

Paget-Schroetter syndrome: treatment of venous thrombosis and outcomes

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Abstract: Thoracic outlet syndrome (TOS) is a rare clinical entity with many etiologies. Venous thoracic outlet syndrome (VTOS), also called Paget-Schroetter syndrome (PSS), is a primary “effort” thrombosis. Here we will focus on the pathophysiology, anatomy, clinical presentation, treatments, and outcomes of VTOS. Treatment involves anticoagulation, catheter-directed thrombolysis, and surgical decompression. Early diagnosis and treatment can improve symptoms and quality of life.

Keywords: Venous thoracic outlet syndrome (VTOS); Paget-Schroetter syndrome (PSS); deep vein thromboses (DVT)

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Introduction

Thoracic outlet syndrome (TOS) describes compression of the structures of the thoracic outlet as they exit the thoracic cavity. Any of the neurovascular structures in this area can be affected, accounting for variations in its presentations: neurogenic (95%), venous (4%), and arterial (1%) (1-3). This review will focus on venous thoracic outlet syndrome (VTOS).

Epidemiology, pathophysiology, anatomy

There are three types of VTOS: intermittent/positional obstruction, secondary subclavian vein thrombosis, and primary “effort thrombosis”. Secondary thrombosis most commonly results from iatrogenic causes such as catheter or pacemaker insertion and is not due to compression (2). Paget-Schroetter syndrome (PSS), also called primary “effort thrombosis”, is associated with both compression and thrombosis of the subclavian vein.

PSS is a rare condition with a yearly incidence of 1–2 per 100,000 people and accounts for 1–4% of all venous thrombosis episodes (2). Young, otherwise healthy, males in the early 30s is the most commonly affected group. At particular risk are athletes, such as baseball players, swimmers, and weight lifters, or workers with repetitive overhead arm motion, such as mechanics or electricians (3-5). It is controversial whether coagulopathy increases the risk of VTOS, but likely thrombotic disorders play a role in idiopathic, unprovoked VTOS (6-9).

PSS is believed to be incited by repeated abnormal and strenuous interaction between the venous system and the structures within the thoracic outlet. The thoracic outlet is bordered by the clavicle superiorly, the first rib inferiorly, the costoclavicular ligament medially, and the anterior scalene muscle laterally. As the axillary vein passes over the first rib and under the clavicle, it becomes the subclavian vein. To reach the internal jugular vein, the subclavian vein passes through the thoracic outlet (10). Chronic compression of the vein between the angle of

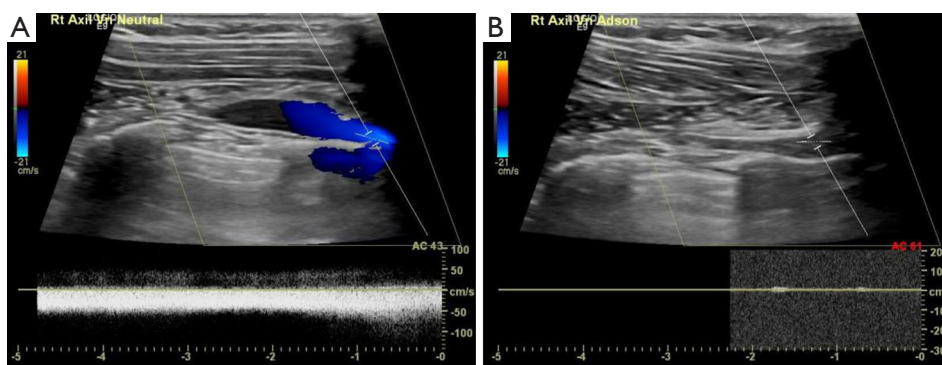


Figure 1 Positive confirmatory ultrasound with provocative occlusion of the axillosubclavian vein. (A) Ultrasound demonstrating flow within the right axillosubclavian vein with arm in neutral position; (B) occlusion of right axillosubclavian flow after provocative Adson maneuver.

the clavicle and first rib with arm abduction leads to venous endothelial cell damage, inflammation, scarring, and potential thrombosis (11). Most patients with VTOS have a costoclavicular ligament which inserts more laterally, contributing to subclavian vein compression (12). Additionally, hypertrophy of muscles in the area, including the subclavius and anterior scalene muscles can also contribute to venous compression and injury (2,3).

Clinical presentation and diagnosis

Patients commonly present within 24 h of an inciting event, with history of excessive activity of the upper extremity and/or dehydration (4,13,14). The upper extremity and chest is painful, congested, and cyanotic appearing. Superficial veins can appear engorged and occasionally thrombosed veins can be palpated in the axilla (15). Pain involving the affected arm is characteristically sudden, involving the dominant extremity. Physical exam provocative tests have a high false positive rate and are more likely to detect neurogenic TOS rather than VTOS (16). PSS can also present with or be complicated by pulmonary embolism (PE). Studies report rates of PE and PSS ranging from 20–30% (17–19). Among upper extremity deep vein thromboses (DVT), PE occurs more often with secondary upper extremity DVT. When considering all DVT, PE is more associated with lower extremity DVT than upper extremity DVT (20,21). Although the risk of PE is smaller in PSS than other DVT states, it is important to be aware of the phenomenon.

Diagnosis is usually achieved with history and physical examination, and can be confirmed with imaging. Initial evaluation includes duplex ultrasonography revealing

partial or complete thrombosis of the axillary and/or subclavian veins (*Figure 1*). Duplex imaging is the gold standard in diagnosis with reports of 80–100% sensitivity and specificity (22).

If duplex ultrasound is inconclusive, other imaging techniques may be used to confirm the diagnosis. Catheter-directed venography was historically the gold-standard for diagnostic imaging, but due to its invasive nature, higher costs, and accuracy of non-invasive ultrasound, it is now reserved for cases with high clinical suspicion and equivocal non-invasive images (2). Venography via computed tomographic (CT) or magnetic resonance (MR) can also be performed in the setting of atypical symptoms or equivocal ultrasound to interrogate the surrounding anatomy. However, both have their drawbacks. CT venography is complicated by risk of contrast and radiation exposure, while MR carries high costs and limited availability. When faced with an inconclusive non-invasive ultrasound and high clinical suspicion for upper extremity DVT, providers have the option of choosing among the above venography techniques. Alla *et al.* propose an algorithm to follow equivocal Doppler ultrasound with MR venogram if a high index of suspicion and no alternative explanation exists. A positive MR venogram is then followed by catheter-directed thrombolysis and early thoracic outlet decompression in patients with symptoms present for less than 2–6 weeks (8).

Plasma D-dimer levels may be elevated with upper extremity DVT, however specificity ranges from 14–60%. As PSS is a rare disorder, no guidelines exist on routine D-dimer testing. It may be useful as an adjunct, but is not recommended as a confirmatory test (23).

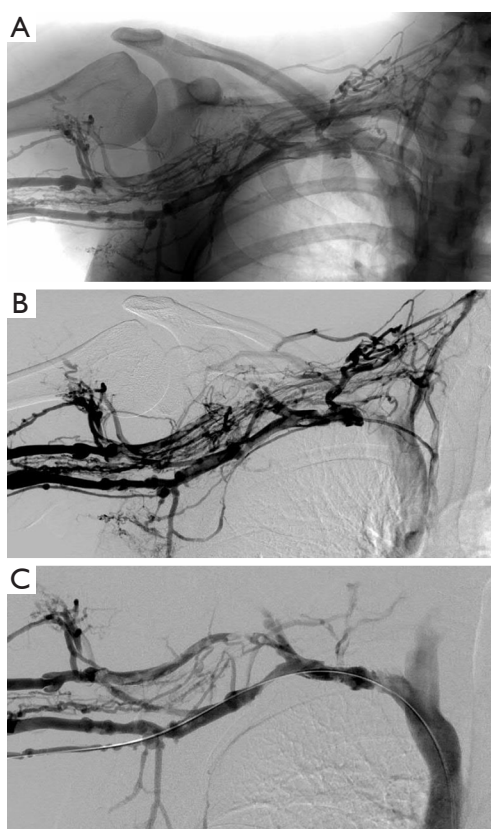


Figure 2 Diagnostic and therapeutic venogram of a patient with Paget-Schroetter syndrome (PSS). (A) Venogram showing occlusion of axillosubclavian vein at the thoracic outlet; (B) catheter-directed thrombolysis of axillosubclavian clot; (C) post-thrombolysis venogram demonstrating patency of subclavian vein.

Patients complaining of neuropathic symptoms warrant nerve conduction studies, although the venous swelling can sometimes produce paresthesias unrelated to neurogenic TOS (16,24). Routine hypercoagulable workup for upper extremity thrombosis is not recommended. However, if a patient presents with an unexplained thrombosis and/or family history, hypercoagulable work-up should be performed (25,26). Hypercoagulable investigations include mutations in factor V Leiden and prothrombin G20210A, and deficiencies in antithrombin, protein C, and protein S. Lupus anticoagulant screening and anticardiolipin/anti- β 2-glycoprotein antibodies may also help direct clinical management (25,27,28).

Cancer screening following unexplained upper extremity thromboses follows similar recommendations for those in the lower extremities. Routine screening is not

recommended, however may be considered in unexplained thromboses (29). In these cases, a thorough history and physical examination, routine laboratory studies, abdominal ultrasound, chest X-ray as well as any other age or gender specific screenings should be performed (25).

Treatment

Treatment of PSS consists of relieving symptoms due to obstruction, preventing complications from DVT, and preventing recurrence. This can be achieved through anticoagulation, thrombolysis, and/or surgical decompression. Initiation of systemic anticoagulation immediately after diagnosis is the first step in treatment. Although not specific for PSS, the 2016 CHEST Guideline and Expert Panel Report on antithrombotic therapy for VTE disease recommends dabigatran, rivaroxaban, apixaban or edoxaban for patients with VTE and no cancer over vitamin K antagonists. Vitamin K antagonists are recommended over low-molecular-weight-heparin (30).

Anticoagulation alone for treatment of PSS is generally not recommended. A more aggressive approach involving thrombolysis and surgery is superior to anticoagulation alone in patient-reported outcomes, such as resolution of symptoms and return to work (31,32). If there are no contraindications, therapeutic anticoagulation for at least 5 days, followed by venography and catheter-directed thrombolysis is optimal if performed within 2 weeks after the onset of symptoms (*Figure 2*) (3,33). Early catheter-directed thrombolysis success rates are reported between 75–84% (34,35). Treatment of a clot older than 2 weeks is less successful as the thrombus is considered chronic and less susceptible to thrombolytic therapy (36,37). One study reported a 29% success rate of thrombolysis 2–12 weeks following onset of symptoms (33).

Despite initial relief of symptoms following anticoagulation and thrombolysis, re-thrombosis can occur in up to one-third of patients (38). Therefore, more definitive treatment with thoracic outlet decompression is recommended for patients who are good surgical candidates (39,40). In the absence of specific anatomic abnormalities, decompression with first rib resection is performed via a transaxillary, supraclavicular or infraclavicular approach. No clinical trials exist to support the superiority of one particular approach. If a cervical rib is present, it should also be removed. If indicated, partial resection of the subclavius and anterior scalene muscle helps to de-bulk the thoracic outlet and prevent recurrence of symptoms (39).

There is no consensus on duration of anticoagulation for PSS. The 2016 CHEST Guideline and Expert Panel Report on antithrombotic therapy for VTE disease recommends a 3-month course of therapy following any upper extremity DVT, regardless of thrombolytic interventions (30). Others suggest a more tailored approach using post-operative venography. If vein patency is demonstrated, no further intervention is required and anticoagulation can be stopped. However, if persistent stenosis or re-thrombosis is identified, anticoagulation is continued and repeat provocative duplex ultrasound examination is performed monthly for 6 months (3,41,42). Additional measures such as surgical thrombectomy, balloon venoplasty, and stenting have been used in the past for persistent stenosis or re-thrombosis, but have fallen out of favor secondary to poor success rates and high morbidity and are generally not recommended as initial treatment (12,43,44).

Outcomes

Following PSS treatment, significant morbidity can occur due to post-thrombotic syndrome (PTS). It is characterized by pain, heaviness and swelling of the affected extremity and can be a chronic, debilitating condition (21,45). PTS occurs in 7–46% of patients with upper extremity DVT and it is more common in primary rather than secondary upper extremity DVT (8,45). It is difficult to prevent all cases of PTS, but data has shown that early treatment correlates with improved patient-reported outcomes.

Success rates of 90–95% have been noted if PSS is diagnosed and intervened quickly with immediate decompression (2). Urschel *et al.* reported 95% of patients indicating “excellent/good” results with early thrombolysis and first rib resection, in regards to pain relief, employment and recreation (12). Other studies have reported similar findings, supporting the use of early surgical decompression (46,47). Patients with VTOS who undergo first rib resection and scalenectomy report improved quality of life, with near full recovery 1 year after surgery (39). Recurrence rates are low, with only 18% of VTOS postoperative patients requiring physical therapy to further reduce symptoms with no further operative interventions required (39). A recent meta-analysis on surgical outcomes of TOS demonstrated surgical intervention to be safe and beneficial with 90% of VTOS patients reporting “excellent/good” outcomes. However, heterogeneity among studies proved difficult to draw many further conclusions (48).

Conclusions

Rapid diagnosis and treatment for PSS is essential for good outcomes. Treatment involves immediate anticoagulation. Venography with catheter-directed thrombolysis can confirm the diagnosis and is potentially therapeutic. Surgical decompression should follow soon after, both for completion of treatment and prevention of recurrent thromboses. Managed in this fashion, the vast majority of patients with VTOS report beneficial outcomes with near full recovery at 1 year.

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Footnote

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