Learning objectives

- Discuss the aetiology of upper limb swelling due to venous thrombosis, including thoracic outlet syndrome (Paget-Schrotter syndrome), iatrogenic causes and thrombosis secondary to thrombophilia.
- Review diagnostic imaging techniques, with examples from our institution.
- Consider treatment pathways for upper limb venous thrombosis.
Background

Upper limb deep vein thrombosis (DVT) is less recognised than its lower limb counterpart however accounts for approximately 10% of all DVTs, with an incidence of 2-3 per 100,000 (1,2). Its lower incidence can be attributed to multiple factors including fewer valves (3) and increased fibrinolytic activity in the endothelium of upper limb veins compared with lower limb (4,5).

It occurs more frequently in younger patients and in those with a lower BMI (6). The subclavian vein is most commonly affected, followed by the axillary vein and then brachial vein (7-9).

In this educational exhibit we will discuss the various causes for upper limb DVT, different imaging techniques used for diagnosis, as well as treatment options and complications.
Findings and procedure details

It is important to understand firstly the difference between primary and secondary venous thrombosis. Primary includes idiopathic, thoracic outlet syndrome and effort thrombosis (Paget-Schroetter syndrome); secondary can be iatrogenic (for example central venous catheter or pacemaker lead), traumatic or related to risk factors that increase the coaguability of blood e.g. thrombophilia, cancer, pregnancy and oral contraceptive medication.

The main primary condition we will discuss is that of effort thrombosis. Described independently by Paget in 1875 and Schroetter in 1884, it was then given the name Paget-Schroetter syndrome by Hughes in 1948 (10). This refers to the poorly understood mechanism of extraluminal compression of the subclavian vein as it traverses the costoclavicular space. This is an anatomical window, bordered by the clavicle and subclavius muscle, first rib and superior border of the scapula. It is believed that in certain individuals repetitive motion involving a lot of thoracic inlet movement causes abrasive force on the vein leading to microtrauma and subsequent stenosis at this point. This stenosis is a risk factor for venous stasis and subsequent thrombosis (one aspect of Virchow's triad).

Central venous catheter or pacemaker insertion can cause either direct trauma to the endoluminal wall or stasis of blood flow, both of which can lead to subsequent thrombosis. Another classic cause is in patients with intrinsic clotting abnormalities, namely the thrombophilias of which there are many. It is outside the scope of this resource to discuss them all, but examples would be Factor V leiden, Protein C/S deficiency, antithrombin III deficiency and Hughes syndrome. Cancer, pregnancy and oral contraceptive medication can also predispose to thrombosis. Although direct trauma is rare it should be considered as venous remodelling changes the laminar flow within a vessel and would increase the risk of subsequent thrombosis.

Investigation of upper limb swelling, following initial history and examination, often begins with ultrasonography, given its availability, low cost and non-invasive nature. Ultrasound, despite its inter-user variability, can be very effective at diagnosing thrombus. Di Nisio et al found that compression ultrasonography performed with a sensitivity of 97% and specificity of 96%; better than both doppler ultrasound and MRI (11). Although Doppler wave form characteristics can be used, visualisation and compression of the subclavian vein, particularly as it passes beneath the clavicle, can be challenging.

Alternative imaging modalities include CT and MR venography however conventional contrast venography is the reference standard. CT and conventional venography both
require injection of contrast medium into a proximal vein in the affected arm. MR may be preferred in cases where ionising radiation or contrast is contraindicated. Stenosis presents as abnormal narrowing of the vein (see figure 1 and 2), which is a somewhat subjective comparison with adjacent segments. Thrombosis manifest as filling defects within the vessel itself (see figure 3). Another feature which would indicate flow disruption and chronicity is collateral vessel formation.

Compared with lower limb DVT, there is a shortage of good quality evidence, in the form of randomised controlled trials, assessing the varying treatment options available for upper limb DVT and thus no consensus algorithm (12). Treatments range from, and may include a combination of, anticoagulation, interventional treatment and surgical approaches.

Anticoagulation usually involves subcutaneous low molecular weight heparin (LMWH) injections administered simultaneously with oral warfarin, with LMWH withdrawn once the international normalised ratio (INR) is in the therapeutic range. Length of treatment will depend on the cause of thrombosis, as well as patient factors such as risk of bleeding and recurrent thrombosis, although current American College of Chest Physician (ACCP) guidelines suggest at least 3 months of anticoagulation (13). Other forms of anticoagulation to be considered are novel anticoagulants (non vitamin K antagonists), so called 'NOACs', such as rivaroxaban. For thrombosis related to central venous catheters, the ACCP suggests catheters do not need to be removed if they are functional and there is an ongoing need for a catheter. If the catheter is not removed, anticoagulation should be continued whilst the catheter remains in situ (13).

Catheter direct thrombolysis (CDT) is now considered a preferrable treatment modality to systemic thrombolysis, where available. CDT involves continuous instillation of a small dose of a thrombolytic agent directly into the thrombus by careful placement of a catheter. For lower limb DVT, the ACCP suggests thrombolysis be used in extensive acute ileofemoral thrombosis presenting within 14 days, where the patient has a good functional status and life expectancy of over 1 year; in these cases and where available, CDT should be performed in preference (13). Although there is currently no evidence directly assesing this option for upper limb DVT, it is likely suggestions for lower limb DVT management can be extended to upper limb.

For Paget Schroetter syndrome, surgical treatment options are available through decompression of the costoclavicular space. Various techniques have been described, with the transaxillary approach being the first reported method (14) and also the most commonly used. The procedure is technically challenging and high risk; these include haemopneumothorax and long thoracic nerve injury. Angioplasty and stenting of the stenosed segment of vein would appear to be a logical solution however the costoclavicular space is in fact more persistent than one would have thought. Both angioplasty and stent insertion have been shown to have a high failure rate if performed
prior to decompressive surgery (15,16). Although available, decompression is still not widely used due to conflicting evidence. Several papers have demonstrated that following thrombolysis, if surgical decompression is not performed 30 day re-stenosis rates can be up to one third (17-20). Kaj Johansen et al however, provide a strong argument against surgical treatment. After mean follow-up of 57 months, of the 50 patients who were thrombolysed and then anticoagulated, but not treated surgically, 82% were completely asymptomatic (21).

Complications include recurrent thromboembolism, post-thrombotic syndrome and pulmonary embolism (PE). Post-thrombotic syndrome is a major complication known to cause significant morbidity and impairment in quality of life (22).

Pulmonary embolism has been documented to occur in up to 36% of cases (23,24) and although death related to PE is rare, it can occur.
Fig. 1: Coronal CT venography demonstrating stenosis of the right subclavian vein as it passes through the costoclavicular space, with large adjacent collateral vessels.

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**Fig. 2:** Conventional venography showing stenosis of the left subclavian vein related to intraluminal pacemaker leads. Multiple axillary collateral vessels are also demonstrated.

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**Fig. 3:** Conventional venography demonstrating a filling defect within the left subclavian vein, representing thrombus. Multiple venous collateral vessels backfill the left braciocephalic vein.

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Conclusion

After reading this review, delegates should have an improved understanding of the various underlying factors which can lead to venous thrombosis and subsequent upper limb swelling. The importance of recognising and diagnosing these causes is to allow timely intervention to prevention of complications, such as PE. The sequelae of upper limb DVT are underestimated, in particular post-thrombotic syndrome, which can have a significant negative effect on patient quality of life.

We have also discussed diagnostic approaches, the gold standard for which is conventional contrast angiography. Due to factors such as availability and cost, the first line tool is often ultrasonography, which has in fact been shown to be highly sensitive and specific.

A range of treatment options do exist, however the mainstay for acute treatment is anticoagulation. Thrombolysis may play a role in certain patient subgroups, for example those who are at high risk of complications. Surgical decompression of the costclavicular space can aid in prevention of re-thrombosis however it is technically challenging and not without risk.
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References


