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'EVIDENCE DRIVEN' CLINICAL SCENARIO

# Preferred Management of Primary Deep Arm Vein Thrombosis

**F.J. Vazquez [a], P. Paulin [a], D. Poodts [a], E. Gándara [b,c,d,*]**

[a] Department of Internal Medicine, Hospital Italiano de Buenos Aires, Instituto Universitario del Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
[b] Department of Medicine, University of Ottawa-Ottawa Hospital, Ottawa, Canada
[c] Ottawa Hospital Research Institute, Ottawa, Canada
[d] Department of Internal Medicine, Hospital Privado de Comunidad, Mar del Plata, Argentina

**CLINICAL VIGNETTE**

In Case 1, a 49 year old male (right handed) presented with 2 days of swelling and pain in his left arm after starting weight lifting. On physical examination his left arm showed clear changes in colour compared with the right. He had pain on palpation of the deep veins, with good pulses and mild venous redistribution in his chest and some tortuous veins in the forearm. Pulses were present without any evidence of venous infarcts. An ultrasound of his right arm confirmed the diagnosis of an upper extremity deep vein thrombosis (DVT) affecting the subclavian and axillary veins. He was started on low molecular weight heparin with a mild symptomatic response after 4 days of treatment. In Case 2, a 23 year old female, who worked as a contemporary dancer, presented with 5 days of mild swelling of her right arm following a session of strenuous physical activity. She noticed that her symptoms had been slowly progressing for the last 3 days. On physical examination her right arm showed clear changes in colour compared with the left. She had pain on palpation of the deep veins, with good pulses and venous redistribution in her chest. Pulses were present without any evidence of venous infarcts. An ultrasound of her right arm confirmed the diagnosis of an upper extremity DVT affecting the subclavian and axillary veins. She was started on low molecular weight heparin with a very good symptomatic response after 4 days of treatment. Both patients wanted to know if a more aggressive approach such as surgery with or without thrombolysis would reduce their risk of developing post-thrombotic syndrome?

**Objective:** Given its rarity, the management of primary upper extremity deep vein thrombosis is controversial. Although anticoagulation alone is commonly advocated for its treatment, it is unclear if this will reduce the risk of developing post-thrombotic syndrome (PTS). The aim of this "Evidence Driven" Clinical Scenario is to evaluate whether more aggressive treatments (including catheter directed thrombolysis or surgery) might help reduce the risk of PTS or recurrent venous thromboembolism in patients with primary upper extremity deep vein thrombosis (DVT).
**Methods:** An electronic systematic review of Ovid MEDLINE and Embase was conducted. Randomised controlled trials and observational studies were eligible. The primary outcome was PTS.
**Results:** The initial search identified 146 articles, and 36 more were identified during a secondary search. In total, 25 studies, reporting the outcome of 1271 patients, were included. None of the studies included was a randomised controlled trial and the large majority of studies were retrospective cohorts. The use of anticoagulation alone was associated with a significant risk of PTS. In patients treated with surgery with or without thrombolysis the incidence of PTS was significantly reduced.
**Conclusion:** Current evidence, albeit with some methodological limitations, suggests that anticoagulation may not be sufficient to prevent PTS in patients with primary upper extremity DVT and that surgery with or without thrombolysis to repair the anatomical defects is needed.

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* Corresponding author. Thrombosis Program-Division of Hematology, University of Ottawa-OHRI, 501 Smyth Road, Box 201A, Rm L2269, Ottawa ONT K1H 8L6, Canada.
*E-mail addresses:* egandara@ohri.ca; gandara.esteban@gmail.com (E. Gándara).

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## INTRODUCTION

Primary upper extremity deep vein thrombosis (DVT) is an uncommon form of venous thromboembolism (VTE), affecting 2 per 100,000 persons.[1] Primary upper extremity DVT is commonly defined as a DVT occurring in patients

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with thoracic outlet syndrome (TOS) or secondary to chronic extrinsic mechanical compression (commonly known as effort thrombosis Paget—Schroetter syndrome).[2] Primary upper extremity DVT occurs secondary to intermittent extrinsic vein compression leading to repeated trauma to the vessel, which produces endothelial damage, stasis, and fibrous scar tissue formation that will compress the vein persistently.[3,4] Extrinsic vein compression is usually secondary to hypertrophied muscles (i.e., secondary to weight lifting), cervical ribs, musculofascial bands, and clavicular or first rib anomalies.[4] The presence of concomitant pulmonary embolism (PE) is less common than in patients with DVT of the legs and the prevalence of post-thrombotic syndrome ranges between 7% and 46%.[5,6] Patients with primary upper extremity DVT who develop post-thrombotic syndrome (especially of the dominant arm) have a significant reduction in quality of life.[7]

The management of primary upper extremity DVT is controversial. Although anticoagulation remains a highly advocated treatment, a lack of data has led to different opinions between experts and guidelines regarding the use surgery and thrombolysis to prevent long-term complications (as shown in Table 1).[4,6,8,9] The aim of this "Evidence Driven" Clinical Scenario is to describe the role of anticoagulation and more aggressive treatments (including catheter directed thrombolysis or surgery) to prevent post-thrombotic syndrome and recurrent venous thromboembolism in patients with primary upper extremity DVT.

## MATERIALS AND METHODS

### Search strategy

An electronic review was conducted of Ovid MEDLINE and Embase from 1946 to December 2014 and updated it to include the period between December 2014 and January 2016. The main key words for the search included "thoracic outlet syndrome and subclavian or axillary or brachiocephalic or innominate or thrombosis OR embolism" (The complete search strategies and PRISMA checklist are presented in the Supplementary material). Hand searches of relevant articles, abstract books from international meetings, and published reviews were also conducted. The language search was restricted to English.

### Study selection

Randomised controlled trials and observational studies were eligible as long as they reported the outcome of at least eight patients diagnosed with a primary upper extremity DVT. For the purpose of this study primary upper extremity DVT was defined as a DVT produced by repetitive effort or thoracic outlet syndrome. In studies reporting mixed populations, data on outcomes were only extracted for the patients with primary upper extremity DVT. If the data could not be extracted for patients with primary upper extremity DVT, the authors of the relevant studies were contacted via e-mail. All potentially relevant articles were reviewed in full text to ensure that they satisfied the inclusion criteria. Two reviewers independently assessed the eligibility of all articles identified in the initial search strategy. A third reviewer adjudicated discrepancies if needed. The primary outcome was post-thrombotic syndrome (PTS). Secondary outcomes were recurrent DVT, PE, death, bleeding, and the need for new or repeated surgical or endovascular intervention. The quality of the studies was assessed using the Newcastle—Ottawa score. Treatments strategies were classified as (1) no treatment (or less than a month of anticoagulation); (2) anticoagulation alone; (3) anticoagulation plus early surgery (less than 4 weeks); (4) anticoagulation plus late surgery (more than 4 weeks); (5) thrombolysis alone (with anticoagulation); (6) thrombolysis plus early surgery (with anticoagulation); and (7) thrombolysis plus late surgery (with anticoagulation). For the purpose of this review first rib resection was considered the standard surgical procedure for patients with primary upper extremity DVT.[9]

**Table 1.** Current treatment recommendations by clinical guidelines.

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| American College of Chest Physicians[9] | In patients with acute upper extremity DVT that involves the axillary or more proximal veins, we suggest anticoagulant therapy alone over thrombolysis (Grade 2C).<br>Remarks: patients who (i) are most likely to benefit t from thrombolysis; (ii) have access to CDT; (iii) attach a high value to prevention of PTS; and (iv) attach a lower value to the initial complexity, cost, and risk of bleeding with thrombolytic therapy are likely to choose thrombolytic therapy over anticoagulation alone.<br>Rib resection is not generally recommended. |
| British Committee for Standards in Haematology 2012[36] | Patients with TOS undergoing surgical decompression should not routinely receive thrombolytic therapy or venoplasty prior to the procedure (2B).<br>Patients with upper extremity DVT should receive anticoagulation with heparin for at least 5 d and warfarin. The optimal duration of warfarin therapy is unknown. Periods of 3—6 months are associated with low risk of recurrence and are likely to be satisfactory (2B). |
| International Society of Thrombosis and Haemostasis[35] | As thoracic outlet syndrome is a risk factor for an upper-limb DVT, imaging studies, such as CT or MR venography of the affected vasculature, can be useful to define the site of obstruction. Vascular surgical intervention can be undertaken for severe thoracic outlet syndrome to obviate consideration of continued anticoagulation. |

CT = computed tomography; DVT = deep vein thrombosis; MRI = magnetic resonance imaging; TOS = thoracic outlet syndrome.

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