Aetiology and Therapeutic Options of Acute Subclavian Vein Thrombosis

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Dear Editor,

We read with interest the two largest registries with multiple studies on upper extremity deep vein thrombosis (UEDVT), namely RIETE and the Japanese COMMAND registries, and consider the importance of reflecting on this matter.[1–4]

UEDVT is a relatively rare phenomenon, accounting for up to 10% of all deep vein thrombosis (DVT).[1–5] Its incidence increases in hospitalised patients, and is often related to central venous catheters.[1–5] To better understand the mechanism of thrombus formation at this specific anatomical level, subclavian DVT has been categorised as primary and secondary.[6]

Primary subclavian DVT, also called effort-thrombosis, is common in young, healthy individuals who play sport or have occupational activities that require repetitive movements elevating the shoulders and arms. The neurovascular bundle is repetitively compressed between the first rib and anterior scalene muscle from below, and the clavicle, subclavius muscle and costocoracoid ligament from above, causing what is known as thoracic outlet syndrome (TOS).[6] Due to the anatomical disposition, neurological symptoms are the most frequent symptoms described in more than 90% of cases.[7] Venous TOS, also known as Paget–Schroetter syndrome, occurs less frequently, with no thrombus formation or subclavian vein thrombosis. Venous TOS prevails in the dominant arm, with an equal sex ratio, as described more recently.[8] Arterial compression symptoms are even more rare.

Secondary thrombosis of the subclavian and axillary veins is a more frequent phenomenon often related to peripherally inserted central venous catheters, tunnelled catheters, subcutaneous ports and pacemaker wires.[6] The ongoing presence of the catheter causes intimal venous wall irritation and inflammation, which can finally lead to thrombosis. Catheter-induced venous thrombosis is relatively frequent, occurring in 5% of central venous catheters with an estimated prevalence of two cases per 1,000 hospital admissions.[9] Cancer, hypercoagulable states, congestive heart failure, mediastinal tumours, local surgery or trauma and nephrotic syndrome conditions can also cause secondary subclavian DVT. Several other factors have proved to increase the risk for DVT. For example, the presence of pacemaker wires with ejection fraction <40% increases the incidence of venous thrombosis.[10] Cancer patients have an eightfold higher risk of presenting UEDVT, whereas obese patients undergoing surgery have a 23-fold increased risk for UEDVT versus non-obese patients.[6,11]

A total of 9% of primary subclavian DVT and 33–60% of secondary subclavian DVT can be asymptomatic. The most common signs are arm swelling and heaviness, and, occasionally, cyanosis, pain and venous claudication. Dilated superficial collateral veins are often present over the shoulder in search of venous hypertension relief.[6] Since clinical findings of UEDVT are non-specific and can be misleading, differential diagnosis spans through arm lymphoedema, muscle haematoma and external venous compression.[6]

Pulmonary embolism (PE) occurs in 12% of patients with primary subclavian DVT. However, the risk for PE rises in patients with catheter-induced subclavian DVT to 15–25% of the cases, with PE being the second most common cause of death in patients with cancer.[9] Oncological patients also have more complications and reduced quality of life.[2] Post-thrombotic syndrome presenting as persistent oedema and pain has been described in 7% of patients.[1] The development of phlegmasia cerulea dolens is extremely rare in both groups, mostly being described in oncological patients and hypercoagulable states.[1]

The recognition of clinical signs and symptoms will be followed by definitive imaging studies.

Duplex ultrasound (DUS), a non-invasive, low-cost, and highly available method with high sensitivity (81–100%) and specificity (82–100%), is the most frequently used diagnostic modality and first step imaging method to confirm UEDVT.[6] However, DUS examination is a subjective method with variable accuracy depending on the operator's experience.

The gold standard is the performance of venography. Although, it is an invasive method requiring contrast medium use, radiation exposure and cannulation of a vein in the affected arm, which can sometimes be impossible due to arm swelling. Venography is only performed when DUS

seems equivocal. Magnetic resonance venography is a non-invasive alternative method correlating well with venography.[9] Magnetic resonance venography presumes time delay and availability. Thus, in patients with high clinical suspicion where no other studies can be performed, the use of CT venography is indicated, especially if PE is suspected.

Anticoagulation alone, rest, and arm elevation in patients with primary subclavian DVT have been associated with high residual functional impairment, significant long-term morbidity and disability.[6] Venous TOS patients are at significant risk for rethrombosis.[12] Thus, thrombolytic therapy emerged as the preferred initial management of venous TOS, followed by surgical decompression. In secondary subclavian DVT, most patients improve with systemic anticoagulation for 3 months and catheter removal. In the case of axillo-subclavian DVT extension and severe symptoms, thrombolysis may be indicated.

Thrombolysis should be performed <14 days after the onset of the symptoms. Thrombolytic therapy can be catheter-directed with local infusion of thrombolytic agents for usually <48 hours, or employing thrombectomy devices. Through basilic vein DUS-guided puncture, a wire is advanced crossing the thrombus. Then, a multiperforated catheter is left to instil physician-specified fluids, usually urokinase.

Thrombectomy devices are more costly, but avoid the side-effects of continuous urokinase infusion, such as cerebral bleeding, while allowing rapid thrombus maceration and aspiration. Several devices are available on the market. The AngioJet PE system (Boston Scientific) functions on the principle of the Venturi effect. It is a rheolytic thrombectomy device that aspirates the generated thrombus fragments after local infusion of urokinase. High-pressure saline is infused through a distal catheter pore while simultaneously aspirated through an adjacent pore.[6] The generated high-flow pressure not only fragments the thrombus, but also destroys blood cells producing haemolysis. Thus, a certain degree of haematuria or frank haematuria are relatively common after treatment with the AngioJet System. However, acute kidney failure has been described in several reports.[13,14] Another thrombectomy device is the Indigo System (Penumbra). This device is advanced and retracted through the CAT catheter to the proximal edge of the thrombus to facilitate the clearing and aspiration. The Rotarex/Aspirex devices (Straub Medical) hold a rotational debulking catheter to fragmentate the cloth and aspirate it, generating negative pressure.

Unsuccessful thrombolytic treatment is rare, being described in patients with rethrombosis and chronic DVT. Anticoagulation and measures to address pain, such as arm elevation, rest and compression, should be applied in these patients. Aggressive surgical treatment in these patients has shown variable results.[6]

When successful re-establishment of axillo-subclavian patency is achieved, positional venography with arm separation would diagnose patients with TOS compression. If there is a remaining venous stenosis, percutaneous balloon angioplasty with or without stenting can be performed. The results of subclavian stenting without thoracic outlet decompression are poor, with a 1-year primary patency of 35%, and a high compression, fracture and thrombosis risk for stents underneath the clavicle. Thus, stenting before surgical decompression in venous TOS plays no role.[6] Some venous stenosis is resistant to dilatation due to intrinsic elastic recoil. Venous TOS patients would benefit from surgical decompression. In patients without extrinsic venous compression, 3–6 months of anticoagulation therapy is indicated.[6]

Some authors recommend immediate surgical decompression as early as 4 hours after thrombolysis to avoid vein rethrombosis.[6] However, systemic anticoagulation treatment avoids rethrombosis risk while awaiting elective surgery to be performed no later than 1 month after thrombolysis. Surgical decompression involves resection of the cervical rib, if present, first rib, anterior scalene muscle and any other anatomical abnormalities as fibromuscular bands, and soft tissue defects. Mainly paraclavicular and transaxillary surgical approaches are favoured. The transaxillary approach allows visualisation of the first rib for resection, whereas the paraclavicular approach (supra- or infraclavicular) facilitates cervical rib, first rib and any other anatomical abnormalities resection.

Finally, UEDVT management depends on the aetiological process. In the presence of external compression, as in venous TOS, thrombolysis and surgical decompression are indicated. Secondary DVT is generally treated by systemic anticoagulation and catheter removal. Comfort measures are indicated for symptomatic patients. The risk of recurrence seems similar when comparing upper extremity and lower extremity DVT, whereas all-cause mortality is significantly higher in the UEDVT group than the lower extremity DVT group (p=0.0338) according to the GARFIELD-VTE registry.[4,15] This latter finding was likely due to the high prevalence of cancer in the UEDVT group.[15] ❑

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