

Long-Term Sequelae of Spontaneous Axillary–Subclavian Venous Thrombosis

Emmanuel Héron, MD; Olivier Lozinguez, MD; Joseph Emmerich, MD, PhD; Claude Laurian, MD; and Jean-Noël Fiessinger, MD

Background: The frequency and severity of post-thrombotic sequelae after spontaneous axillary–subclavian venous thrombosis remain poorly known.

Objective: To determine the late sequelae of conventionally treated spontaneous axillary–subclavian venous thrombosis.

Design: Cross-sectional study.

Setting: University department of vascular medicine.

Patients: 54 patients seen during an 18-year period (mean follow-up, 5 years).

Measurements: Scores for the severity of post-thrombotic symptoms were graded on a numerical rating scale ranging from 0 to 10 and on a 6-point verbal rating scale. Ultrasonographic sequelae were classified as grade 0, normal flow; grade 1, moderate obstruction; or grade 2, severe obstruction or occlusion.

Results: Verbal scores were “nil/negligible” in 47% of patients and “severe/intolerable” in 13%; numerical scores were 0 to 3 in 78% of patients and 7 to 10 in 9%. Grade 2 ultrasonographic sequelae were found in 22% of cases. No relation was seen between ultrasonographic sequelae and symptom severity scores.

Conclusion: The overall clinical outcome of spontaneous axillary–subclavian venous thrombosis is good, and there is no relation between the severity of late symptoms and ultrasonographic sequelae.

Spontaneous axillary–subclavian venous thrombosis is a rare, nonfatal disease that mainly affects young, active, and otherwise healthy patients. The main complication is the possibility of long-term sequelae causing residual disability (1–8). However, the exact rate, severity, and consequences of these sequelae are unknown (6). Many authors (7–10) recommend thrombolytic therapy for this condition under the assumption that restoring venous patency is essential for reducing late sequelae. However, because this recommendation is not evidence based (owing to a lack of properly randomized trials), the use of thrombolysis remains controversial. We conducted a study to determine 1) the precise long-term clinical sequelae of spontaneous axillary–subclavian venous thrombosis treated with anticoagulants alone and 2) the relation between the severity of residual symptoms and ultrasonographic sequelae.

Methods

Study Sample

Between April 1980 and November 1998, 56 consecutive patients were referred to the thrombosis unit of Broussais Hospital in Paris, France, for treatment or investigation of spontaneous axillary–subclavian venous thrombosis. The thromboses occurred in ambulatory patients with no history of venous injection, catheterization, major trauma, cancer, or overt organ deficiency. Two patients were lost to follow-up; thus, the study sample consisted of the remaining 54 patients. Four patients had bilateral thromboses, but only the arm with the more severe symptoms was considered in the final analysis. The diagnosis was confirmed by phlebography in 34 cases and by duplex ultrasonography in 20 cases. Most patients were treated with anticoagulants; none received thrombolytic therapy. Six patients underwent first-rib resection 3 months to 2 years after the thrombosis.

Evaluation of Clinical Sequelae

All 54 patients responded to a standardized written questionnaire administered between February 1996 and November 1998; 49 patients (91%) completed the questionnaire at a follow-up visit in our department, and 5 completed it by mail after a telephone interview. The following information was obtained: 1) presence or absence of residual symptoms; 2) main symptom; 3) symptom severity scores, obtained by using two simple, reliable verbal and numerical rating scales (11); 4) presence or absence of cutaneous collateral venous circulation; and 5) significant and durable modifications in occupational or recreational activities (at least 1 year of

Ann Intern Med. 1999;131:510-513.

For author affiliations and current addresses, see end of text.

follow-up was required). The two scales were used to measure chronic pain secondary to the thrombosis. The 11-point (0 to 10) numerical scale provided an optimal level of discrimination for grading pain intensity (11, 12), and the 6-point verbal scale (which consisted of the following categories: nil, negligible, mild, moderate, severe, and intolerable) provided a better idea of functional status. These two pain scales have been validated in cases of chronic rheumatic diseases (11) with symptoms (pain, swelling, and paresthesia) similar to those in our patients.

Evaluation of Ultrasonographic Sequelae

The 49 patients who attended a follow-up visit underwent ultrasonography that was done by a single experienced operator using a high-resolution real-time scanner (HDI 3000, ATL Ultrasound, Inc., Bothell, Washington) and a 7-4 MHz linear probe. After echographic analysis of morphologic sequelae (venous retraction, wall thickening or calcification, and endoluminal echoes), venous hemodynamics were compared on the two sides by means of duplex ultrasonography. The permeability of the vein was verified by color Doppler ultrasonography (13) before duplex ultrasonography was done to analyze venous flow at the axillary-subclavian junction during respiratory movements of increasing amplitude. Ultrasonographic sequelae were divided into three grades: grade 0, normal flow; grade 1, moderate obstruction (reduction in normal respiratory flow modulation); and grade 2, venous occlusion or severe obstruction (reduced basal flow and absence or near-absence of respiratory modulation). Phlebography was performed in 10 patients.

Results

The **Table** shows the main characteristics of the patients, the type and duration of treatment, the length of follow-up, and post-thrombotic sequelae. The thrombi involved the axillary or subclavian veins, or both, in all 54 patients; the brachial vein in 12; the brachiocephalic trunk in 13; and the internal jugular vein in 4. Twenty-six percent of the patients had documented pulmonary embolism, which was asymptomatic in 36% of cases; other investigators have prospectively observed similar findings (14). No patients died.

The patients' rating of symptom severity with the verbal and numerical scales is shown in the left panel of the **Figure**. Nearly half the patients rated their symptoms as nil or negligible, and 78% gave numerical symptom scores of 0 to 3. Symptoms were severe or intolerable in 13% of patients (scores of 7 through 10 in 9% of patients). One

Table. Main Characteristics of 54 Patients with Spontaneous Axillary-Subclavian Venous Thrombosis and Long-Term Sequelae

Variable	Data*
Patients (men/women), <i>n</i> (<i>n/n</i>)	54 (25/29)
Median age at time of thrombosis (range), <i>y</i>	32 (15-86)
Strenuous muscular activity of involved arm, <i>n</i> (%)	23 (43 [30-57])
Thrombosis involving the dominant arm, <i>n</i> (%)	33 (61 [47-74])
Hypercoagulable states, <i>n</i> (%)	
Pregnancy or oral contraceptive use (women only)	18 (62 [42-79])
Genetic clotting defect†	8 (15 [7-28])
Antiphospholipid antibody†	10 (19 [10-32])
Patients with thoracic symptoms, <i>n</i> (%)‡	11 (20 [11-34])
Documented pulmonary embolism, <i>n</i> (%)‡	14 (26 [15-40])
Initial heparin therapy, <i>n</i> (%)§	51 (94 [84-99])
Median duration of heparin therapy (range), <i>d</i> §	7.6 (4-30)
Total duration of anticoagulant therapy, <i>n</i> (%)	
No anticoagulation	3 (6 [2-16])
<3 months	4 (7 [2-19])
3-11 months	44 (81 [68-90])
≥12 months	3 (6 [2-16])
Mean follow-up (range), <i>mo</i>	60 (3-324)
Presence of collateral venous circulation, <i>n</i> (%)	35 (65 [51-77])
Ultrasonographic sequelae (49 patients), <i>n</i> (%)	
Echographic (morphologic) sequelae	35 (71 [57-83])
Axillary-subclavian venous hemodynamics	
Grade 0 (normal flow)	20 (41 [27-56])
Grade 1 (moderate obstruction)	18 (37 [24-52])
Grade 2 (severe obstruction or occlusion)	11 (22 [12-37])
Verbal symptom scores, <i>n</i> (%)	
Nil or negligible	25 (46 [33-60])
Mild or moderate	22 (41 [28-55])
Severe or intolerable	7 (13 [6-25])
Durable (≥1 <i>y</i>) lifestyle changes (43 patients), <i>n</i> (%)	7 (16 [7-31])

* Values in square brackets are 95% CIs.

† Six patients had the factor V Leiden mutation, and two others had protein S deficiency. One patient had lupus anticoagulant, high titers of anticardiolipin antibodies, and recurrent thromboembolism. Nine patients had borderline-elevated anticardiolipin antibody titers (up to 3.5 times the upper limit of normal in our laboratory) of unknown clinical significance.

‡ Two patients with thoracic symptoms had no documented pulmonary embolism on the basis of findings on lung scanning, helicoidal computed tomography, or pulmonary angiography.

§ Twenty-five patients received intravenous unfractionated heparin, and 26 received subcutaneous low-molecular-weight heparin. Two women (excluded from the calculation of the median duration of heparin therapy) received subcutaneous fractionated heparin during 6 months of pregnancy.

patient had to change his occupation, and 6 others changed a sport activity. Among the 6 patients who underwent first-rib resection, 3 had severe clinical sequelae, 1 had mild sequelae, and 2 had no sequelae. A case of severe lymphedema with normal findings on ultrasonography was a postoperative complication.

The right panel of the **Figure** shows the lack of a relation between ultrasonographic sequelae and symptom severity. The hemodynamic sequelae, assessed blindly by two experienced operators in 7 cases, were identically classified by the two operators as grade 0 (*n* = 2), grade 1 (*n* = 2), or grade 2 (*n* = 3). The 10 phlebographies showed residual subclavian occlusion in 4 cases, marked endoluminal sequelae in 2 cases, and short narrowed fibromatous subclavian stenosis in 4 cases. The correlative ultrasonographic studies showed grade 1 (*n* = 4) or grade 2 (*n* = 6) hemodynamic sequelae. In these 10 arms, verbal symptom scores ranged from nil to intolerable despite similar degrees of phlebographic venous obstruction.

Discussion

An important component of any comprehensive evaluation of pain is self-measurement of its intensity (15, 16). This was the main strength of our study. Patient ratings of symptom intensity a mean of 5 years after spontaneous axillary-subclavian venous thrombosis showed that nearly 50% were almost asymptomatic and that 13% had severe symptoms. Durable lifestyle modifications (16% of patients) did not seem to be a good marker of altered well-being: Only one young tennis player found this change bothersome. Symptom scores did not correlate with ultrasonographic sequelae, an observation explained by the abundant collateral pathways in the upper extremities (17). These findings agree with previous phlebographic observations, notably in the study by Machleder (7). In that study, 50 consecutive patients with spontaneous axillary-subclavian venous thrombosis were treated by a combination of thrombolysis, 3 months of anticoagulation, and first-rib resection. Sixty-four percent of the 22 patients whose veins remained phlebographically suboccluded at the final evaluation at 2 years were essentially free of symptoms.

The literature on axillary-subclavian venous thrombosis mainly consists of case reports and small retrospective series (6, 18). We reviewed the main series published since 1950 (1-5, 14)—that is, those with at least 10 conservatively treated patients. Linblad and colleagues' series (1) is particularly interesting because it concerns the entire unselected

population of Malmö, Sweden, a town served by a single hospital. A low rate (25%) of mild to moderate sequelae was found among 73 patients with spontaneous thromboses. A similar low rate of sequelae (21% of patients; in 1 of 4 of these patients, sequelae were severe) occurred in 27 patients prospectively studied by Prandoni and colleagues (14). Only 14 patients had spontaneous thromboses, however, and the sequelae were not separated into etiologic categories. By contrast, Adams (2) and Tilney (3) and their colleagues reported high rates (73%) of sequelae. Likewise, the rate of severe sequelae varied among these studies, ranging from 0% (1) to 55% (3). In addition to particular deficiencies (for example, 35% of patients in Tilney and coworkers' study were lost to follow-up), the major limitation of these studies was the form of outcome assessment, which was mainly based on retrospective chart review.

One limitation of our study is that the patients were evaluated at various times after the event (that is, cross-sectionally). Of interest, however, the relative proportions of patients subdivided according to the severity of residual symptoms did not vary by the length of follow-up 6 months after the event or longer (for example, the rates of severe symptoms between 6 and 11, 12 and 59, and 60 months or longer were 10%, 16%, and 11%, respectively). Another potential limitation is the nonuniformity of treatment, but we observed no difference in clinical outcomes according to the type of initial (fractionated or unfractionated) heparin therapy. One of the three untreated patients had severe sequelae, which

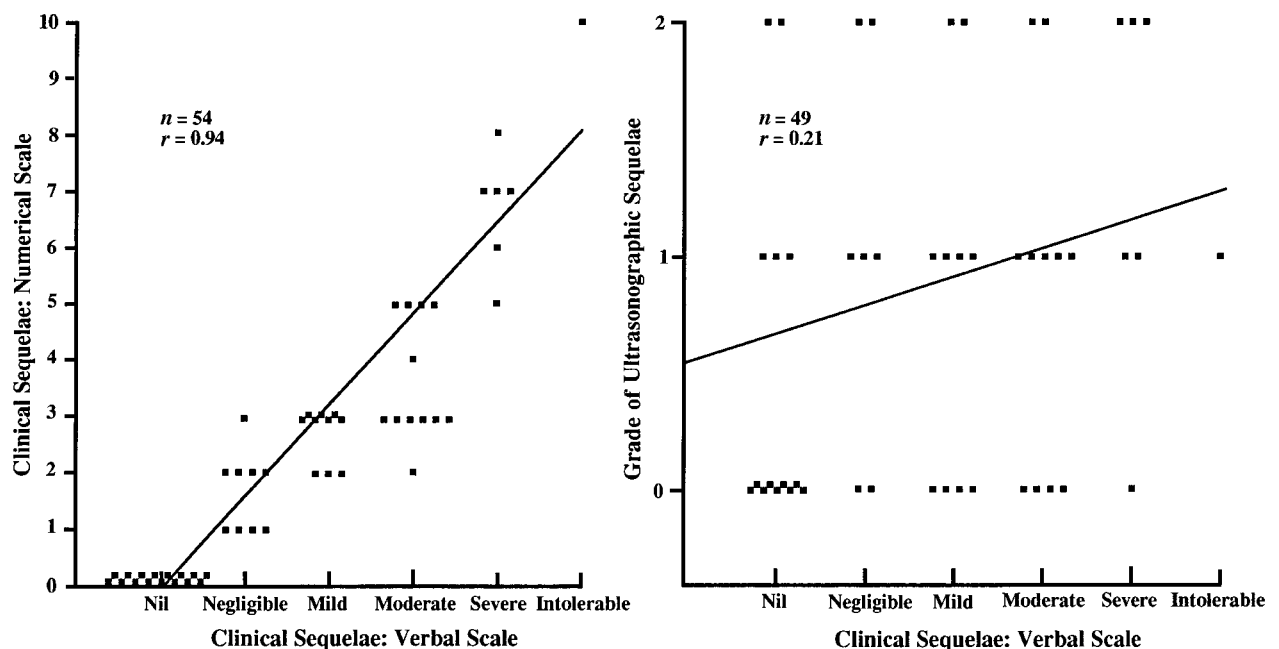


Figure. Left. Patients' ratings of long-term symptom severity in 54 arms with spontaneous axillary-subclavian venous thrombosis. Scores from an 11-point numerical rating scale are plotted against ratings on a 6-point descriptive scale. Right. Relation between clinical and ultrasonographic sequelae in 49 arms. Grade 0, normal flow; grade 1, moderate obstruction; grade 2, severe obstruction or occlusion of the axillary-subclavian vein.

could have worsened our results but did not affect the final conclusion.

A challenging issue is the treatment of spontaneous axillary–subclavian venous thrombosis, particularly the use of thrombolysis in the acute phase. The best series (8) of “aggressively” treated patients published so far is that by Machleder (7). In this study, 6 patients (12%) remained disabled because of severe symptoms after a mean follow-up of 3 years. Thus, patient outcomes in Machleder’s study, which were similar to those in our study, and the lack of any relation between residual symptoms and vein patency both suggest that the potential clinical value of thrombolysis for this indication would be small at best. Until the benefit of thrombolysis is demonstrated in a well-designed randomized trial, we believe that anticoagulation alone remains the first-line treatment of choice for spontaneous axillary–subclavian venous thrombosis; severe residual symptoms seem to occur only in about 1 in 10 patients.

From Hôpital Broussais and Hôpital Saint-Joseph, Paris, France.

Acknowledgment: The authors thank Professor Gilles Chatellier (Service d’Informatique Médicale, Hôpital Broussais) for help with the statistical analyses.

Requests for Reprints: Jean-Noël Fiessinger, MD, Service de Médecine Vasculaire, Hôpital Broussais, 96 rue Didot, 75674 Paris Cedex 14, France.

Current Author Addresses: Drs. Héron, Lozinguez, Emmerich, and Fiessinger: Service de Médecine Vasculaire and Centre Claude Bernard de Recherche sur les Maladies Vasculaires Périphériques, Hôpital Broussais, 96 rue Didot, 75674 Paris Cedex 14, France.

Dr. Laurian: Service de Chirurgie Vasculaire, Hôpital Saint-Joseph, 185 rue Raymond Losserand, 75674 Paris Cedex 14, France.

References

1. 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;2:161-5.
 2. Adams JT, McEvoy RK, DeWeese JA. Primary deep venous thrombosis of upper extremities. *Arch Surg.* 1965;91:29-42.
 3. Tilney NL, Griffiths HJ, Edwards EA. Natural history of major venous thrombosis of the upper extremity. *Arch Surg.* 1970;101:792-6.
 4. Gloviczki P, Kazmier FJ, Hollier LH. Axillary-subclavian venous occlusion: the morbidity of a nonlethal disease. *J Vasc Surg.* 1986;4:333-7.
 5. Ameli FM, Minas T, Weiss M, Provan JL. Consequences of “conservative” conventional management of axillary vein thrombosis. *Can J Surg.* 1987;30:167-9.
 6. Becker DM, Philbrick JT, Walker FB 4th. Axillary and subclavian venous thrombosis. Prognosis and treatment. *Arch Intern Med.* 1991;151:1934-43.
 7. Machleder HI. Evaluation of a new treatment strategy for Paget-Schroetter syndrome: spontaneous thrombosis of the axillary-subclavian vein. *J Vasc Surg.* 1993;17:305-17.
 8. Haire WD. Arm vein thrombosis. *Clin Chest Med.* 1995;16:341-51.
 9. Molina JE. Need for emergency treatment in subclavian vein effort thrombosis. *J Am Coll Surg.* 1995;181:414-20.
 10. Meier GH, Pollack JS, Rosenblatt M, Dickey KW, Gusberg RJ. Initial experience with venous stents in exertional axillary-subclavian vein thrombosis. *J Vasc Surg.* 1996;24:974-83.
 11. Downie WW, Leatham PA, Rhind VM, Wright V, Branco JA, Anderson JA. Studies with pain rating scales. *Ann Rheum Dis.* 1978;37:378-81.
 12. Jensen MP, Turner JA, Romano JM. What is the maximum number of levels needed in pain intensity measurement? *Pain.* 1994;58:387-92.
 13. Grassi CJ, Polak JF. Axillary and subclavian venous thrombosis: follow-up evaluation with color Doppler flow US and venography. *Radiology.* 1990;175:651-4.
 14. Prandoni P, Polistena P, Bernardi E, Cogo A, Casara D, Verlato F, et al. Upper-extremity deep vein thrombosis. Risk factors, diagnosis, and complications. *Arch Intern Med.* 1997;157:57-62.
 15. Huskisson EC. Measurement of pain. *Lancet.* 1974;2:1127-31.
 16. Houde RW. Methods for measuring clinical pain in humans. *Acta Anaesthesiol Scand.* 1982;74(Suppl):25-9.
 17. Richard HM 3d, Selby JB, Gay SB, Tegtmeier CJ. Normal venous anatomy and collateral pathways in upper extremity venous thrombosis. *Radiographics.* 1992;12:527-34.
 18. Elliott G. Upper-extremity deep vein thrombosis. *Lancet.* 1997;349:1188-9.
- © 1999 American College of Physicians–American Society of Internal Medicine