

Thrombolysis and Balloon Venoplasty for Subclavian Vein Thrombosis

63

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Abstract

Venous thrombosis due to thoracic outlet syndrome (VTOS) is often managed initially with thrombolysis since this provides some immediate relief of symptoms plus removing the thrombus allows for a more localized decompressive operation and decreases the risk of a pulmonary embolus. Thrombolysis can be achieved with either catheter directed infusion of a thrombolytic drug or by pharmacomechanical thrombolysis which uses mechanical devices to augment the thrombolytic effect and to help remove thrombus. Technical success rates are very high with only rare complications reported. Advances in pharmacomechanical technique have decreased both procedure times and use of thrombolytic drug.

3–5 Critical Take-Home Messages

1. The technical success of thrombolysis for venous thoracic outlet thrombosis is about 95% if done with 2 weeks of symptom onset.

- 2. Mechanical thrombectomy devices can be used to augment thrombolysis or even completely replace the need for t-PA infusion.
- 3. Pharmacomechanical thrombolysis signifcantly speeds up the thrombolysis and makes it feasible to perform complete thrombolysis n a single session.
- 4. Pharmacomechanical thrombolysis can be done with very low complication rates.
- 5. While effective at removing the thrombus, pharmacomechanical thrombolysis does not deal with the extrinsic compression of the subclavian vein for which surgical decompression is the best option.

63.1 Introduction

Interventional radiologic procedures have become an integral part of managing patients with venous thoracic outlet syndrome (VTOS). This chapter will focus on initial management as the endovascular techniques used after decompressive surgeries are dealt with in a later chapter. Interventional radiology is typically involved with VTOS therapeutically. Catheter venography is rarely needed to make the initial diagnosis of VTOS since other imaging modalities can usu-M. Darcy (\boxtimes) ally make the diagnosis [[1\]](#page-10-0).

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63.2 Pre Thrombolysis

Prior to undertaking thrombolysis one should assess the extent of the thrombosis, the chronicity of the occlusion, and what risk factors might contraindicate the use of a thrombolytic drug. As the frst step, imaging of the vein is important to assess if the vein is thrombosed, the extent of thrombosis, and if it is an acute or chronic occlusion. This will inform whether to undertake lysis and to help plan the procedure.

Duplex ultrasound is often the frst step in a patient with VTOS, because it is inexpensive, readily available, easy for the patient to tolerate, and totally non-invasive. However there are several disadvantages to ultrasound. Visualization of the vein as it passes beneath the clavicle may be diffcult. If chronic occlusion is present it may be diffcult to distinguish a large collateral vein from the subclavian vein. Compressing the subclavian may be diffcult because of the overlying clavicle. Finally a high grade stenosis may slow flow so much that it can mimic thrombosis. For the above reasons it can be diffcult to assess the length of the occlusion, and it may be diffcult to distinguish acute from sub-acute thrombosis by

ultrasound. The sensitivity of ultrasound has been reported to be in the range of 71–100% and specificity ranges from 82 to 100% [\[2](#page-10-1), [3](#page-10-2)].

When ultrasound visualization is inadequate, computed tomographic angiography (CTA) or magnetic resonance venography (MRV) can demonstrate thrombosis and can be also used to document venous compression. Unlike ultrasound, both CT and MR are able to consistently visualize the subclavian vein under the clavicle. Both CT and MR can also readily defne anatomy extrinsic to the vein that may be responsible for compression of the vein such as hypertrophy of the anterior scalene muscle. MR can be done without iodinated contrast and does not involve ionizing radiation. Also with MR it is possible to do provocative maneuvers (Fig. [63.1](#page-1-0)) to reveal subclavian compression not evident on standard images with the patient's arms at their side. MR has been reported to have a sensitivity for detecting stenoses and obstructions of 100% with a specificity of 97% $[4]$ $[4]$.

It is important to try to determine the chronicity of the occlusion since occlusions older than 2 weeks are less likely to respond to thrombolysis [\[5](#page-10-4)]. A good history can determine the time from

Fig. 63.1 (**a**) MR scan with the arms in neutral position at the side. The right subclavian vein appears to be normal. (**b**) Repeat MR after abducting and raising the arms shows narrowing (*arrow*) of the right subclavian vein

onset of thrombosis to presentation. But if a good history cannot be obtained there are still other clues. Physical exam may reveal large chest wall collaterals which typically take some time to develop. Imaging can also help determine the chronicity of the occlusion. An acute thrombosis often shows a distended vein with tram tracking of contrast around some of the thrombus plus collaterals are usually not well developed. Over time the clot retracts and the subclavian vein may shrink or even become obliterated with concordant development of larger collaterals (Fig. [63.2\)](#page-2-0). Acute or sub-acute presentation is more common but in one study of 73 patients undergoing venography for VTOS, 77% had acute or subacute thrombosis but 23% had venographic evidence of chronic venous occlusion [[6\]](#page-10-5). At the time of venography, the ability to pass a wire through the thrombosed segment also helps determine the chronicity of the occlusion since wires pass more easily through acute thrombus than chronically organized clot.

Prior to undertaking thrombolysis, a careful history should be taken to assess for contraindications to use of a thrombolytic drug like tissue plasminogen activator (t-PA). Even with a local infusion, there is some systemic effect which can precipitate bleeding elsewhere. The most common contraindications typically include an intra-

Fig. 63.2 Right subclavian venogram shows an occluded right subclavian and axillary vein with no discernable intra-luminal flling defects but large collaterals (*arrow*) indicating a more chronic thrombosis

cranial process such a tumors, malformations, or aneurysms; active bleeding such as ongoing gastrointestinal bleeding or vaginal hemorrhage; and recent major surgery. While there are no studies analyzing how soon after surgery t-PA is safe to use, most physicians would prefer to not use t-PA within the first 2–3 weeks after major surgery.

As soon as subclavian thrombosis has been diagnosed, systemic anticoagulation should be started. The rationale for starting anticoagulation prior to thrombolysis is twofold. First is to prevent extension of the thrombus which could make a thrombolysis procedure lengthier and more diffcult. The second goal is to avoid pulmonary embolism which is very rare but has been reported [\[7](#page-10-6), [8](#page-10-7)].

63.3 Rationale for Lysis

Prior to starting thrombolysis it is important to set the expectations for the patient. They should understand that thrombolysis is not intended to be a solo therapy. Subsequent decompressive surgery is likely and does not mean that the thrombolysis failed since thrombolysis alone does not treat the underlying stenosis (Fig. [63.3](#page-3-0)).

Series exploring thrombolysis alone are illustrative. In one, 25 patients were treated with thrombolysis, 12 of them with adjunctive PTA, while only 2 underwent operative decompression [\[9](#page-10-8)]. At 3 years of follow-up only 28% were symptom free while 72% had mild or severe symptoms. Another series of 35 patients treated non-operatively with thrombolysis and anticoagulation resulted in a 23% rate of recurrent thrombosis within 13 months post treatment [\[10](#page-10-9)].

Angioplasty without operative decompression is futile as the problem is *extrinsic* compression of the vein at the costoclavicular junction. Stenting the subclavian vein without surgical decompression also generally fails, as rates of failure approach 100% [\[11](#page-10-10), [12\]](#page-10-11). Lee et al. showed that presence of a stent in the subclavian vein was an important contributor to re-thrombosis after intervention [\[10](#page-10-9)], and the presence of a stent compromises the ability to surgically reconstruct the vein when the stent fails.

a b

Fig. 63.3 (**a**) Venogram showing acute left subclavian and axillary vein thrombosis. (**b**) Venogram done after complete clot lysis reveals persistent subclavian vein stenosis (*arrow*)

Given that surgery is almost inevitable why do thrombolysis in the frst place? Clearing the vein of thrombus allows the most defnitive means of accurately diagnosing VTOS. If the subclavian vein is occluded by thrombus then it is impossible to demonstrate compression and it has been shown that only 60% of primary upper extremity DVT is TOS related [[13\]](#page-10-12). The extrinsic compression can only be demonstrated when there is fow of contrast within the vein and this allows visualization of a reduced venous lumen at the thoracic outlet. Additionally, reducing the extent of occluded vein allows for a more focal surgical lysis of scar or residual occlusion and reducing clot burden can decrease the chance of pulmonary embolism.

While pre-operative thrombolysis is generally considered to be beneficial, one report of thrombolysis in VTOS patients is the subacute and chronic time frame showed no beneft [\[14](#page-10-13)]. In this retrospective study 45 patients underwent thrombolysis prior to frst rib resection but 65 patients were treated with anticoagulation alone before the surgery. Both the lysis and heparinization groups had similar need for venoplasty when routine venograms were done 2 weeks after surgery. More importantly at follow-up, 91% of both groups had patent veins and were free of symptoms regardless of which pre-operative treatment was used. Importantly, however, this series included a large number of patients who presented with subacute or even chronic thrombus, so these results should be applied only to this group.

63.4 Thrombolysis Technique

Thrombolysis starts with gaining venous access. Access is almost always via a brachial or basilic vein in the upper arm. These veins can be easily punctured with ultrasound guidance. The distance from the access to the subclavian occlusion is quite short. Also the smaller caliber of the brachial or basilic veins supports the catheter and reduces buckling. These factors enhance manipulations and the ability to cross the occlusion. Femoral access is less desirable because the long distance to the occlusion decreases catheter control and the relatively large space in the right atrium and chest veins allow catheter buckling to occur when trying to push across a tough occlusion.

Venography is then done to assess the length and chronicity of the occlusion. The length of the thrombotic occlusion ranged in one study from 3 to 25 cm [\[15](#page-10-14)]. Short occlusions might be managed in a single session whereas longer occlusions might require overnight thrombolysis. Also the appearance of the occlusion, acute or chronic, will determine what tools to use. Thus venography helps formulate the therapeutic plan.

There are two main techniques for thrombolysis: catheter-directed infusion (CDT) of a thrombolytic agent and pharmacomechanical thrombolysis (PMT). Many centers use a combi-

nation of techniques depending on the morphology of the occlusion and patient clinical factors. In a study of 41 patients 5 were treated with t-PA alone, 6 had mechanical lysis alone, and 30 underwent PMT with both t-PA and mechanical devices [[6\]](#page-10-5).

63.5 Catheter-Directed Thrombolysis (CDT)

CDT is performed by placing a multi-side hole catheter into the clot and running thrombolytic agent through it for 6–48 h. This obviously requires that the thrombus be soft enough to traverse with the catheter; if the occlusion cannot be traversed, most interventionalists would abandon the attempt. However, a simple end-hole catheter can be embedded in the clot and lytic infusion started. While this can sometimes work, more frequent catheter checks are required to keep advancing the catheter into the thrombus as the peripheral thrombus dissolves.

A common catheter used for CDT is the Unifuse (Angiodynamics; Queensbury, NY). This is a multi-sidehole catheter with a tip occluding wire to force the t-PA to infuse out the side holes into the clot rather than taking the path of least resistance which would be through the end hole of the catheter if it was not occluded. Another available mutli-sidehole catheter is the Cragg-Mcnamara catheter (Medtronic; Minneapolis, MN). This utilizes a valve at the end of the catheter rather than a tip occluding wire to force the t-PA to exit through the sideholes. For simple CDT, the dose of t-PA commonly used is 0.5–1 mg per hour. Zurkiya et al. [\[6](#page-10-5)] reported that the mean amount of t-PA used was 20.5 mg, with mean thrombolysis duration of 15 h. Vik et al. used a slightly different regimen and infused t-PA at 0.01 mg/kg h. In this study the median duration of thrombolysis was 70 h and the median amount of t-PA infused was 52 mg (range, 19–225 mg) [[16\]](#page-10-15).

The main advantage of catheter infusion is that it is simple, less labor intensive, and does not take much time in the angiography suite. The main disadvantage is that clot dissolution may

take several days although if signifcant progress is not made after 48 h of infusion most physicians tend to terminate the procedure. Another disadvantage is that the patient has to be monitored in an observation unit or ICU during this whole time due to the risk of bleeding. Labs need to be monitored serially (usually every 6–8 h) including hemoglobin/hematocrit to watch for evidence of bleeding and fbrinogen levels to assess fbrinolytic effect. If the fbrinogen level falls below 100 mg/dl the t-PA infusion is typically reduced or temporarily held. The likelihood of successful lysis depends on how old the thrombus is. While there are anecdotes of month old clot being successfully lysed, some have reported no success when the patient's symptoms indicated that the clot was present for over 2 weeks [\[17](#page-11-0)].

63.6 Pharmacomechanical Thrombolysis (PMT) and Mechanical Thrombectomy

PMT is a generic term for use of a mechanical thrombolytic device in combination with infusion of a thrombolytic drug. The main beneft of using mechanical devices is that they can signifcantly speed up the process of clearing the entire clot. There are several mechanisms by which this occurs. First, some of the mechanical devices help disperse the lytic agent over a wider area and/or actually force lytic drug into the thrombus. Some mechanical devices also cause fragmentation of thrombus, which carries with it two benefts: Fragmentation can in some cases be effcient enough that the particles created are small enough to aspirate or safely pass into the pulmonary circulation, and, secondly, such fragmentation creates a greater surface area for lytic drug to work on and speeds the lytic effect. Some of the newer devices are designed to remove thrombus by either suction or purely mechanical means thus avoiding the use of t-PA.

PMT allows for shorter procedure times. Vik et al. [[16\]](#page-10-15), utilizing t-PA infusion via a multi-side hole catheter reported a mean procedure duration of 70 h compared to 15 h procedure time for ultrasound accelerated thrombolysis reported by Struck et al. [\[18](#page-11-1)]. PMT now makes it possible to sometimes lyse the thrombus in a single session (Fig. [63.4\)](#page-5-0). Kim et al. [[19\]](#page-11-2) compared standard lytic infusions to PMT with the Angiojet device (Boston Scientifc; Maple Grove, Mn), and found that PMT yielded signifcantly shorter lysis treatment times (26.3 vs. 48 h for standard infusion). The mean endovascular procedure time in another PMT study was just 105 min [\[15](#page-10-14)].

Single session thrombolysis has several advantages. First it is potentially easier for the patient to tolerate as a prolonged indwelling infusion catheter is not needed. This also obviates the need to send the patient to a higher acuity observation unit or ICU since there is no prolonged infusion, and the risk of pericatheter bleeding, higher with prolonged infusion time, is virtually eliminated. The main disadvantage of single session thrombolysis is that these cases can take several hours, thus tying up the proceduralist and interventional suite time.

Some interventionalists adopt a hybrid strategy where an infusion catheter is placed in the morning and the patient is infused in an observation unit for 4–6 h. They are then brought back to the angiography suite in the afternoon and the

remaining clot is cleared with PMT techniques. After several hours of thrombolytic infusion the thrombus is not only reduced in volume but is also generally softer and more readily fragmented with mechanical devices. This approach is a little less labor intensive but still generally accomplishes complete lysis in a single work-day.

PMT also allows lower overall doses of lytic drugs. As an example, one study [\[16](#page-10-15)] of simple catheter infusion utilized a mean t-PA dose of 52 mg compared to 20 mg needed for ultrasound accelerated thrombolysis and 10 mg for single session PMT [\[18](#page-11-1)]. In an older study the total urokinase dose was signifcantly decreased (2.7 vs. 5.6 million units) by utilizing the Angiojet for PMT [\[19](#page-11-2)]. Lowering the dose should decrease the chance of hemorrhagic complications.

63.7 Devices

The mechanical devices available for thrombectomy have signifcantly changed in recent years. Several devices that used to be mainstays for managing VTOS are no longer available. These include the Amplatz Thrombectomy Device (EV3; Plymouth, MN) and the Trellis catheter

Fig. 63.4 (**a**) Pre thrombolysis left subclavian venogram showing thrombus and collaterals. (**b**) After thrombolysis the underlying stenosis (*arrow*) is present but the throm-

bus and collateral fow is no longer seen. This was accomplished in one 2-h session using an Angiojet device for pharmacomechanical thrombolysis

(Bacchus Vascular; Santa Clara, CA). However as these devices went away, several newer devices have been introduced.

63.8 Ultrasound Accelerated Thrombolysis

The Ekosonic Endovascular System (EKOS Corporation, Bothell, WA) is not strictly a mechanical device like others we will discuss. Ultrasound energy is used to accelerate lysis. While the lytic agent is infused, the EKOS wire generates ultrasound along the length of the device. This "sonication" increases the thrombolytic effect by increasing penetration of the lytic agent into thrombus [\[20](#page-11-3)]. There are several reported benefts to this approach, including penetration of lytic effect into diffcult–to-reach places (such as behind valves) where a purely mechanical device might not reach, and reportedly allows diffuse penetration of the thrombus without causing macroscopic fragmentation of the clot that could lead to embolization. Since this process is not mechanical there is no damage to the vessel wall or valves and no red cell hemolysis [[21\]](#page-11-4). Because of the lack of hemolysis, there is no adenosine release and thus no increased risk of arrhythmias, as well. There is little data for use of EKOS for VTOS and this device is more commonly utilized to manage deep vein thrombosis and pulmonary emboli.

63.9 Mechanical Fragmentation Devices

The Trerotola percutaneous thrombectomy device (PTD) (Arrow International; Reading, PA) and the Cleaner (Argon Medical; Athens, Tx) are pure fragmentation devices with slight design differences. Both have a motor which rotates a drive shaft. The PTD (Fig. [63.5](#page-6-0)) has a basket at the end of the drive shaft whereas the Cleaner ends in a sinusoidal shaped wire. The high speed rotation acts somewhat like an egg-beater and fragments the thrombus into very small pieces that can be aspirated or can pass centrally.

Fig. 63.5 The Arrow Percutaneous Thrombectomy Device being used in the subclavian vein. The *arrow* points to the rotating basket that macerates the clot

Because the rotating basket has potential for wall contact this device could theoretically cause endothelial damage but this has not been shown to be an issue. These devices provide slightly more aggressive clot fragmentation and are sometimes useful when the thrombus is a little older and more organized. While the device itself is purely mechanical, t-PA can be infused either through the side port of the device or into the thrombus prior to activating the device. Thus during activation the rotating device can disperse the t-PA in addition to mechanically fragmenting the thrombus.

63.10 Suction and Mechanical Removal Devices

Several devices allow aspiration or purely mechanical removal of lysed clot. The oldest of these, the AngioJet system (Boston Scientifc; Maple Grove, Mn) uses a pump system that works in several ways. In power-pulse mode the lytic agent is power injected into the clot leading to better penetration than can be accomplished by a standard IV infusion pump. In regular mode, saline is pumped in near the catheter tip while suction is applied to a more proximal port. The vortex created by this fuid circuit helps to macerate clot and facilitates aspiration through the suction lumen. There have been reports of bradyarrhythmias and even heart block when this

device is used close to the heart [[22,](#page-11-5) [23](#page-11-6)]. This led to the FDA issuing a black box warning against using the Angiojet for pulmonary emboli lysis. There are several theories as to the cause of the bradyarrhythmias including activation of stretch receptors or release of excessive amounts of ATP from the lysed clot. While the black box warning specifcally applies to use of the Angiojet during thrombolysis of pulmonary emboli, it is prudent to use it with caution in the subclavian vein. Thus it is recommended that the device be activated for only short periods of time in susceptible patients.

Relatively recent additions to the thrombectomy armamentarium include the Indigo thrombectomy system (Penumbra; Alameda, CA), the JETi thrombectomy catheter (Walk Vascular; Irvine, CA), and the ClotTriever and FlowTriever (both from Inari Medical; Irvine, CA). The Indigo systems consist of catheters of various sizes that are hooked to a continuous suction pump. A separator, which is a small basket shaped device attached to a wire passed through the catheter, is used to break up and help pull thrombus into the catheter.

The JETi system is an 8 Fr catheter hooked to suction but within the distal tip of the catheter is a focused saline jet that helps macerate the clot that is sucked into the catheter. Since the saline jet only macerates clot that has already been sucked into the catheter it should not lead to hemolysis as can occur with the Angiojet.

The 2 devices from Inari medical function slightly differently. The FlowTriever which is approved for retrieval of pulmonary emboli utilizes a catheter with 3 self-expanding nitinol disks that expand into the thrombus, not only disrupting the thrombus but also engaging it so it can be pulled into the large aspiration catheter. At 20 Fr this system might be a bit large for introduction through upper extremity veins. The ClotTriever was intended for peripheral venous thrombi or emboli. The catheter is advanced past the clot and opened exposing a nitinol coring element and the attached braided collection bag. The coring element separates thrombus from the vessel wall which is then captured in the collection bag. Clot is then pulled into the 13 Fr braided nitinol funnel sheath which is supposed to prevent distal embolization. The captured thrombus is pulled out through the sheath in a purely mechanical fashion.

The advantage of these newer devices (Indigo, JETi, ClotTriever) are that they are designed to remove thrombus without needing t-PA as an adjunct. Theoretically this could allow successful clot removal in patients who have contraindications to pharmacologic thrombolysis. However, none of these devices were specifcally designed with VTOS in mind and there is currently no signifcant data yet on their safety or effcacy for managing VTOS related subclavian thrombosis.

63.11 After Thrombolysis

In general the end point for thrombolysis or PMT is >90% resolution of the thrombus based on the venographic appearance [[24\]](#page-11-7). There is no literature to defne the role of intravascular ultrasound (IVUS) in the assessment of these patients immediately post lysis. One recent paper that looked at patients being evaluated after frst rib resection, did note that IVUS was able to identify signifcant venous stenosis in 94.4% of patients but venography showed stenosis in only 66.7% of those same patients [\[25](#page-11-8)]. This is not surprising given experience in other vascular beds has shown that IVUS reveals more about luminal narrowing than venography. However, it is not known if that additional information would impact how patients are managed immediately after lysis.

Once the thrombus has been lysed it is controversial as to whether balloon angioplasty should be done to treat any residual stenosis. Some authors [[6\]](#page-10-5) report that they do not angioplasty any residual stenosis seen after lysis whereas others perform angioplasty in the majority of cases [\[15](#page-10-14)]. Size of balloon used also varies with some authors advocating small low pressure balloons to avoid trauma to the vein since the angioplasty is a temporizing measure [\[26](#page-11-9)]. Others utilize larger 10–12 mm balloon [\[15](#page-10-14)] however there is no study that has compared the results with different sizes of balloons.

The theoretic beneft to balloon angioplasty of residual stenosis would be to enhance the luminal patency and improve flow (Fig. 63.6). Low flow may predispose to repeat thrombosis so by improving patency, PTA might reduce the chance

Fig. 63.6 (**a**) Acute right subclavian thrombosis. The venogram demonstrates that it is acute by the contrast tracking around the intraluminal thrombus. (**b**) A multi side hole infusion catheter The has been positioned across the thrombus. The infusion side holes are between the markers (*arrows*) on the catheter. (**c**) After an overnight infusion of t-PA, the The venogram shows the thrombus is mostly gone but there is a residual stenosis (*large arrow*) of the subclavian vein. The presence of collaterals (*small arrows*) indicates continued restriction of blood fow and a risk for re-thrombosis. (**d**) Spot flm showing a 10 mm balloon dilatingThe the subclavian stenosis. (**e**) Post angioplasty venogram The shows that while there is some residual stenosis, the luminal caliber is improved and the collaterals no longer fll, thus indicating improved fow

of re-thrombosis. Angioplasty can disrupt residual webs or synechiae. However, there is little chance that angioplasty will signifcantly improve the primary stenosis that incited thrombosis since that stenosis is due to extrinsic compression which will recoil right after the balloon is defated. Intravascular stenting is not a viable alternative to frst rib resection for managing residual stenosis as the extrinsic compression can compress or even fracture a stent [\[11](#page-10-10)].

63.12 Results of Thrombolysis

The technical success rates for thrombolysis reported in some older studies ranged widely from 62 to 100% [\[5](#page-10-4), [17,](#page-11-0) [27,](#page-11-10) [28](#page-11-11)]. Two more recent studies utilizing PMT reported technical success rates of 95% [\[15](#page-10-14), [29\]](#page-11-12). There are no good studies comparing the different techniques but it is apparent that the likelihood of successful lysis varies with the length of time the patient has symptoms prior to presenting for treatment. Molina et al. [\[5](#page-10-4)] described outcomes in 97 patients who presented for treatment within 2 weeks after the onset of symptoms. These patients had 100% technical success with thrombolysis and 100% patency on post op duplex imaging. In the same series were 17 patients frst seen 2 weeks–3 months after the onset of symptoms, and only fve such patients (29%) were able to undergo successful lysis and subsequent surgery. There are no frm guidelines regarding how long thrombolysis should be pursued before deciding that the thrombus will not lyse but one group [\[30](#page-11-13)] has suggested that if 20–25 mg of t-PA have been given without substantial lysis then the procedure should be terminated.

The long-term clinical results of thrombolysis followed by surgical decompression are quite good. Primary and secondary patency rates at 1 year are 92 and 96% respectively [\[31](#page-11-14)]. In a huge series of 506 extremities treated over the course of 50 years, 96% of patients were improved during follow-up periods ranging from 1 to 32 years with an average follow-up of 7.2 years [\[12](#page-10-11)]. Several studies have reported that 100% of athletes treated for VTOS were able to

resume unrestricted use of the treated extremity [\[3](#page-10-2), [32](#page-11-15)]. A more recent study of high-performance athletes showed that by using a combined approach of thrombolysis followed by surgical decompression, 93% were able to return to full athletic ability within their sport [[33\]](#page-11-16).

With appropriate patient selection, thrombolysis can be done for VTOS with minimal complication rates. Multiple series of PMT have reported no thrombolysis related complications [\[18](#page-11-1), [24](#page-11-7), [29\]](#page-11-12). Zurkiya et al. [\[6](#page-10-5)] reported no complications from venography, thrombolysis, or PTA except for one case of heparin induced thrombocytopenia. One of the worst reported rates was from an older study of pure t-PA infusion, no adjunctive mechanical thrombectomy, with 9% major bleeding although there were no intra-cerebral bleeds [\[16](#page-10-15)]. Thus use of mechanical devices seems to provide a risk beneft by lowering or eliminating the use of t-PA.

63.13 Post Thrombolysis Management

While thrombolysis may provide initial relief of symptoms, proper management includes planned frst rib resection and decompression of the thoracic outlet. Without surgical decompression, the extrinsic obstruction can lead to recurrent thrombosis and persistent symptoms. An analysis of 12 series including 684 patients [\[34](#page-11-17)] found that long term symptom relief was signifcantly more likely in patients who underwent frst rib resection compared to those who did not (93–95 vs. 54%). Subclavian vein patency was signifcantly better in those in the rib resection cohort and more than 40% of patients who had not undergone planned rib resection ultimately had a rib resection for recurrent symptoms. Given the risk of recurrent thrombosis, patients should be anticoagulated after thrombolysis until their rib resection surgery occurs.

One question is how soon after thrombolysis should decompressive surgery be done. Early investigators [[35\]](#page-11-18) recommended delaying operation for 2–3 months after thrombolysis to reduce the risk of bleeding, however, most investigators

feel that this is not a major problem. Some authors report no major surgical complications resulting from the prior lysis. One study [[30\]](#page-11-13) of 60 patients only had minor complications in 3 patients (5%). These consisted of 1 peri-catheter bleed, 1 minor hemoptysis, and 1 case of back pain, none of which caused any long-term problems. In another study in which 23 patients were operated on within 24 h after thrombolysis, wound hematomas occurred in 3 patients (13%), one of whom required thoracotomy for drainage [\[36](#page-11-19)]. Molina et al., however, reported only one bleeding complication in 97 cases in which early operation was performed [[5\]](#page-10-4).

Operating soon after lysis is often recommended since this decreases the chance of rethrombosis caused by unrelieved stenosis of the subclavian vein. Also it may allow quicker return to full activity. Melby et al. [[3\]](#page-10-2) showed that as the time interval from diagnosis to operation increases the overall duration of management and time to full recovery also lengthens. In a large study of 56 patients, early surgery (<30 days after lysis) led to a signifcantly better objective clinical outcome scores compared to patients who had delayed surgery [\[28](#page-11-11)]. This was partially because the delayed surgery group had a higher rate of re-thrombosis.

63.14 Conclusion

Thrombolysis can effectively treat acute thrombosis which can decrease patient symptoms, better defne the extent of the occlusion, and allow for more focal surgical correction of the compression. Thrombolysis is not effective against chronic thrombosis but imaging and symptom duration should help distinguish chronic from acute occlusions. While useful, effective, and low risk thrombolysis alone is insuffcient and needs to be followed by surgical decompression.

References

1. Raptis CA, Sridhar S, Thompson RW, Fowler KJ, Bhalla S. Imaging of the patient with thoracic outlet syndrome. Radiographics. 2016;36(4):984–1000.

- 2. Chin EE, Zimmerman PT, Grant EG. Sonographic evaluation of upper extremity deep venous thrombosis. J Ultrasound Med. 2005;24(6):829–38; quiz 39–40.
- 3. Melby SJ, Vedantham S, Narra VR, Paletta GA Jr, Khoo-Summers L, Driskill M, et al. Comprehensive surgical management of the competitive athlete with effort thrombosis of the subclavian vein (Paget– Schroetter syndrome). J Vasc Surg. 2008;47(4):809– 20; discussion 21.
- 4. Chang YC, Su CT, Yang PC, Wang TC, Chiu LC, Hsu JC. Magnetic resonance angiography in the diagnosis of thoracic venous obstruction. J Formos Med Assoc. 1998;97(1):38–43.
- 5. Molina JE, Hunter DW, Dietz CA. Paget–Schroetter syndrome treated with thrombolytics and immediate surgery. J Vasc Surg. 2007;45(2):328–34.
- 6. Zurkiya O, Donahue DM, Walker TG, Ganguli S. Safety and efficacy of catheter-directed therapies as a supplement to surgical decompression in venous thoracic outlet syndrome. AJR Am J Roentgenol. 2018;210(2):W80–W5.
- 7. Glavich G, Gourley J, Fong V. Paget–Schroetter syndrome with bilateral pulmonary emboli. Radiol Case Rep. 2018;13(1):28–31.
- 8. Kaczynski J, Sathiananthan J. Paget–Schroetter syndrome complicated by an incidental pulmonary embolism. BMJ Case Rep. 2017;2017:bcr-2017.
- 9. Lokanathan R, Salvian AJ, Chen JC, Morris C, Taylor DC, Hsiang YN. Outcome after thrombolysis and selective thoracic outlet decompression for primary axillary vein thrombosis. J Vasc Surg. 2001;33(4):783–8.
- 10. Lee JT, Karwowski JK, Harris EJ, Haukoos JS, Olcott C. Long-term thrombotic recurrence after nonoperative management of Paget–Schroetter syndrome. J Vasc Surg. 2006;43(6):1236–43.
- 11. Maintz D, Landwehr P, Gawenda M, Lackner K. Failure of Wallstents in the subclavian vein due to stent damage. Clin Imaging. 2001;25(2):133–7.
- 12. Urschel HC Jr, Patel AN. Surgery remains the most effective treatment for Paget–Schroetter syndrome: 50 years' experience. Ann Thorac Surg. 2008;86(1):254– 60; discussion 60.
- 13. Flinterman LE, Van Der Meer FJ, Rosendaal FR, Doggen CJ. Current perspective of venous thrombosis in the upper extremity. J Thromb Haemost. 2008;6(8):1262–6.
- 14. Guzzo JL, Chang K, Demos J, Black JH, Freischlag JA. Preoperative thrombolysis and venoplasty affords no beneft in patency following frst rib resection and scalenectomy for subacute and chronic subclavian vein thrombosis. J Vasc Surg. 2010;52(3):658–62; discussion 62–3.
- 15. Karkkainen JM, Nuutinen H, Riekkinen T, Sihvo E, Turtiainen J, Saari P, et al. Pharmacomechanical Thrombectomy in Paget–Schroetter syndrome. Cardiovasc Intervent Radiol. 2016;39(9):1272–9.
- 16. Vik A, Holme PA, Singh K, Dorenberg E, Nordhus KC, Kumar S, et al. Catheter-directed thrombolysis for treatment of deep venous thrombosis in the

upper extremities. Cardiovasc Intervent Radiol. 2009;32(5):980–7.

- 17. Doyle A, Wolford HY, Davies MG, Adams JT, Singh MJ, Saad WE, et al. Management of effort thrombosis of the subclavian vein: today's treatment. Ann Vasc Surg. 2007;21(6):723–9.
- 18. Stuck AK, Engelberger RP, Saengprakai W, Kucher N. Pharmacomechanical or ultrasound-assisted thrombolysis, balloon angioplasty and provisional surgical decompression for upper extremity deep vein thrombosis due to thoracic outlet syndrome. Thromb Res. 2016;145:109–11.
- 19. Kim HS, Patra A, Paxton BE, Khan J, Streiff MB. Catheter-directed thrombolysis with percutaneous rheolytic thrombectomy versus thrombolysis alone in upper and lower extremity deep vein thrombosis. Cardiovasc Intervent Radiol. 2006;29(6):1003–7.
- 20. Francis CW, Blinc A, Lee S, Cox C. Ultrasound accelerates transport of recombinant tissue plasminogen activator into clots. Ultrasound Med Biol. 1995;21(3):419–24.
- 21. Soltani A, Singhal R, Garcia JL, Raju NR. Absence of biological damage from prolonged exposure to intravascular ultrasound: a swine model. Ultrasonics. 2007;46(1):60–7.
- 22. Dwarka D, Schwartz SA, Smyth SH, O'Brien MJ. Bradyarrhythmias during use of the AngioJet system. J Vasc Interv Radiol. 2006;17(10):1693–5.
- 23. Fontaine AB, Borsa JJ, Hoffer EK, Bloch RD, So CR, Newton M. Type III heart block with peripheral use of the Angiojet thrombectomy system. J Vasc Interv Radiol. 2001;12(10):1223–5.
- 24. Trenor CC 3rd, Fisher JG, Khan FA, Sparks EA, Duzan J, Harney K, et al. Paget–Schroetter syndrome in 21 children: outcomes after multidisciplinary care. J Pediatr. 2015;166(6):1493–7 e1.
- 25. Kim TI, Sarac TP, Orion KC. Intravascular ultrasound in venous thoracic outlet syndrome. Ann Vasc Surg. 2019;54:118–22.
- 26. Ryan CP, Mouawad NJ, Vaccaro PS, Go MR. A patient-Centered approach to guide follow-up and adjunctive testing and treatment after frst rib resection for venous thoracic outlet syndrome is safe and effective. Diagnostics (Basel). 2018;8(1):4.
- 27. Beygui RE, Olcott C, Dalman RL. Subclavian vein thrombosis: outcome analysis based on etiology and modality of treatment. Ann Vasc Surg. 1997;11(3):247–55.
- 28. Taylor JM, Telford RJ, Kinsella DC, Watkinson AF, Thompson JF. Long-term clinical and functional outcome following treatment for Paget–Schroetter syndrome. Br J Surg. 2013;100(11):1459–64.
- 29. Mahmoud O, Sihvo E, Rasanen J, Vikatmaa L, Vikatmaa P, Venermo M. Treatment of Paget– Schroetter syndrome with a three-stage approach including thoracoscopic rib resection at the second stage. J Vasc Surg Venous Lymphat Disord. 2018;6(1):75–82.
- 30. Thompson JF, Winterborn RJ, Bays S, White H, Kinsella DC, Watkinson AF. Venous thoracic outlet compression and the Paget–Schroetter syndrome: a review and recommendations for management. Cardiovasc Intervent Radiol. 2011;34(5):903–10.
- 31. Schneider DB, Dimuzio PJ, Martin ND, Gordon RL, Wilson MW, Laberge JM, et al. Combination treatment of venous thoracic outlet syndrome: open surgical decompression and intraoperative angioplasty. J Vasc Surg. 2004;40(4):599–603.
- 32. Feugier P, Aleksic I, Salari R, Durand X, Chevalier JM. Long-term results of venous revascularization for Paget–Schroetter syndrome in athletes. Ann Vasc Surg. 2001;15(2):212–8.
- 33. Chandra V, Little C, Lee JT. Thoracic outlet syndrome in high-performance athletes. J Vasc Surg. 2014;60(4):1012–7; discussion 7–8.
- 34. Lugo J, Tanious A, Armstrong P, Back M, Johnson B, Shames M, et al. Acute Paget–Schroetter syndrome: does the frst rib routinely need to be removed after thrombolysis? Ann Vasc Surg. 2015;29(6):1073–7.
- 35. Machleder HI. Evaluation of a new treatment strategy for Paget–Schroetter syndrome: spontaneous thrombosis of the axillary-subclavian vein. J Vasc Surg. 1993;17(2):305–15; discussion 16–7.
- 36. Kreienberg PB, Chang BB, Darling RC 3rd, Roddy SP, Paty PS, Lloyd WE, et al. Long-term results in patients treated with thrombolysis, thoracic inlet decompression, and subclavian vein stenting for Paget–Schroetter syndrome. J Vasc Surg. 2001;33(2 Suppl):S100–5.