested that local thrombolysis is the delivery method of choice for lower limb DVT, and this probably holds true for venous thrombosis of the upper limb.

Most authors give a bolus dose of lytic agent initially and follow this with an infusion. The length of time of infusion depends on the degree of lysis observed on serial venography and on the infusion technique but is typically in the range of 6 to 48 hours.[6,80,87] Intravenous heparin is usually given simultaneously to prevent rethrombosis and thrombus cuff formation around the catheter. Actual doses and infusion regimens vary greatly between authors from a low dose of 10 000 IU (streptokinase) per hour[84] to a high dose of 100 000 IU (streptokinase) per hour,[86] with infusions up to 96 hours. There is probably little to recommend infusion for longer than 12 hours if clot lysis is not progressing.

Mechanical disruption of the clot may help its dissolution. The pulse-spray technique has this effect and is now becoming more widely used in peripheral arterial and dialysis access graft thrombolysis.[93–95] It can be employed if available.

Which lytic agent?

The 2 main thrombolytic agents used in the treatment of patients with SAVT are streptokinase and urokinase. Their method of action and administration have been previously described by Bell and Meek.[96]

There have been no controlled trials directly comparing the action of lytic agents in SAVT. However, Kunkel and Machleder[80] found that urokinase was better than streptokinase in establishing early patency. Also, urokinase does not have the allergy problems associated with streptokinase. In a series of 4 patients treated with streptokinase for SAVT, all had to have their infusion terminated because of a combination of high antibody levels and fever. In all 4 cases, treatment was successfully completed using urokinase.[10]

Ruckley, Boulton and Redhead[82] described 6 cases of spontaneous SAVT treated with *p*-anisoylated streptokinase-plasminogen complex (APSAC) with partial or total lysis occurring in 5, and Pires and Jay[97] described a similar case with a good result.

Tissue plasminogen activator (rt-PA) does not appear to have been widely used in treating SAVT, although its use for lower limb venous thrombosis has been summarized.[98]

Regardless of which drug is used, the longer the history of the thrombosis the less likely it is that lytic therapy will be successful because of cellular infiltration and organization of the thrombus.[99] Therefore, lytic therapy should be confined to acute cases of

Table II

Management and Sequelae in Patients With Primary Subclavian-Axillary Vein Thrombosis

Series	No. of patients	Mean age, yr	Treatment	Duration of follow-up	No. of patients with persistent symptoms after treatment
AbuRahma et al, 1991[6]	10	35	AC 6, AC + SK 2, AC + UK 2	1 yr+	AC 5, SK 1
Adams, McEvoy and DeWeese, 1965[2]	25	39	AC 10, Con 12, Thr 2, Stell 1	6 mo–24 yr	AC 8, Con 9, Thr 1, Stell 1
Ameli et al, 1987[63]	17	?	AC 17	42 mo	AC 4
Aziz, Straehley and Whelan, 1986[18]	4	25	TOD 4	6 mo–20 yr	None
Campbell et al, 1977[23]	8	41	Con 5, AC 2, TOD 1	6 mo+	Con 5, AC 1, TOD 1
Cohen and Dubin, 1988[62]	5	42	Con 1, AC 4	1–6 yr	AC 2 of 3
DeWeese, Adams and Gaiser, 1970[68]	5	30	AC + Thr + TOD 5	1–12 yr	None
Donayre et al, 1986[22]	9	35.3	AC 8, TOD 1, Thr 2	?	7 of 9
Druy et al, 1985[87]	5	24	SK/UK 5, SK/UK + TOD 2	4 mo–4 yr	SK/UK 1, SK/UK + TOD 1
Dunant, 1981[17]	25	19–44*	Lysis + TOD 25	?	8 of 25
Koot and Veen, 1991[74]	3	26	SK + AC 3	1–3 mo	None
Kunkel and Machleder, 1989[80]	25	29	SK 8, UK 3, AC 9, TOD 17	?	18 of 25
Landercasper et al, 1987[64]	4	41	SK/UK + AC 3, SK/UK + TOD 1	2 wk–4yr	None
Lindblad, Tengborn and Bergqvist, 1988[21]	73	?	AC 59, SK 5, Con 8, other 1	?	AC 13, SK 2, Con 3
Machleder 1993[8]	50	29	UK/SK 29, AC 14, Con 7, TOD 36	10 mo–7 yr	19 of 50
Malcynski et al, 1993[81]	12	31	UK 7, SK 2, UK/SK + TOD 8	2 yr (av.)	UK/SK 3
Molina, 1992[13]	28	?	AC + UK + TOD 28	6 mo–3 yr	4
Painter and Karpf, 1984[27]	8	22	AC 2, SK 2, Thr 2, TOD 1, Con 1	?	3 (4 of 8 lost)
Pittam and Darke, 1987[112]	8	30	AC 2, SK + TOD 1, TOD 5	4 mo–3 yr	AC 1, TOD 2
Prescott and Tikoff, 1979[19]	3	33	AC 3	1–17 mo	1
Steed et al, 1986[69]	2	26	SK 2	2 yr	1
Swinton, Edgett and Hall, 1968[5]	23	24	AC 8, Con 15	3 wk–17 yr	AC 2, Con 7
Thompson et al, 1992[103]	6	38	TOD 6, (+ UK 2)	9 mo–14 yr	None
Urschel and Razzuk, 1991[65]	71 limbs	32	AC 14, SK 1, AC + TOD 21, SK + TOD 35	0–25 yr	AC + TOD 26, SK + TOD 4
Wilson, Zahn and Newman, 1990[11]	8	27.5	SK 7, AC 1	Max. 5 yr	1 of 8

*Age range
AC = anticoagulation, Con = conservative management, SK = streptokinase, UK = urokinase, Thr = thrombectomy, TOD = thoracic outlet decompression, Stell = stellate ganglion block, lysis = thrombolysis with unspecified agent

SAVT. The need for prompt treatment is emphasized by Coon and Willis.[26] They found that 80% of patients who presented and were treated (with anticoagulation) within 7 days of the onset of symptoms had no residual symptoms.

Complications of thrombolysis

Morbidity associated with thrombolysis includes hemorrhage (intracranial, retroperitoneal, gastrointestinal, genitourinary, pulmonary and at sites of invasive procedures), fever, headaches and anaphylaxis. The allergic types of reactions are more common with streptokinase than with urokinase. There are few data on the incidence of these types of complications when thrombolysis is used for SAVT, although Machleder8 has described 2 episodes of allergic reaction and 1 minor hemorrhage in a series of 50 patients treated with catheter-directed streptokinase. In a review of streptokinase therapy for DVT of all types, Rogers and Lutcher[100] concluded that streptokinase is not only beneficial in DVT but that "when patients are carefully selected and invasive procedures minimized, major bleeding events including intracerebral haemorrhage are no more frequent with streptokinase than with conventional heparin therapy."

Adjuvant treatment

A number of authors have emphasized the importance of identifying and treating any underlying cause of primary SAVT,[8,81,87,101–103] whether it is an intrinsic stenosis or an extrinsic compression. Otherwise, residual symptoms, with or without rethrombosis of the vein, will remain. Identification of a stenosis or area of extrinsic compression is facilitated by lysis of thrombus in that area.

Adjuvant surgical intervention for

Table III

Management and Sequelae in Patients With Thrombosis due to Systemic Disease

Series	No. of patients	Mean age, yr	Treatment	Duration of follow-up	No. of patients with persistent symptoms after treatment
Cohen and Dubin, 1988[62]	3	35	AC 2, Con 1	4wk–1 yr	None
Donayre et al, 1986[22]	7	36	AC 7	?	1
Mason, 1981[45]	12	58	AC 9, Rad 2, Con 1	?	1
Painter and Karpf, 1984[27]	5	48	AC 5	?	2 (3 of 5 lost)
Prescott and Tikoff, 1979[19]	7	43	AC 7	10–43 mo	2

AC = anticoagulation, Con = conservative management, SK = streptokinase, UK = urokinase, Thr = thrombectomy, TOD = thoracic outlet decompression, Stell = stellate ganglion block, lysis = thrombolysis with unspecified agent

Table IV

Management and Sequelae of Patients With Thrombosis due to Catheter and Local Irritant

Series	No. of patients	Mean age, yr	Treatment	Duration of follow-up	No. of patients with persistent symptoms after treatment
Ameli et al, 1987[63]	3	?	AC 3	42 mo	None
Campbell et al, 1977[23]	10	52	AC 7, Con 2, Thr 1	> 6 mo	None of 8 (2 of 10 died)
Cohen and Dubin, 1988[62]	2	84	AC 1, Con 1	3 mo–2 yr	None
Donayre et al, 1986[22]	21	42	AC 21	?	3
Druy et al, 1985[87]	3	55	SK 3	4–8 mo	None
Kerr et al, 1990[49]	31	?	AC 22, Con 9	1–38 mo	AC 5, Con 2 (2 of 31 died)
Painter and Karpf, 1984[27]	5	53	AC 4, SK 1	?	AC 3 (1 of 5 lost)
Steed et al, 1986[69]	5	58	SK 5	6 mo	None (2 of 5 died)

AC = anticoagulation, Con = conservative management, SK = streptokinase, UK = urokinase, Thr = thrombectomy, TOD = thoracic outlet decompression, Stell = stellate ganglion block, lysis = thrombolysis with unspecified agent

SAVT usually takes the form of first rib resection or some other thoracic outlet decompression procedure, with or without venoplasty. Balloon angioplasty of residual stenoses after the decompressive surgery has been found useful provided that any extrinsic compression has been relieved.[104] In contrast, if angioplasty is performed before such surgery it is associated with a high restenosis rate[8] and may in fact be detrimental; Kunkel and Machleder[80] reported 4 out of 4 thrombotic occlusions in veins that were previously only stenotic. Balloon angioplasty has been applied to venous stenosis secondary to central venous catheterization in patients undergoing dialysis[4] but results in low long-term patency (35% at 1 year and 6% at 2 years). However, the use of repeated angioplasty is recommended[4,105] for patients who have limited access sites for dialysis.

The use of stents has been described and appears to have a better success rate in treating stenoses due to catheterization and those associated with arteriovenous dialysis fistulae than does angioplasty alone.[106–109] Stenting in primary SAVT is unlikely to be of benefit unless a short, localized intravenous lesion is identified.

Molina[13,44] and Urschel and Razzuk[65] have proposed a protocol for the management of SAVT, involving a combination of thrombolysis and early surgery to remove the first rib in all patients with "effort" thrombosis. We do not find this a logical approach because not all patients with "effort" thrombosis have an identifiable extrinsic compression and because positional extrinsic compression does not necessarily cause venous thrombosis. This latter point is supported by Dunant,[17] who found that venous obstruction could be demonstrated in up to 70% of healthy people when the shoulder was hyperabducted and retracted. Similar shoulder movement caused a significant rise in axillary vein pressure in 88% of healthy people. However, in a similar study, Stevenson and Parry[110] found no evidence of venous compression in abduction and adduction venograms of healthy subjects, but only 10 subjects were included.

Rauwerda and colleagues[111] reported on a series of patients who underwent thrombolysis followed, after a 3-month delay, by first rib resection. Venography and plethysmographic determination of venous outflow, venous capacity and impedance were performed postoperatively and showed good results, but no measurements were taken preoperatively for comparison. A similar approach was taken by Machleder,[14] who also suggests waiting 3 months to reassess symptoms, and by Pittam and Darke,[112] who advocated a 6-month delay.

When contemplating first rib resection, it must be remembered that this procedure may be associated with serious complications and that it is a potent source of litigation. Symptoms must be assessed very carefully and "lesser" procedures considered, if appropriate.

It must also be remembered that some patients with primary SAVT have thoracic outlet obstruction but with symptoms of neurologic origin.[14,80] Such symptoms can be confused with those of venous origin, and postoperative improvement may be due to relief of nerve compression rather than relief of venous obstruction.

Table V

Sequelae According to Etiology of Thrombosis. Summary of Studies

Etiology	Patients, no. Total	Median no./study	Range in studies	Mean age, yr	No. (%) of patients with persistent symptoms
Primary	437	8	2–73	31.4	165 (37.8)
Systemic disease	34	7	3–12	44	6 (17.6)
Catheter and local irritant	80	5	2–31	57	13 (16.3)

Table VI

Summary of Sequelae According to Type of Treatment

Treatment	No. of patients treated	No. (and %) of patients with persistent symptoms
Conservative	50	26 (52)
Anticoagulation	133	42 (32)
Thrombolysis	31	8 (26)
Thoracic outlet decompression plus lysis	67	13 (19)
Thoracic outlet decompression	19	3 (16)
Other	4	2 (50)

Primary versus secondary

There is little hard evidence to indicate whether primary and secondary SAVT should be managed differently because patient numbers in series are

small, and definitions and classifications of SAVT vary between authors. Donayre and associates[22] suggested that patients with primary SAVT be treated aggressively with thrombolysis and surgery (if indicated) to prevent chronic disability, but that those with secondary causes of SAVT require only anticoagulation, as their long-term morbidity is low.[113] This latter point seems sensible when one considers the degree of comorbidity in patients with thrombosis secondary to cardiac failure, cancer and venous catheterization that is used in a variety of chronic illnesses. This comorbidity may preclude thrombolysis and surgery in many patients. Such an approach is supported by Campbell and associates,[23] who reported that none of their 8 patients who had secondary thrombosis complained of persistent symptoms whether or not they received anticoagulation.

Patients who require repeated central catheterization for dialysis access, total parenteral nutrition or chemotherapy may be an exception to this rule of minimal intervention because of the absolute necessity to maintain adequate venous access.[87]

Long-term sequelae

Tables II to VI summarize the management and long-term sequelae of SAVT. Multiple publications and individual case reports have been excluded, as have those that lack adequate follow-up of symptomatology (less than 6 months) or adequate subclassification of the cause of thrombosis and its management.

Conclusions

The management of patients with SAVT remains controversial. A number of options are available, varying from the conservative heparinization followed by oral anticoagulation, through thrombolysis, to aggressive early surgical intervention. For patients with primary SAVT, the prevention of the chronic symptoms of pain, swelling and limitation of movement

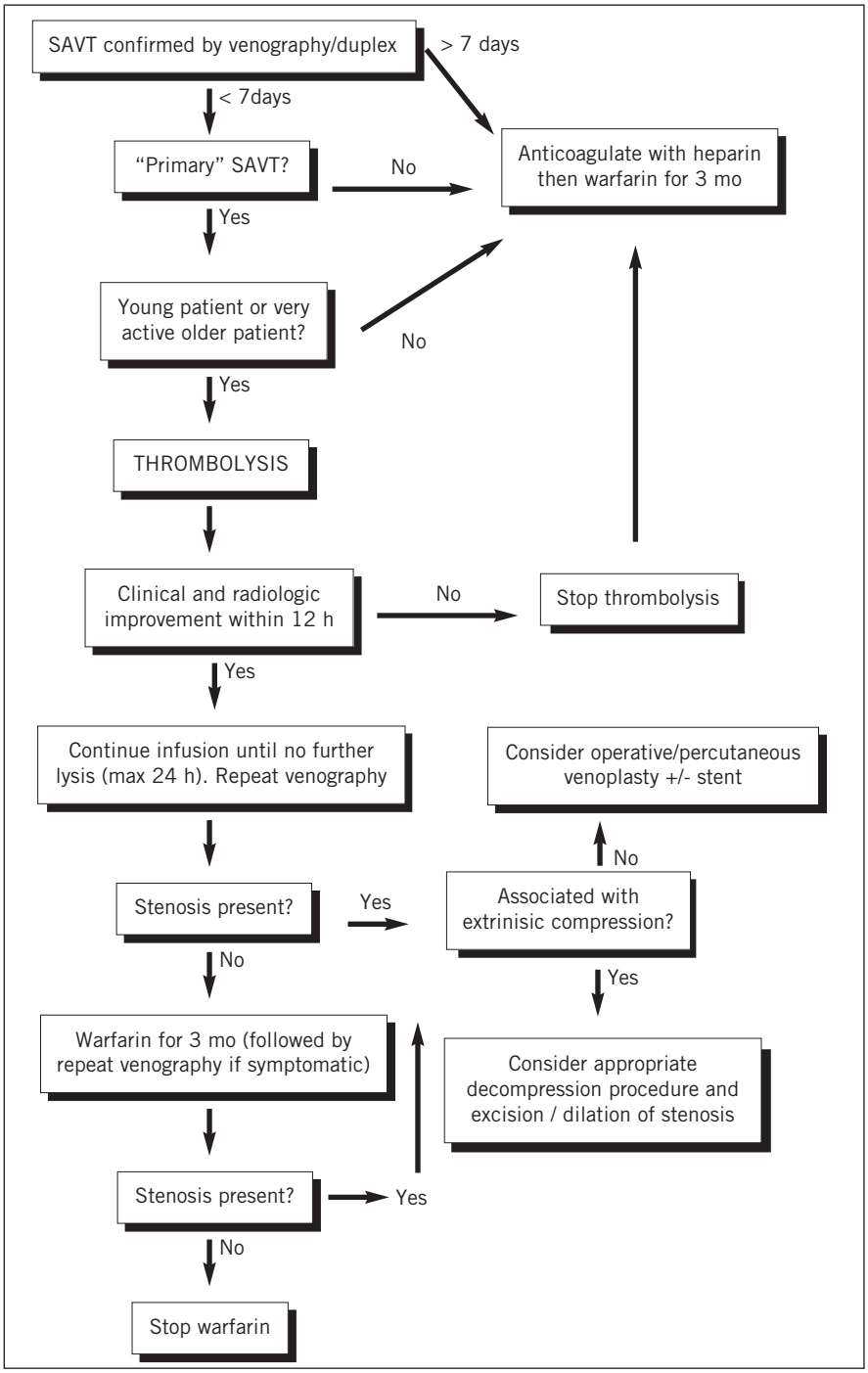

FIG. 1. Algorithm for the management of acute subclavian-axillary vein thrombosis. Patients with thrombosed access for hemodialysis, those receiving total parenteral nutrition or chemotherapy may need thrombolysis and should be considered as special cases. Young = 65 years of age or less, older = more than 65 years of age. For a definition of "primary" see text.

is of major importance, although the degree of long-term morbidity in published series varies greatly. For these patients, the only predictors of chronic symptoms appear to be the etiology of the thrombosis, the presence (or not) of extrinsic compression or venous stenosis and length of history. The acceptability of chronic symptoms depends on the activity level of the individual patient, which in turn is related to age, employment and recreational interests. Therefore, the type of treatment chosen for any particular patient should be tailored both to this and to the cause of the thrombosis.

Thrombolysis is becoming widely used in the management of SAVT. However, its side effects must be considered; problems with hemorrhage, allergy and catheter placement have all been recorded.[99,114] When used correctly, thrombolytic drugs appear to be safe, but it must be remembered that local infusions require skilled catheter placement and that monitoring must be adequate and dosages carefully calculated. Financial implications must also be considered, as radiology time and equipment, beds in the intensive care unit and the drugs themselves are associated with significant cost. It has, however, to be compared with the overall cost to society of a young patient who cannot contribute economically over his or her lifetime because of chronic symptoms of arm swelling and pain.

Although the prevalence of SAVT is increasing, it remains uncommon. Becker, Philbrick and Walker[66] have suggested that a multicentre trial would be justified to evaluate the management of SAVT. The purpose of such a trial should be specifically to define whether anticoagulation is adequate to prevent both the early and late sequelae of SAVT, whether thrombolysis should be more widely adopted or whether its use should be confined to specified groups of patients. The role of surgery would be more difficult to assess, partly because all patients should initially receive some form of pharmacologic intervention regardless of whether surgery is scheduled, and partly because of ethical considerations.

However, until such a trial is undertaken, on the basis of this review we propose the following management strategy and an algorithm (Fig. 1) similar to that suggested by Haire:[115]

- Anticoagulation remains the mainstay of treatment in the early stages and should be used in cases of acute thrombosis and continued for 3 months.
- Chronic thromboses may require only conservative management; thrombolysis is not indicated.
- Thrombolysis should be confined to specific categories of patients with primary SAVT: young patients, some patients with venous access requirements and older patients whose employment or recreational activity would be severely limited by chronic arm swelling or pain.
- SAVT should be confirmed by venography even if Doppler ultrasonography is negative, and should be further investigated if no obvious cause is found.
- Catheter-guided local administration of the lytic agent is the delivery method of choice. Urokinase has certain advantages over streptokinase.
- After the acute episode, surgery should be considered if there is symptomatic extrinsic venous compression, and angioplasty of residual stenoses should only be performed postoperatively.

References

1. Hughes ES. Venous obstruction in the upper extremity: review of 320 cases. *Int Abstr Surg* 1949;88:89-127.
2. Adams JT, McEvoy RK, DeWeese JA. Primary deep venous thrombosis of upper extremity. *Arch Surg* 1965; 91:29-42.
3. Hurlbert SN, Rutherford RB. Basic data underlying clinical decision making — primary subclavian-axillary vein thrombosis. *Ann Vasc Surg* 1995;9(2):217-23.
4. Glanz S, Gordon DH, Lipkowitz GS, Butt KMH, Hong J, Sclafani SJA. Axillary and subclavian vein stenosis: percutaneous angioplasty. *Radiology* 1988;168(2):371-3.
5. Swinton NW, Edgett JW, Hall RJ. Primary subclavian-axillary vein thrombosis. *Circulation* 1968;38:737-45.
6. AbuRahma AF, Sadler D, Stuart P, Khan MZ, Boland JP. Conventional versus thrombolytic therapy in spontaneous (effort) axillary-subclavian vein thrombosis. *Am J Surg* 1991; 161(4):459-65.
7. Baron B, Kiproff PM, Khoury MB. Local thrombolysis and percutaneous transluminal venoplasty for the venous complications of thoracic outlet syndrome: case report. *Angiology* 1992;43(11):957-60.
8. Machleder HI. Evaluation of a new treatment strategy for Paget–Schroetter syndrome: spontaneous thrombosis of the axillary-subclavian vein. *J Vasc Surg* 1993;17(2):305-17.
9. Taylor LM, McAllister WR, Dennis DL, Porter JM. Thrombolytic therapy followed by first rib resection for spontaneous ("effort") subclavian vein thrombosis. *Am J Surg* 1985; 149(5):644-7.
10. Becker GJ, Holden RW, Rabe FE, Castaneda-Zuniga WR, Sears N, Dilley RS, et al. Local thrombolytic therapy for subclavian and axillary vein thrombosis. *Radiology* 1983;149(2): 419-23.
11. Wilson JJ, Zahn CA, Newman H. Fibrinolytic therapy for idiopathic subclavian-axillary vein thrombosis. *Am J Surg* 1990;159(2):208-11.
12. Adams JT, DeWeese JA. "Effort" thrombosis of the axillary and subclavian veins. *J Trauma* 1971;11(11):

923-30.
13. Molina JE. Surgery for effort thrombosis of the subclavian vein. *J Thorac Cardiovasc Surg* 1992;103(2):341-6.
14. Machleder HI. Effort thrombosis of the axillosubclavian vein: a disabling vascular disorder. *Compr Ther* 1991; 17(5):18-24.
15. Inahara T. Surgical treatment of "effort" thrombosis of the axillary and subclavian veins. *Am Surg* 1968; 34(7):479-83.
16. Giordano A, Muzi M, Massaro M, Rulli F. Scintigraphic assessment of "effort" axillary-subclavian vein thrombosis. *Clin Nucl Med* 1992;7:933-5.
17. Dunant JH. Effort thrombosis, a complication of thoracic outlet syndrome. *Vasa* 1981;10(4):322-4.
18. Aziz S, Straehley CJ, Whelan TJ. Effort-related axillosubclavian vein thrombosis. A new theory of pathogenesis and a plea for direct surgical intervention. *Am J Surg* 1986;152 (1):57-61.
19. Prescott SM, Tikoff G. Deep venous thrombosis of the upper extremity: a reappraisal. *Circulation* 1979;59(2): 350-5.
20. Sanders RJ, Haug C. Subclavian vein obstruction and thoracic outlet syndrome: a review of etiology and management. *Ann Vasc Surg* 1990;4(4): 397-410.
21. Lindblad B, Tengborn L, Bergqvist D. Deep vein thrombosis of the axillary-subclavian veins: epidemiologic data, effects of different types of treatment and late sequelae. *Eur J Vasc Surg* 1988;2(3):161-5.
22. Donayre CE, White GE, Mehringer SM, Wilson SE. Pathogenesis determines late morbidity of axillosubclavian vein thrombosis. *Am J Surg* 1986;152(2):179-84.
23. Campbell CB, Chandler JG, Tegtmeyer CJ, Bernstein EF. Axillary, subclavian, and brachiocephalic vein obstruction. *Surgery* 1977;82(6):816-26.
24. Ben-Shlomo I, Azogui G, Prober A, Cozacov C, Zohar S. Axillary vein thrombosis during pregnancy: a case report. *Obstet Gynecol* 1992;80(3): 495-7.
25. Laguna P, Sanchez M-A, Moya M. Subclavian vein thrombosis in a patient with Raynaud's disease [letter]. *Postgrad Med J* 1994;70(822):312.
26. Coon WW, Willis PW. Thrombosis of axillary and subclavian veins. *Arch Surg* 1967;94(5):657-63.
27. Painter TD, Karpf M. Deep venous thrombosis of the upper extremity five years experience at a university hospital. *Angiology* 1984;35(11): 743-9.
28. Lokich JJ, Becker B. Subclavian vein thrombosis in patients treated with infusion chemotherapy for advanced malignancy. *Cancer* 1983;52(9): 1586-9.
29. Dickey W, Callender ME, Mayne EE. Upper limb venous thrombosis complicating amyloidosis. *Ir J Med Sci* 1986;155(12):437-8.
30. Warden GD, Wilmore DW, Pruitt BA. Central venous thrombosis: a hazard of medical progress. *J Trauma* 1973;13(7):620-6.
31. Vanherweghem JL, Yassine T, Goldman M, Vandenbosch G, Delcour C, Struyven J, et al. Subclavian vein thrombosis: a frequent complication of subclavian vein cannulation for hemodialysis. *Clin Nephrol* 1986;26(5): 235-8.
32. Bozzetti F, Scarpa D, Terno G, Scotti A, Ammatuna M, Bonalumi MG, et al. Subclavian venous thrombosis due to indwelling catheters: a prospective study on 52 patients. *J Parenter Enter Nutr* 1983;7(6):560-2.
33. Koo Seen Lin C, Taube D, Al-Kutoubi A. Acute management of subclavian vein thrombosis [letter]. *Br J Surg* 1995;82:1140.
34. Lisse JR, Davis CP, Thurmond-Anderle ME. Upper extremity deep venous thrombosis: increased prevalence due to cocaine abuse. *Am J Med* 1989;87:457-8.
35. Wolfe BM, Ryder MA, Nishikawa RA, Halsted CH, Schmidt BF. Complications of parenteral nutrition. *Am J Surg* 1986;152:93-9.
36. Mashiah A, Liebergall M, Pasik S, David A, Bar-Khayim Y. Axillary vein thrombosis: a rare complication following creation of arteriovenous fistula for hemodialysis. *J Cardiovasc Surg (Torino)* 1986;27:291-3.
37. Horattas MC, Wright DJ, Fenton AH, Evans DM, Oddi MA, Kamienski RW, et al. Changing concepts of deep venous thrombosis of the upper extremity — report of a series and review of the literature. *Surgery* 1988; 104(3):561-7.
38. AbuRahma AF, Sadler DL, Robinson PA. Axillary-subclavian vein thrombosis. Changing patterns of etiology, diagnostic, and therapeutic modalities. *Am Surg* 1991;57(2):101-7.
39. Burihan E, Poli de Figueiredo LF, Francisco JJ, Miranda FJ. Upper-extremity deep venous thrombosis: analysis of 52 cases. *Cardiovasc Surg* 1993;1(1):19-22.
40. Lindblad B. Thromboembolic complications and central venous catheters [letter]. *Lancet* 1982;2:936.
41. Rochester JR, Beard JD. Acute management of subclavian vein thrombosis. *Br J Surg* 1995;82:433-4.
42. Adams JT, DeWeese JA, Mahoney EB, Rob CG. Intermittent subclavian vein obstruction without thrombosis. *Surgery* 1968;63(1):147-65.
43. Scher LA, Veith FJ, Samson RH, Gupta SK, Ascer E. Vascular complications of thoracic outlet syndrome. *J Vasc Surg* 1986;3(3):565-8.
44. Molina JE. Need for emergency treatment in subclavian vein effort thrombosis. *J Am Coll Surg* 1995;181:414-20.
45. Mason BA. Axillary-subclavian vein occlusion in patients with lung neoplasms. *Cancer* 1981;48(8):1886-9.
46. Pollak EW, Walsh J. Subclavian-axillary venous thrombosis: role of noninvasive diagnostic methods. *South Med J* 1980;73(11):1503-6.
47. Tilney NL, Griffiths HJG, Edwards EA. Natural history of major venous thrombosis of the upper extremity. *Arch Surg* 1970;101(6):792-6.
48. Whelan TJ Jr. Management of vascular disease of the upper extremity. *Surg Clin North Am* 1982;62(3): 373-89.
49. Kerr TM, Lutter KS, Moeller DM, Hasselfeld KA, Roedersheimer LR, McKenna PJ, et al. Upper extremity venous thrombosis diagnosed by duplex scanning. *Am J Surg* 1990; 160:202-6.
50. Bernier V, Scott AA, Glynn MFX. Thrombosis in the upper extremity: use of Doppler ultrasound for diagnosis. *Can Anaesth Soc J* 1981;28(6):

579-84.
51. Bonnet F, Loriferne JF, Texier JP, Texier M, Salvat A, Vasile N. Evaluation of Doppler examination for diagnosis of catheter-related deep venous thrombosis. *Intensive Care Med* 1989;15:238-40.
52. Haire WD, Lynch TG, Lund GB, Lieberman RP, Edney JA. Limitations of magnetic resonance imaging and ultrasound-directed (duplex) scanning in the diagnosis of subclavian vein thrombosis. *J Vasc Surg* 1991;13(3):391-7.
53. Haire WD, Lynch TG, Lieberman RP, Lund GB, Edney JA. Utility of duplex ultrasound in the diagnosis of asymptomatic catheter-induced subclavian vein thrombosis. *J Ultrasound Med* 1991;10:493-6.
54. Killewich LA, Martin R, Cramer M, Beach KW, Strandness DE Jr. An objective assessment of the physiologic changes in the postthrombotic syndrome. *Arch Surg* 1985;120:424-6.
55. Gardner GP, Cordts PR, Gillespie DL, LaMorte W, Woodson J, Menzoian JO. Can air plethysmography accurately identify upper extremity deep venous thrombosis? *J Vasc Surg* 1993;18:808-13.
56. Chengelis DL, Glover JL, Bendick P, Ellwood R, Kirsch M, Fornatoro D. The use of intravascular ultrasound in the management of thoracic outlet syndrome. *Am Surg* 1994;60(8):592-6.
57. Tello R, Scholz E, Finn JP, Costello P. Subclavian vein thrombosis detected with spiral CT and three-dimensional reconstruction. *AJR Am J Roentgenol* 1993;160(1):33-4.
58. Scott DJA, Farmilo W, Horrocks M, Taylor P. Venous thrombolysis [letter]. *Eur J Vasc Surg* 1988;2(4):274.
59. Scott DJA, Farmilo RW, Taylor PC. The place of first rib resection in the management of axillary-subclavian thrombosis [letter]. *Eur J Vasc Surg* 1987;1(5):363.
60. Sundqvist S-B, Hedner U, Kullenberg HKE, Bergentz S-E. Deep venous thrombosis of the arm: a study of coagulation and fibrinolysis. *BMJ* 1981;283(6286):265-7.
61. Gloviczki P, Kazmier FJ, Hollier LH. Axillary-subclavian venous occlusion: the morbidity of a nonlethal disease. *J Vasc Surg* 1986;4(4):333-7.
62. Cohen JR, Dubin M. Deep venous thrombosis of the upper extremity. *NY State J Med* 1988;88:177-9.
63. Ameli FM, Minas T, Weiss M, Provan JL. Consequences of "conservative" conventional management of axillary vein thrombosis. *Can J Surg* 1987;30(3):167-9.
64. Landercasper J, Gall W, Fischer M, Boyd WC, Dahlberg PJ, Kisken WA, et al. Thrombolytic therapy of axillary-subclavian venous thrombosis. *Arch Surg* 1987;122(9):1072-5.
65. Urschel HC, Razzuk MA. Improved management of the Paget–Schroetter syndrome secondary to thoracic outlet syndrome. *Ann Thorac Surg* 1991;52:1217-21.
66. Becker DM, Philbrick JT, Walker FB. Axillary and subclavian venous thrombosis. prognosis and treatment. *Arch Intern Med* 1991;151: 1934-43.
67. Lindblad B, Bergqvist D. Heparin for axillary vein thrombosis [letter]. *Eur J Vasc Surg* 1991;5(4):487-8.
68. DeWeese JA, Adams JT, Gaiser DL. Subclavian venous thrombectomy. *Circulation* 1970;41-42(Suppl. II): II158-64.
69. Steed DL, Teodori MF, Peitzman AB, McAuley CE, Kapoor WN, Webster MW. Streptokinase in the treatment of subclavian vein thrombosis. *J Vasc Surg* 1986;4(1):28-32.
70. Rabinowitz R, Goldfarb D. Surgical treatment of axillosubclavian venous thrombosis: a case report. *Surgery* 1971;70(5):703-6.
71. Jacobson JH, Haimov M. Venous revascularization of the arm: report of three cases. *Surgery* 1977;81(5):599-604.
72. Hansen B, Feins RS, Detmer DE. Simple extra-anatomic jugular vein bypass for subclavian vein thrombosis. *J Vasc Surg* 1985;2(6):921-3.
73. Sanders RJ, Cooper MA. Surgical management of subclavian vein obstruction, including six cases of subclavian vein bypass. *Surgery* 1995; 118:856-63.
74. Koot HWJ, Veen HF. Local thrombolytic therapy for axillary subclavian vein thrombosis *Neth J Surg* 1991; 43(3):71-4.
75. Duckert F, Müller G, Nyman D, Benz A, Prisender S, Madar G, et al. Treatment of deep vein thrombosis with streptokinase. *BMJ* 1975;1 (5956):479-81.
76. Elliot MS, Immelman EJ, Jeffery P, Benatar SR, Funston MR, Smith JA, et al. A comparative randomized trial of heparin versus streptokinase in the treatment of acute proximal venous thrombosis: an interim report of a prospective trial. *Br J Surg* 1979;66: 838-43.
77. Hill SL, Martin D, Evans P. Massive venous thrombosis of the extremities. *Am J Surg* 1989;158:131-5.
78. Sasahara AA, Sharma GVRK, Tow DE, McIntyre KM, Parisi AF, Cella G. Clinical use of thrombolytic agents in venous thromboembolism. *Arch Intern Med* 1982;142(4):684-8.
79. Comerota AJ, Aldridge SC. Thrombolytic therapy for deep venous thrombosis: a clinical review. *Can J Surg* 1993;36(4):359-64.
80. Kunkel JM, Machleder HI. Treatment of Paget–Schroetter syndrome: a staged, multidisciplinary approach. *Arch Surg* 1989;124(10):1153-8.
81. Malcynski J, O'Donnell TF Jr, Mackey WC, Millan VA. Long-term results of treatment for axillary subclavian vein thrombosis. *Can J Surg* 1993;36(4):365-71.
82. Ruckley CV, Boulton FE, Redhead D. The treatment of venous thrombosis of the upper and lower limbs with "APSAC" (*p*-anisoylated streptokinase-plasminogen complex). *Eur J Vasc Surg* 1987;1(2):107-12.
83. Smith-Behn J, Althar R, Katz W. Primary thrombosis of the axillary/subclavian vein. *South Med J* 1986;79(9): 1176-8.
84. van Leeuwen PJCM, Huisman AB, Hohmann FR. Selective low-dose thrombolysis in patients with an axillary-subclavian vein thrombosis. *Eur J Vasc Surg* 1990;4(5):503-6.
85. Richard HM 3d, Selby JB, Gay SB, Tegtmeyer CJ. Normal venous anatomy and collateral pathways in upper extremity venous thrombosis. *Radiographics* 1992;12:527-34.

86. Albrechtsson U, Anderson J, Einarsson E, Eklöf B, Norgren L. Streptokinase treatment of deep venous thrombosis and the postthrombotic syndrome. Follow-up evaluation of venous function. *Arch Surg* 1981; 116:33-7.
87. Druy EM, Trout HH 3d, Giordano JM, Hix WR. Lytic therapy in the treatment of axillary and subclavian vein thrombosis. *J Vasc Surg* 1985; 2(6):821-7.
88. Smith BM, Shield GW, Riddell DH, Snell JD. Venous gangrene of the upper extremity. *Ann Surg* 1985;201 (4):511-9.
89. Harley DP, White RA, Nelson RJ, Mehringer CM. Pulmonary embolism secondary to venous thrombosis of the arm. *Am J Surg* 1984; 147:221-4.
90. Monreal M, Lafoz E, Ruiz J, Valls R, Alastrue A. Upper-extremity deep venous thrombosis and pulmonary embolism. A prospective study. *Chest* 1991;99(2):280-3.
91. Black MD, French GJ, Rasuli P, Bouchard AC. Upper extremity deep venous thrombosis. Underdiagnosed and potentially lethal. *Chest* 1993; 103(6):1887-90.
92. Persson AV, Robichaux WT, Jaxheimer EC, DiPronio EM. Burst therapy. A method of administering fibrinolytic agents. *Am J Surg* 1984; 147:531-6.
93. Bookstein JJ, Valji K. Pulse-spray pharmacomechanical thrombolysis. *Cardiovasc Intervent Radiol* 1992; 15:228-33.
94. Roberts AC, Valji K, Bookstein JJ, Hye RJ. Pulse-spray pharmacomechanical thrombolysis for treatment of thrombosed dialysis access grafts. *Am J Surg* 1993;166(2):221-6.
95. Yusuf SW, Whitaker SC, Gregson RHS, Wenham PW, Hopkinson BR, Makin GS. Experience with pulse-spray technique in peripheral thrombolysis. *Eur J Vasc Surg* 1994;8(3): 270-5.
96. Bell WR, Meek AG. Guidelines for the use of thrombolytic agents. *N Engl J Med* 1979;301(23):1266-70.
97. Pires LA, Jay G. Upper-extremity deep-vein thrombosis: thrombolytic therapy with antistrepalase. *Ann Emerg Med* 1993;22(4):748-50.
98. Kwaan HC. Thrombolytic therapy for deep vein thrombosis. *J Lab Clin Med* 1992;119(5):450-1.
99. Francis CW, Marder VJ. Fibrinolytic therapy for venous thrombosis. *Prog Cardiovasc Dis* 1991;34(3):193-204.
100. Rogers LQ, Lutcher CL. Streptokinase therapy for deep vein thrombosis: a comprehensive review of the English literature. *Am J Med* 1990; 88:389-95.
101. Glass BA. The relationship of axillary venous thrombosis to the thoracic outlet compression syndrome. *Ann Thorac Surg* 1975;19(6):613-21.
102. Etheredge S, Wilbur B, Stoney RJ. Thoracic outlet syndrome. *Am J Surg* 1979;138:175-82.
103. Thompson RW, Schneider PA, Nelken NA, Skioldebrand CG, Stoney RJ. Circumferential venolysis and paraclavicular thoracic outlet decompression for "effort thrombosis" of the subclavian vein. *J Vasc Surg* 1992; 16(5):723-32.
104. Perler BA, Mitchell SE. Percutaneous transluminal angioplasty and transaxillary first rib resection. A multidisciplinary approach to the thoracic outlet syndrome. *Am Surg* 1986;52 (9):485-8.
105. Criado E, Marston WA, Jaques PF, Mauro MA, Keagy BA. Proximal venous outflow obstruction in patients with upper extremity arteriovenous dialysis access. *Ann Vasc Surg* 1994; 8:530-5.
106. Irving JD, Dondelinger RF, Reidy JF, Schild H, Dick R, Adam A, et al. Gianturco self-expanding stents: clinical experience in the vena cava and large veins. *Cardiovasc Intervent Radiol* 1992;15:328-33.
107. Arrieta J, DeBlas M, Merino S, Olivar E. Central-vein stenosis affecting AV fistula function. Correction with a self-expanding intravascular stent. *Nephrol Dial Transplant* 1994;9:192-5.
108. Kovalik EC, Newman GE, Suhocki P, Knelson M, Schwab SJ. Correction of central venous stenoses: use of angioplasty and vascular Wallstents. *Kidney Int* 1994;45:1177-81.
109. Shoenfeld R, Hermans H, Novick A, Brener B, Cordero P, Eisenbud D, et al. Stenting of proximal venous obstructions to maintain hemodialysis access. *J Vasc Surg* 1994;19(3):532-9.
110. Stevenson IM, Parry EW. Radiological study of the aetiological factors in venous obstruction of the upper limb. *J Cardiovasc Surg (Torino)* 1975;16:580-5.
111. Rauwerda JA, Bakker FC, van den Broek TAA, Dwars BJ. Spontaneous subclavian vein thrombosis: a successful combined approach of local thrombolytic therapy followed by first-rib resection. *Surgery* 1988;103 (4):477-80.
112. Pittam MR, Darke SG. The place of first rib resection in the management of axillary-subclavian vein thrombosis. *Eur J Vasc Surg* 1987;1(1):5-10.
113. Hill SL, Berry RE. Subclavian vein thrombosis: a continuing challenge. *Surgery* 1990;108:1-9.
114. Elliot J. Greater use of fibrinolytic agents urged. *JAMA* 1980;243(22): 2275-6.
115. Haire WD. Arm vein thrombosis. *Clin Chest Med* 1995;16(2):341-51.