Same Admission Hybrid Treatment of Primary Upper Extremity Deep Venous Thrombosis with Thrombolysis, Transaxillary Thoracic Outlet Decompression, and Immediate Endovascular Evaluation

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Background: Multiple algorithms exist for treating acute primary upper extremity deep venous thrombosis (pUEDVT) caused by venous thoracic outlet syndrome (VTOS). In this case series, we present the results of our dedicated same admission treatment algorithm.

Methods: All patients between January 2015 and December 2019 with an established acute upper extremity deep venous thrombosis (symptoms < 14 days) caused by VTOS were treated according to an algorithm consisting of same admission thrombolysis, transaxillary thoracic outlet decompression (TA-TOD) with extensive venolysis, and venography. If a residual stenosis of the subclavian vein was identified on venography, including by means of low-pressure diagnostic balloon inflation, correction by percutaneous transluminal angioplasty (PTA) was performed. The thoracic outlet syndrome disability scale, the Dutch language version of the disabilities of the arm, shoulder, and hand, and the VEINES—quality of life (VEINES-QOL/VEINES-symptoms) questionnaires were collected during follow-up.

Results: In total, 10 patients were treated for acute pUEDVT. After successful thrombolysis (100%) and TA-TOD, immediate venography showed residual stenosis of the subclavian vein in 8 of 10 patients (80%). Low-pressure dilatation of a balloon suited to the geometry of the axillosubclavian vein showed significant tapering in all cases (10/10) after which a formal venous PTA was performed. No stents were used. Mean time to discharge was 6.4 days. All patients were free of symptoms at a mean follow-up period of 34.4 months. Eight of the 10 patients completed follow-up questionnaires and reported a mean thoracic outlet syndrome scale of 0.6, mean disabilities of the arm, shoulder, and hand score of 4.2, and a median VEINES-Symptoms of 55.23 (IQR, 12.13), and VEINES-QOL of 55.29 (IQR, 15.42).

Conclusions: A same admission treatment algorithm for acute pUEDVT in patients with VTOS including thrombolysis, TA-TOD with extensive venolysis, and immediate venography with PTA is effective with promising intermediate results.

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INTRODUCTION

Venous thoracic outlet syndrome (VTOS) is caused by repetitive compressive injury to the axillosubclavian vein (ASV) that results in a cycle of inflammation and fibrosis of the vein wall and its adjacent structures.1 This compression is often the consequence of an abnormal inserted costoclavicular ligament and/or hypertrophy of the anterior scalene muscle and/or subclavius muscle that narrow(s) the thoracic inlet. Ultimately, acute primary upper extremity deep venous thrombosis (pUEDVT) may result and this characteristically affects young, healthy, and active people with an incidence of approximately 1–2 per 100,000 people per year.1–3

The management of acute pUEDVT is controversial. Most guidelines suggest the use of anticoagulant therapy as primary treatment.4,5 However, some experts suggest that full recovery after acute pUEDVT and prevention of chronic VTOS with post-thrombotic syndrome (PTS) complaints is best established by a more aggressive approach consisting of anticoagulant therapy in combination with thrombolysis and surgical thoracic outlet decompression (TOD), preferably within the first 14 days after the onset of symptoms.1,12 Although some favor this aggressive treatment, different opinions regarding surgical approach, timing of TOD, and management after TOD with percutaneous transluminal angioplasty (PTA), stents, and/or venous bypass procedures remain.6–8

Correcting the anatomic substrate by TOD is, besides a fast start of initial treatment, thought to be helpful in preventing PTS and recurrent venous thromboembolism in patients with acute pUEDVT.1,5 However, residual lesions in the subclavian vein after TOD are a common finding.10–11 The residual stenosis can be treated by patch venoplasty, venous bypass grafting during paracervical TOD surgery, or PTA with or without stent placement. Thrombolysis followed by TOD, with immediate PTA addresses both the anatomic substrate and the residual stenosis in patients with acute pUEDVT. In this study, we present the results of a same admission algorithm in a case series of 10 patients.

METHODS

Study Design and Participants

We evaluated all patients that were referred to the Department of Vascular Surgery of the Catharina Hospital Eindhoven, The Netherlands, between January 2015 and December 2019 for diagnosis and treatment of upper extremity deep venous thrombosis (UEDVT) caused by VTOS. Patients were identified in a prospectively collected database. This study was approved by the local ethics committee and informed consent was obtained from all individuals after treatment.

According to the Reporting Standards for TOS, patients were classified into acute (<14 days), subacute (14 days–3 months), or chronic (≥3 months) VTOS.14 Patients were included in this study if they presented with an acute pUEDVT (<14 days) in the ASV with relation to compression on venography and no other explanation for UEDVT (e.g., malignancy, catheter). Patients presenting with chronic or subacute symptoms, or secondary causes of UEDVT (e.g., catheter or malignancy based) were excluded from these series.

Data collection included medical history, demographics, clotting disorders, dominant hand, side of symptoms, time between event and presentation, provoking factors, and findings of clinical examination. All patients were clinically evaluated by a dedicated TOS surgeon (J.A.W.T. or M.R.H.M.S.). During history and physical examination there was explicit attention for the presence of coexisting neurogenic TOS. Chest X-ray of the superior thoracic aperture was made to reveal possible bony anatomic abnormalities (e.g., cervical ribs, abnormal first ribs, or an elongated transverse process of C7). Finally, both duplex ultrasonography and digital subtraction contrast venography of the upper extremity were performed to identify the venous occlusion and to assess its extent.

After presentation and identification of axillo-subclavian thrombus, thrombolysis was started as soon as possible. First, the thrombus was passed with a guidewire after which a thrombolysis catheter was put in place for delivery of the thrombolytic agent. Alteplase (Boehringer Ingelheim, Ingelheim, Germany) therapy was used in all patients by first giving a lacing bolus of 5 mg. Thereafter, infusion with Alteplase was continued with 1 mg/hr for 12 hr followed by 0.5 mg/hr after 12 hr until there was no progression of thrombolysis on sequential examinations, or until complete thrombus dissolution was achieved. If high-grade stenosis was visible on sequential venography studies despite thrombolysis, a 6 mm PTA was performed preoperatively to enhance post-TOD catheterization. After stopping thrombolysis, low-molecular-weight heparin (LMWH; Nadroparin, Fraxodi; GlaxoSmithKline, Brentford, UK) prophylaxis was continued until the evening before TOD surgery. However, in patients treated in 2015 and 2016 (n = 4) LMWH prophylaxis was continued periprocedurally.
After successful thrombolysis, same admission transaxillary thoracic outlet decompression (TATOD) was performed in a hybrid operating room. The procedure was performed under general anesthesia with the addition of interfascial plane blockade to reduce postoperative pain as described previously. During this procedure, a complete first rib resection from the costochondral junction to the articulation with the vertebral body’s transverse process (the neck of the first rib remains), a partial anterior and medial scalenectomy (15–20 mm lower part), medial 3–4 cm removal of the subclavius muscle, and a thorough circumferential venolysis of the ASV was performed. After closure of the axillary wound, a venography through the basilic vein or brachial vein was performed to assess the patency of the vein. In addition, an 8 × 40 mm balloon (Passeo-35; Biotronik, Berlin, Germany) was advanced to the level of the thoracic inlet/outlet and slowly inflated to 2 atm under fluoroscopic guidance to visualize the presence of residual stenosis. If a stenosis was identified on this diagnostic balloon inflation, as evidenced by tapering of the balloon, a formal PTA (with nominal to burst pressures of the balloon) was performed with a balloon suitable to the geometry of the vessel. Postoperative therapeutic anticoagulation with rivaroxaban 20 mg once daily (Xarelto; Bayer, Leverkusen, Germany) was initiated directly after TOD surgery and continued for 6 weeks in all patients. A summary of the complete VTOS care pathway including the pUEDVT treatment algorithm is displayed in Figure 1.

All patients were evaluated 6 weeks after surgery and then yearly. No additional duplex ultrasonography or venography was performed in patients without sequelae or complaints during physical examination. However, a low threshold venography was performed if a patient reported even minimal sequelae or when abnormalities during physical examination were observed. Sequelae were defined as swelling, edema, pain, discoloration, and heaviness in rest or during strenuous activity. If venography in these patients showed a reduced diameter of the vein, a re-PTA was performed. Patients were seen 6 weeks after intervention and thereafter in case of sequelae. Additional follow-up data were obtained by questionnaires consisting of the thoracic outlet...
syndrome (TOS) disability scale, the Dutch language version of the disabilities of the arm, shoulder, and hand (DASH) score, return to work, and quality of life by VEINES-symptoms (VEINES-SYM) and VEINES-quality of life (VEINES-QOL). The mean DASH score in a general population with comparable age is 5 ± 10 points. VEINES-SYM and VEINES-QOL scores for patients with PTS are reported around 34 points compared with 53 points for patients without PTS symptoms.17

### Statistical Analysis

The statistical analysis was performed using Statistical Product and Service Solutions (SPSS) 25 (IBM Corporate, Armonk, New York, USA). Data are presented as the means with ranges and medians with interquartile ranges for VEINES scores. The VEINES-QOL/VEINES-SYM was calculated using the intrinsic method, allowing comparison between other cohorts.18

### RESULTS

In total, 52 patients were surgically treated for VTOS during the study period of which 10 of 52 patients had acute symptoms related to pUEDVT and were eligible for inclusion based on duration of complaints <14 days. Mean age was 34 years (range, 22–59), and 6 patients (60%) were men. The mean time between initial complaints and presentation in our outpatient clinic was 7.2 days (1–12). Clotting disorders were not found in our cohort. One patient had 2 previous episodes of acute pUEDVT on the same side. Symptoms of neurologic or arterial TOS were not found in this series. All baseline characteristics following the reporting standards for TOS are summarized in Table I.14

In all patients (10/10), a diagnostic venography was performed showing a thrombus in the ASV in all cases (Fig. 2). Collateralization as evidenced by visible vessels on the thoracic wall was seen in 8 of 10 patients. Subsequently, thrombolysis was initiated in all individuals within 24 hr after presentation. Thrombolysis was continued with a mean duration of 39 hr (range, 19–66). Progression of thrombus dissolution was seen in all patients (100%) but a remaining high-grade stenosis was seen in 2 patients, requiring preoperative PTA with a 6 × 40 mm balloon (Passeo-35; Biotronik) to enhance post-TOD catheterization.

After thrombolysis, TA-TOD with circumferential venolysis was performed in all (10) patients. No cervical rib or fibrous band was assessed in this series. During the intraoperative venography a residual stenosis of the ASV was visualized in 8 of 10 patients (Fig. 3). Moreover, tapering during the low-pressure diagnostic balloon inflation revealed persisting stenosis in all (10/10) patients (Fig. 4). Therefore, a formal angioplasty was executed in every case (2 times an 8 mm balloon, 6 times a 10 mm balloon, and 2 times a 12 mm balloon) (Powerflex; Cordis, Miami, FL). In all patients this approach resulted in a patent ASV without residual stenosis at the end of the procedure (Fig. 5). Complete disappearance of collaterals after PTA was seen in 6 patients, and partial in the remaining 4 patients. The overall
length of stay was 6.4 days (range, 2–15 days). Mean time from presentation to TOD surgery was 89 hr (range, 45–142). Postoperative length of stay was 3.2 days (range, 1–12 days). Surgical data are summarized in Table II.

Postoperative complications included 2 patients with hematoma formation requiring reexploration. In 1 patient, a small active bleeding vessel was found, which was controlled during reintervention. No active bleeding was found in the second patient and removal of hematoma was performed. Other complications such as pneumothorax, wound infection, phrenic or long thoracic nerve palsies, or brachial plexus injuries were not seen.

At the time of writing, all patients were asymptomatic without symptoms of PTS with a mean follow-up of 34.4 months (range, 6–58). However, recurrent symptoms were reported during follow-up in 3 of 10 patients and consisted of swelling (3/3 patients), pain (2/3 patients), and discoloration (1/3 patients). Venography showed a decrease in diameter without rethrombosis of the ASV in all these patients and a second PTA was performed.

This re-PTA resulted in relief of complaints in all 3 patients, resulting in a primary patency of 70% and primary assisted patency of 100% in this cohort. The mean time to reintervention was 32 days (range, 11–49).

The follow-up questionnaires were completed in 80% (8/10) of the patients and showed an improvement in function of the arm in all these patients at 38.9 months (range, 20–58). All (10/10) these patients were able to return to work and sport without limitations. Moreover, the mean TOS disability scale was 0.6 and the mean DASH score was 4.2 suggesting minor disabilities of the arm, shoulder, or hand. Quality of life measured with the adapted VEINES-SYM and VEINES-QOL resulted in a median VEINES-SYM score of 55.23 (IQR, 12.13) and VEINES-QOL score of 55.29 (IQR, 15.42).

### Table II. Surgical data

<table>
<thead>
<tr>
<th>Surgical data</th>
<th>n = 10 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean delay to presentation in our clinic (days)</td>
<td>7.2 (1–12)</td>
</tr>
<tr>
<td>Successful wire passage</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Intraoperative PTA performed</td>
<td>10 (100)</td>
</tr>
<tr>
<td>Re-PTA after initial TOD + PTA</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Mean time to Re-PTA (days)</td>
<td>32.3 (11–49)</td>
</tr>
<tr>
<td>Complications</td>
<td></td>
</tr>
<tr>
<td>Brachial plexus injury</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Superficial infection</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Postoperative bleeding</td>
<td>2 (20)</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Scapula alata</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Mean operative time (min)</td>
<td>96.1 (58–160)</td>
</tr>
<tr>
<td>Mean ASA score</td>
<td>2 (1–3)</td>
</tr>
<tr>
<td>Overall length of stay including thrombolysis (days)</td>
<td>6.4 (2–15)</td>
</tr>
<tr>
<td>Length of stay after TOD surgery (days)</td>
<td>3.2 (1–12)</td>
</tr>
<tr>
<td>Mean follow-up time (months)</td>
<td>34.4 (6–58)</td>
</tr>
</tbody>
</table>

ASA, American Society of Anesthesiologists.

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**Fig. 3.** Situation after thrombolysis and TOD with venolysis.

**Fig. 4.** Example of tapering during test-PTA after thoracic outlet decompression surgery.

**Fig. 5.** Situation after same admission thrombolysis, TOD with venolysis, and PTA.
DISCUSSION

The proposed algorithm including thrombolysis, TA-TOD surgery, venolysis, and immediate PTA is effective with promising short and intermediate results. Using this treatment algorithm, both the anatomic substrate and the residual lesions can be effectively treated in the same admission. This ensures minimization of the risk of recurrent thrombosis and less in hospital days compared with other treatment algorithms. Follow-up by DASH score suggests equal functional outcomes compared with more invasive treatment algorithms. Moreover, the high return to work percentage and high quality of life score show minimal sequelae after adequate treatment in these patients with acute pUEDVT.

Our same admission treatment protocol is based on 3 principles: immediate thrombolysis within 24 hr after presentation, transaxillary TOD with venolysis in the same admission, and intraoperative venography with immediate PTA to treat residual lesions. We try to accomplish thrombolysis within 24 hr after presentation for all patients with acute pUEDVT because thrombolysis has the highest success rate if performed in patients with acute symptoms. Thrombolysis is followed by TOD surgery as soon as possible, because delayed surgery after thrombolysis can potentially lead to poorer functional outcomes and higher rates of recurrent thrombosis in patients with acute pUEDVT. Although we advocate fast initiation of treatment by thrombolysis and TOD surgery, a mean of 7 days between the symptom onset and presentation in our clinic is present because of the delay of both patient and doctor. Because thrombolysis is proven useful within 14 days of onset, we believe this delay significant but acceptable. However, as fast initiation of adequate treatment is of importance, also delay of patient and doctor should be addressed to optimize treatment for patients with acute pUEDVT.

The preferred surgical approach differs between centers and is greatly dependent on the surgeon’s preference and the method of treating residual stenosis. These intrinsic residual lesions of the ASV found after TOD surgery are relatively underexposed in the literature. The vein may remain stenotic because of fibrotic changes in the vein itself despite thrombolysis, surgical decompression, and venolysis. Besides, the ASV can lose the ability to dilate, which consequently causes sequelae especially during strenuous activities. Intrinsic residual lesions are commonly found after TOD surgery in patients with acute pUEDVT with percentages varying from 35% to 95%. These patients are presumed to be more at risk to develop a recurrent venous thromboembolism or chronic stenosis resulting in PTS. Evidence to subsequently guide treatment in these patients is limited and it remains unclear if the addition of PTA or vein patch placement after TOD surgery has a favourable effect on PTS rates and long-term functional outcome compared with TOD surgery alone. However, treatment algorithms with the best long-term outcome include a control venography and treatment of residual stenosis after TOD surgery. Moreover, the complication rates of these treatment modalities are not higher compared with TOD alone. Therefore, we also choose to assess the subclavian vein patency directly after TOD and subsequently treat residual stenosis in all patients.

Most treatment algorithms use intraoperative or postoperative venography to demonstrate patency or occlusion of the subclavian vein. We prefer an approach with intraoperative venography in a hybrid operating room. This allows for TOD surgery and endovascular treatment in the same procedure, resulting in same admission treatment for patients.

Although management of residual lesions is becoming of more importance, debate exists about the best approach. Different treatment algorithms with PTA, stents, vein patch placement, and/or venous bypass procedures have been published with varying results because restenosis can occur. Besides, the optimal timing for these procedures is debatable. Venous reconstruction procedures, in particular vein patch placements, are described in several cohorts with excellent patency rates. To adequately place a patch on the ASV, at least an infraclavicular approach should be performed. Some experts advise even a paraclavicular approach. These approaches combined with vein patch placement add time and complexity to the procedure. However, the results of this case series and other cohorts are comparable with vein patch placement and require a less invasive transaxillary approach combined with an endovascular intervention. We prefer the transaxillary approach allowing complete resection of the first rib from the costochondral junction to the articulation with the vertebral body’s transverse process, leaving the neck of the first rib in situ, and access to the anterior scalene and subclavius muscles. This offers excellent ability to remove all compressive elements in the thoracic inlet/outlet. Although complete first rib resection is not necessary for full venous decompression, both anterior and posterior residual rib stumps are associated with higher recurrence rates of neurogenic TOS.
and VTOS complaints and should therefore be avoided. In addition to the operative advantages, the transaxillary approach also has the best cosmetic effect. However, this approach does not allow reconstruction of the ASV by vein patch placement or jugular vein turn-down procedures. The infraclavicular approach is also used as primary approach in algorithms with endovascular repair of residual lesions and has its own advantages. We do not primarily choose for this approach because it does not allow for complete first rib resection with thorough venolysis and has inferior cosmetic results.

We perform a PTA immediately after TOD surgery because this leads to faster functional recovery and less days of anticoagulant therapy compared with algorithms with delayed PTA. The long-term results defined by the recurrence rate of PTS must be awaited. Some clinicians use stents to treat (short segment) residual lesions. There is a lot of controversy on this issue. In some articles there is concern about long-term patency or limited options for later venous reconstruction, whereas another article claims excellent results. We reserve stent placement for persistent residual lesions in patients with severe sequelae despite several PTAs.

Surgical reexploration was required in 2 of 10 patients because of hematoma formation. Although no hemodynamic instability was reported, the question arises if recent thrombolysis puts patients at an increased risk for bleeding complications. On the basis of the pharmacokinetics of Alteplase, surgery can be performed safely after an interval of 4 hr. In our cohort, these 2 patients were operated on when we continued LMWH perioperatively and before the routine use of the Ligasure sealing device (Valleylab, Boulder, CO). Currently, we stop LMWH prophylaxis the evening before surgery. We did not have any bleeding complications after these changes in our protocol. Nonetheless, the regular postoperative prescription of anticoagulants in combination with recent surgical trauma and endovascular treatment of fibrotic veins may pose the patients at an increased risk for bleeding complications.

**Limitations**

This case series has several limitations. First, the patency of the vein during follow-up is not checked in all patients with venography. However, routine venography during follow-up in the absence of symptoms is difficult to justify. Some use duplex ultrasonography to assess vein patency during follow-up but the results and sensitivity to assess significant stenosis in the ASV is limited. Therefore, we stopped with the routine use of duplex ultrasonography recently and only use venography as diagnostic imaging technique in patients with acute pUEDVT. We consider a daily activity questionnaire and the Dutch language version of the DASH score as best outcome measures during follow-up considering the limitations of duplex ultrasonography and venography. Second, we did not use the modified Villalta scale as outcome measure to assess severity of PTS complaints. The Villalta scale is originally developed for the assessment of lower-extremity PTS. It is suggested that a modified Villalta scale is superior to the DASH score in assessing outcome after acute pUEDVT. Unfortunately, the modified Villalta scale is not yet validated. Third, baseline questionnaire scores were not obtained before TOD surgery. Therefore, comparison of all used scores before and after surgery is not possible in this cohort. However, follow-up scores can be used to determine the level of functional disability and quality of life, and allow for comparison with other cohorts.

The “test-PTA” is used in addition to venography to assess vein patency after TOD surgery. However, this approach has not been validated to determine vein patency as whether it is combined with venography. Future studies should validate this diagnostic PTA and compare it to venography alone and/or intravascular ultrasound methods.

**CONCLUSIONS**

A same admission treatment algorithm for acute pUEDVT in patients with VTOS including thrombolysis, TA-TOD with extensive venolysis, and immediate venography with PTA is effective with promising short and intermediate results.

**CREDIT AUTHORSHIP CONTRIBUTION STATEMENT**


**REFERENCES**


