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False-negative upper extremity ultrasound in the initial evaluation of patients with suspected subclavian vein thrombosis due to thoracic outlet syndrome (Paget-Schroetter syndrome)

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ABSTRACT

Objective: To assess the utilization and consequences of upper extremity Duplex ultrasound in the initial diagnostic evaluation of patients with suspected subclavian vein (SCV) thrombosis and venous thoracic outlet syndrome (VTOS).

Methods: A retrospective single-center review was conducted for patients that underwent primary surgical treatment for VTOS between 2008 and 2017, in whom an upper extremity ultrasound had been performed as the initial diagnostic test (n = 214). Clinical and treatment characteristics were compared between patients with positive and false-negative ultrasound studies.

Results: There were 122 men (57%) and 92 women (43%) that had presented with spontaneous idiopathic arm swelling, including 28 (13%) with proven pulmonary embolism, at a mean age of 30.7 ± 0.8 years (range 14-69). Upper extremity ultrasound had been performed 23.8 ± 12.2 days after the onset of symptoms, with confirmation of axillary-SCV thrombosis in 169 patients (79%) and negative results in 45 (21%). Of the false-negative ultrasound study reports, only 8 (18%) acknowledged limitations in visualizing the central SCV. Definitive imaging diagnostic (DDI) had been obtained by upper extremity venography in 175 (82%), computed tomography angiography in 24 (11%), and magnetic resonance angiography in 4 (2%). Patients with false-negative initial ultrasound studies were significantly more likely to have DDI within 48 hours than those with a positive ultrasound (44% vs 24%; P = .02). At the time of surgical treatment, the SCV was widely patent following paraclavicular decompression and external venolysis alone in 74 patients (35%). Patch angioplasty was performed for focal SCV stenosis in 76 (36%) and bypass graft reconstruction for long-segment axillary-SCV occlusion in 63 (29%). Patients with false-negative initial ultrasound studies were significantly more likely to require SCV bypass reconstruction than those with a positive ultrasound (44% vs 25%; P = .02).

Conclusions: Duplex ultrasound has significant limitations in the initial evaluation of patients with suspected SCV thrombosis, with false-negative results in 21% of patients with proven VTOS. This is rarely acknowledged in ultrasound reports, but false-negative ultrasound studies have the potential to delay definitive imaging, thrombolysis, and further treatment for VTOS. Initial false-negative ultrasound results are associated with progressive thrombus extension and a more frequent need for SCV bypass reconstruction at the time of surgical treatment. (J Vasc Surg: Venous and Lym Dis 2020;8:118-26.)

Keywords: Subclavian vein; Duplex ultrasound; Upper extremity; Deep vein thrombosis; Thrombolysis; Surgical treatment

Upper extremity deep vein thrombosis (UE-DVT) is relatively uncommon, representing only 10% of all DVT, and is most frequently associated with an underlying secondary cause, such as a central venous catheter, pacemaker wire, malignancy, or pro-thrombotic hematological condition. In contrast, idiopathic “primary” UE-DVT is estimated to occur in approximately 20% to 30% of patients. The most prevalent form of primary UE-DVT is
due to extrinsic compression of the central subclavian vein (SCV) at the level of the costoclavicular space, also termed venous thoracic outlet syndrome (VTOS), which leads to SCV “effort” thrombosis (Paget-Schroetter syndrome).4

The pathophysiology of VTOS is currently understood to involve repetitive dynamic compression and localized injury of the SCV between the first rib, clavicle, anterior scalene muscle, subclavius muscle, and the costoclavicular ligament.4-6 Gradual fibrous constriction of the SCV is accompanied by expansion of collateral vein pathways, such that patients are typically asymptomatic during early stages of this condition. Eventually, thrombosis occurs in the narrowed SCV, along with thrombus propagation into the axillary vein and obstruction of critical venous collaterals, resulting in abrupt clinical symptoms. SCV thrombus forming central to the point of obstruction may also lead to pulmonary embolism, but this is rarely hemodynamically significant and usually asymptomatic. The onset of upper extremity symptoms is frequently perceived to be associated with recent exertion, heavy lifting, or repetitive vigorous overhead use of the upper extremity, which historically gave rise to the term “effort” thrombosis; however, SCV thrombosis is better viewed as an acute or subacute event superimposed on chronic gradual venous obstruction. VTOS thereby represents a “mechanical” anatomical condition secondary to vein compression and injury that is amenable to surgical treatment, rather than a hematomal condition to be managed primarily by anticoagulation.

Clinical suspicion of axillary-SCV thrombosis resulting from VTOS is typically prompted by presentation of an otherwise healthy, relatively young person with the sudden, spontaneous, onset of whole-arm swelling, with or without cyanotic discoloration, in the absence of a known malignancy, central venous catheter, recent arm injury or surgery, or history of DVT.7 Prompt diagnosis of VTOS is important to direct initial anticoagulation and catheter-based venography within a timeframe that permits the potential use of thrombolytic treatment (ideally within 6-8 weeks after the onset of symptoms), as an intermediate step toward definitive surgical treatment.8-16

Duplex ultrasound has been described to have a high level of sensitivity and specificity in the diagnosis of UE-DVT and is widely considered the standard for initial evaluation of this condition.17-21 However, even the strongest advocates of venous ultrasound acknowledge that “…an important limitation of ultrasonography is that visualization and compression of the subclavian and brachiocephalic veins are hampered by the clavicle, which limits the accuracy of ultrasonography in these segments.”21 This limitation makes ultrasonography unsuited for early diagnosis of VTOS, when focal central SCV obstruction has not yet led to distal thrombus extension, and its widespread use raises the likelihood that VTOS will be unrecognized and undertreated. In a previous study of competitive athletes with VTOS, we found that 21 of 32 patients (66%) had a duplex ultrasound as the initial diagnostic study, with false-negative results in 29%.22 Although this raises concern that a false-negative ultrasound might be associated with treatment delay and unsatisfactory outcomes, there is otherwise little information available on ultrasound in evaluation of patients found to have axillary-SCV thrombosis resulting from VTOS.

The purpose of this study was to better assess the utilization and consequences of using upper extremity ultrasound in the initial evaluation of patients with suspected SCV thrombosis and VTOS. To address these issues, we examined clinical and treatment characteristics in a relatively large series of patients that underwent surgical treatment for VTOS, in whom an upper extremity ultrasound had been performed as the initial diagnostic test, and compared these features between patients with positive and false-negative ultrasound studies.

**METHODS**

The study population was derived from patients referred to the Washington University Center for Thoracic Outlet Syndrome at Barnes-Jewish Hospital (St. Louis, Mo) for evaluation and surgical treatment of VTOS between January 2008 and March 2017. Patients with the neurogenic or arterial forms of TOS were excluded from review, as were patients with VTOS undergoing reoperative procedures or operations for threatened hemodialysis access. Detailed information regarding each patient was obtained from a prospectively maintained database and summarized from office notes, hospital charts, imaging studies, operative findings and records from treating physicians, therapists, and vascular laboratories. The study protocol and informed consent were approved by the Human Research Protection Office at Washington
University in St. Louis; each patient provided written informed consent.

Data were collected regarding the initial symptoms and clinical presentation of each patient. Printed ultrasound reports were evaluated for the methods used to identify DVT or venous flow abnormalities, the specific veins involved, and the presence of any statements regarding limitations of the ultrasound study. Certification status of the specific laboratories performing each ultrasound study were obtained by accessing the Inter-societal Accreditation Commission (IAC) website (https://www.intersocietal.org/iac/facilitylist/search.htm). The timing, findings, and results of definitive diagnostic imaging (DDI) studies, such as catheter-based venography, computed tomography angiography (CTA) or magnetic resonance angiography, and any catheter-directed thrombolytic treatment, were determined from printed reports of the relevant investigations and procedures.

Patients were maintained on anticoagulation following evaluation for surgical treatment of VTOS, including physical examination and review of the most recent venography studies. The level of functional disability was assessed using the 11-item version of the Disabilities of the Arm, Shoulder, and Hand (QuickDASH) survey instrument, which has been designed and validated for use in a variety of upper extremity disorders including TOS. Surgical treatment for VTOS was generally recommended within 4 to 6 weeks of thrombolytic therapy to allow time for resolution of acute perivenous inflammation while minimizing the risk of rethrombosis.

All patients underwent standardized paracervical thoracic outlet decompression, including complete anterior and middle scalenectomy, mobilization of the brachial plexus nerve roots, subclavius muscle resection, and complete first rib resection from the transverse process posteriorly and to the level of the sternum anteriorly.23,24 Exposure through the infraclavicular incision was used to initiate external venolysis of the axillary-SCV, which was then continued through the supraclavicular incision to the junction of the SCV with the internal jugular and innominate veins. Inspection, palpation, and intraoperative venography were used to assess the axillary-SCV and direct vein reconstruction was performed if necessary, using patch angioplasty for focal stenosis or bypass graft placement for long-segment occlusion, as previously described.23,24 For occlusions extending into the distal axillary vein, concomitantpectoralis minor tenotomy was used to identify a suitable inflow vein for bypass graft reconstruction. No patients required division of the sternocleidomastoid muscle, partial resection of the clavicle, disruption of the sternoclavicular joint, or transmanubrial extension of the exposure.

Descriptive group data are presented as the mean ± standard error or the frequency (percent incidence). Comparisons between two groups were made using the unpaired t-test with Welch correction (for data with continuous variables) or Fisher’s exact test (for categorical data). All statistical tests were performed using Prism version 4.0c (GraphPad Software Inc, San Diego, Calif), with P values < .05 considered significant.

RESULTS

There were 339 patients who underwent primary operations for VTOS in our institution between January 2008 and March 2017, representing 21% of 1630 surgical procedures performed for all forms of TOS (Fig 1, A). There were 255 patients with VTOS (75%) that had undergone upper extremity ultrasound as the initial diagnostic test, with incomplete data for 41 (only verbal results or insufficiently detailed reports), leaving 214 patients available for the purposes of this study.

The study population consisted of 122 men (57%) and 92 women (43%) with a mean age of 30.7 ± 0.8 years (median 28.0, range 14-69). The age distribution of patients included 54 (25%) younger than age 21 and 160 (75%) older than age 21, with 95% younger than 55 years of age (Fig 1, B). The majority of patients were right-hand dominant (n = 191; 89%) with the dominant side affected in 153 (71%). Patients in the study population described their primary occupation as student (n = 42; 20%), office-based deskwork (n = 42; 20%), athlete (n = 41; 19%), skilled labor (n = 24; 11%), nurse or therapist (n = 15; 7%), manager (n = 12; 6%), homemaker (n = 9; 4%), manual labor (n = 7; 3%), physician (n = 7; 3%), unemployed (n = 7; 3%), or executive (n = 5; 2%). There were 55 patients (26%) referred from the St. Louis metropolitan area, 105 (49%) from the central Midwest region, and 54 (25%) from more distant locations in the United States. The presenting symptoms consisted of arm swelling alone in 122 (57%) and arm swelling with cyanotic discoloration in 92 (43%), with 118 patients (55%) initially presenting to an emergency room and 96 (45%) to a primary care physician. There were 28 patients (13%) with radiographic evidence of pulmonary embolism. The overall mean QuickDASH score upon referral was 26.2 ± 1.6.

Using SVS reporting standards definitions, the timing of clinical presentation was characterized as acute (0 to 14 days) in 195 patients (91%), subacute (14 to 90 days) in 9 patients (4%), and chronic (>90 days) in 10 patients (5%).25 The mean time interval between the onset of arm swelling symptoms and the initial ultrasound was 23.8 ± 12.2 days. The upper extremity ultrasound performed at initial presentation was positive in 169 patients (79%) and negative in 45 (21%).

The positive ultrasound study reports described the distribution of DVT in both the axillary and subclavian veins (n = 59; 35%); the subclavian vein alone (n = 52; 31%); the basilic, axillary, and subclavian veins (n = 41; 24%); the basilic and axillary veins (n = 5; 3%); the axillary vein alone (n = 2; 1%); flow abnormalities consistent with proximal
obstruction but no defined thrombosis \( (n = 4; 2\%) \); and unspecified \( (n = 6; 3\%) \). Thirteen \( (8\%) \) of the positive ultrasound study reports indicated the potential presence of SCV compression within the thoracic outlet. Of the false-negative ultrasound study reports, only 8 \( (18\%) \) included a description of limitations of the study to visualize the central SCV or the possibility of central venous obstruction at the thoracic outlet, although 14 \( (31\%) \) of the laboratories performing these studies had current IAC certification for vascular testing. There were no significant differences between the positive and false-negative ultrasound groups with regard to age, gender, side affected, pattern or timing of symptomatic presentation, incidence of pulmonary embolism, or QuickDASH scores (Table I).

For the overall study population, DDI was obtained by catheter-based upper extremity venography in 175 \( (82\%) \). CTA was performed in 24 \( (11\%) \) and magnetic resonance angiography in 15 \( (7\%) \) patients, primarily when there had been longstanding symptoms. The interval between the initial ultrasound and DDI was 48.9 ± 14.2 days and the interval between the onset of symptoms and DDI was 72.7 ± 18.7 days. There were only 86 patients \( (40\%) \) that had DDI within 48 hours of ultrasound examination, whereas there were 58 \( (27\%) \) in whom DDI was performed more than 14 days after the initial ultrasound. Venous thrombolysis was performed in 142 patients \( (66\%) \), with inclusion of balloon angioplasty in 115 \( (54\%) \). There were no significant differences between the positive and false-negative ultrasound groups with regard to the interval between symptoms and initial ultrasound, the interval between initial ultrasound and DDI, the proportion of patients having DDI within 14 days of the onset of symptoms or the initial ultrasound, or the proportion of patients undergoing thrombolysis or balloon angioplasty treatment; however,
patients with a positive initial ultrasound were significantly more likely to have DDI performed within 48 hours than those with a false-negative ultrasound (44% vs 24%; \( P = .02 \); Table II).

All patients were maintained on anticoagulation after DDI with a mean interval between DDI and surgical treatment of 68.2 ± 7.5 days. For those that had undergone thrombolysis (n = 142), the mean interval between

Table I. Presenting characteristics of 214 patients with subclavian vein thrombosis and venous thoracic outlet syndrome that had undergone upper extremity ultrasound as the initial diagnostic test

<table>
<thead>
<tr>
<th></th>
<th>U/S positive (n = 169)</th>
<th>U/S negative (n = 45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30.4 ± 0.9</td>
<td>31.9 ± 2.0</td>
<td>495°</td>
</tr>
<tr>
<td>Male</td>
<td>99 (59)</td>
<td>23 (51)</td>
<td>400°</td>
</tr>
<tr>
<td>Right side affected</td>
<td>126 (75)</td>
<td>32 (71)</td>
<td>703°</td>
</tr>
<tr>
<td>Presented to ER vs PCP</td>
<td>96 (57)</td>
<td>22 (49)</td>
<td>400°</td>
</tr>
<tr>
<td>Local metropolitan area patient</td>
<td>44 (26)</td>
<td>11 (24)</td>
<td>1.00°</td>
</tr>
<tr>
<td>Regional area referral</td>
<td>86 (51)</td>
<td>19 (42)</td>
<td>319°</td>
</tr>
<tr>
<td>Distant (out-of-region) referral</td>
<td>39 (23)</td>
<td>15 (33)</td>
<td>178°</td>
</tr>
<tr>
<td>Acute presentation (0-14 days)</td>
<td>157 (93)</td>
<td>38 (84)</td>
<td>0.84°</td>
</tr>
<tr>
<td>Subacute presentation (14-90 days)</td>
<td>5 (3)</td>
<td>4 (9)</td>
<td>0.95°</td>
</tr>
<tr>
<td>Chronic presentation (&gt;90 days)</td>
<td>7 (4)</td>
<td>3 (7)</td>
<td>442°</td>
</tr>
<tr>
<td>Arm swelling alone</td>
<td>94 (56)</td>
<td>28 (62)</td>
<td>499°</td>
</tr>
<tr>
<td>Swelling and cyanotic discoloration</td>
<td>75 (44)</td>
<td>17 (38)</td>
<td>499°</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>21 (12)</td>
<td>7 (16)</td>
<td>620°</td>
</tr>
<tr>
<td>Initial QuickDASH</td>
<td>26.4 ± 1.8</td>
<td>25.7 ± 3.4</td>
<td>856°</td>
</tr>
</tbody>
</table>

ER, Emergency room; PCP, primary care physician. QuickDASH, 11-item version of the Disabilities of the Arm, Shoulder, and Hand survey instrument. SCV, subclavian vein; U/S, ultrasound; VTOS, venous thoracic outlet syndrome.

Patients were identified that had primary surgical treatment for VTOS between 2008 and 2017 and had U/S performed as the initial diagnostic test (n = 214). For each item assessed, the data shown indicate the mean ± standard error for continuous measures or the number of patients (%) for categorical variables.

°Unpaired t-test.

Table II. Diagnosis and initial treatment of 214 patients with subclavian vein thrombosis and venous thoracic outlet syndrome

<table>
<thead>
<tr>
<th></th>
<th>U/S positive (n = 169)</th>
<th>U/S negative (n = 45)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms to U/S (days)</td>
<td>23.3 ± 15.1</td>
<td>25.5 ± 12.6</td>
<td>911°</td>
</tr>
<tr>
<td>Symptoms to U/S &gt;14 days</td>
<td>12 (7)</td>
<td>6 (13)</td>
<td>224°</td>
</tr>
<tr>
<td>Symptoms to U/S &gt;90 days</td>
<td>7 (4)</td>
<td>3 (7)</td>
<td>442°</td>
</tr>
<tr>
<td>U/S to DDI (days)</td>
<td>43.0 ± 13.8</td>
<td>71.1 ± 43.9</td>
<td>544°</td>
</tr>
<tr>
<td>U/S to DDI &lt;48 hours</td>
<td>75 (44)</td>
<td>11 (24)</td>
<td>.017°</td>
</tr>
<tr>
<td>U/S to DDI &gt;14 days</td>
<td>44 (26)</td>
<td>14 (31)</td>
<td>351°</td>
</tr>
<tr>
<td>U/S to DDI &gt;90 days</td>
<td>13 (8)</td>
<td>5 (11)</td>
<td>544°</td>
</tr>
<tr>
<td>Symptoms to DDI (days)</td>
<td>66.3 ± 20.4</td>
<td>96.6 ± 45.9</td>
<td>549°</td>
</tr>
<tr>
<td>Symptoms to DDI &gt;14 days</td>
<td>50 (30)</td>
<td>18 (40)</td>
<td>208°</td>
</tr>
<tr>
<td>Symptoms to DDI &gt;90 days</td>
<td>20 (12)</td>
<td>7 (16)</td>
<td>461°</td>
</tr>
<tr>
<td>DDI Type: venogram</td>
<td>140 (83)</td>
<td>35 (78)</td>
<td>514°</td>
</tr>
<tr>
<td>DDI Type: MRA</td>
<td>11 (7)</td>
<td>4 (9)</td>
<td>525°</td>
</tr>
<tr>
<td>DDI Type: CTA</td>
<td>18 (11)</td>
<td>6 (13)</td>
<td>600°</td>
</tr>
<tr>
<td>Thrombolysis performed</td>
<td>114 (67)</td>
<td>28 (62)</td>
<td>595°</td>
</tr>
<tr>
<td>Balloon angioplasty</td>
<td>94 (56)</td>
<td>21 (47)</td>
<td>315°</td>
</tr>
</tbody>
</table>

ER, Emergency room; PCP, primary care physician. QuickDASH, 11-item version of the Disabilities of the Arm, Shoulder, and Hand survey instrument. SCV, subclavian vein; U/S, ultrasound; VTOS, venous thoracic outlet syndrome.

Patients were identified that had primary surgical treatment for VTOS between 2008 and 2017 and had U/S performed as the initial diagnostic test (n = 214). For each item assessed, the data shown indicate the mean ± standard error for continuous measures or the number of patients (%) for categorical variables.

°Unpaired t-test.

ēFisher’s exact test.

ēP < .05.
thrombolysis and surgical treatment was $50.3 \pm 6.8$ days: $27.2 \pm 4.7$ days for local patients ($n=40$), $47.3 \pm 6.2$ days for regional referral patients ($n=63$) and $80.6 \pm 22.2$ days for distant referral patients ($n=38$). Each patient underwent paraclavicular thoracic outlet decompression with complete resection of the first rib and external venolysis of the axillary SCV. In 74 patients (35%), the axillary SCV was widely patent, by visual inspection, palpation, and intraoperative venography, following decompression and external venolysis alone. In 76 patients (36%), there remained a focal high-grade SCV stenosis that was treated by patch angioplasty, whereas 63 patients (29%) had a long-segment SCV occlusion for which axillary-innominate vein bypass was performed. In 52 of these patients (24%), the venous occlusion extended laterally underneath the pectoralis minor muscle, such that pectoralis minor tenotomy was required to expose a patent axillary vein of suitable caliber for bypass reconstruction.

Although there were no significant differences between the positive and false-negative ultrasound groups with regard to the incidence of external venolysis alone or patch angioplasty reconstruction, patients that had a false-negative ultrasound as the initial diagnostic study were significantly more likely to require axillary-SCV bypass than those who had a positive ultrasound as the initial diagnostic test (44% vs 25%; $P=0.017$; Fig 2).

DISCUSSION

The approach to diagnosis and management of VTOS varies between different physicians and institutions, and the most effective strategy for this condition continues to elicit debate. In this study, we examined the clinical presentation for a large number of patients with proven VTOS to assess the utilization and consequences of using upper extremity ultrasound in the initial evaluation of patients with suspected SCV thrombosis. The most important findings were: (1) initial duplex ultrasound studies were false negative in 21% of patients with VTOS; (2) the incidence of documented pulmonary embolism was 13%; (3) there were disappointingly long intervals between symptom onset, clinical suspicion, and definitive diagnosis; (4) patients with a positive initial ultrasound were nearly twice as likely to have definitive imaging performed within 48 hours than those with a false-negative ultrasound; (5) there was relatively low utilization of thrombolysis as part of initial management; and (6) at the time of surgical treatment, patients with a false-negative ultrasound as the initial diagnostic study were significantly more likely to have a long-segment SCV occlusion requiring bypass reconstruction than those who initially had a positive ultrasound.

Treatment protocols for idiopathic UE-DVT that are based on anticoagulation alone are flawed by extrapolation from regimens designed for lower extremity DVT, often not taking into account the mechanical (surgically correctable) pathophysiology underlying VTOS. Studies of treatment for VTOS with anticoagulation alone have consistently demonstrated suboptimal outcomes, whereas better outcomes for this condition are reported with prompt SCV thrombolysis and definitive surgical treatment. Based on the present study and other investigations, we have developed a comprehensive management algorithm for the diagnosis and treatment of SCV thrombosis (Fig 3). Satisfactory thrombolysis allows
clearing of clot from the axillary and distal subclavian veins but is unlikely to be successful more than 6 to 8 weeks after the onset of symptoms. Prompt recognition of axillary-SCV thrombosis is therefore crucial to direct patients toward early venography and thrombolysis. Hematologic and oncologic evaluations are generally not needed in this population and should not delay definitive imaging, thrombolysis, or surgery. The optimal timing is still uncertain, but surgical treatment should generally be performed within 4 to 6 weeks of thrombolysis to minimize the chance of rethrombosis. Surgical treatment within the same hospitalization as thrombolysis is also an acceptable approach.\(^\text{29}\) Once surgical decompression has been achieved, direct or indirect (endovascular) intervention to restore a patent subclavian vein can be successfully undertaken, either in the operating room or in a delayed manner through interventional approaches, as described in some protocols.\(^\text{5,6,26,27,30}\) The principal limitation in the treatment of VTOS is for patients who have long-segment occlusion of the SCV that persists despite adequate decompression; in nearly every published series, such patients represent 5% to 20% of those presenting for surgery.\(^\text{6}\) Although this situation is managed differently in different protocols, there remain some patients who cannot be satisfactorily treated and for whom long-term anticoagulation may be the only remaining option. Overall management of VTOS should consequently be aimed at minimizing the number of patients with chronic long-segment occlusions. The methods used in
the initial evaluation of patients with suspected axillary-SCV thrombosis are therefore important to permit prompt and effective treatment toward this goal, and a negative duplex ultrasound should not be used to exclude a diagnosis of VTOS.

There are inherent technical limitations in the use of duplex ultrasound for evaluation of the central SCV. These include the abbreviated acoustic window through which to visualize the SCV due to the overriding clavicle, the inability to compress the SCV because of anatomic constraints, the presence of large transverse collateral veins that may be misinterpreted to represent the SCV, and high flow through venous collaterals that may minimize hemodynamic alterations even in the presence of central SCV obstruction. Although these limitations are acknowledged by experts in the field and in various publications, they are often overlooked in clinical practice and only rarely mentioned in clinical ultrasound reports. It is not clear that these limitations are unique to noncertified vascular laboratories because 31% of the false-negative ultrasound evaluations in this study were performed in IAC-certified laboratories. The usefulness of ultrasound in the initial evaluation of patients with suspected SCV thrombosis is thereby often misunderstood and overstated. Although not addressed in this study, the same concerns exist for the use of ultrasound in postoperative follow-up of patients after treatment for VTOS, where reports describing SCV patency based solely upon ultrasound should be interpreted with caution.

Clinicians ordering upper extremity ultrasound testing to exclude DVT may not be aware of the limitations of these studies and, as found in the current study, the reports of ultrasound testing infrequently state the limitations in assessing the central SCV. This may lead clinicians to forego further evaluation or specialist referral when ultrasound testing is reported to be “negative,” rather than treat with presumptive anticoagulation and obtain definitive imaging. For patients with SCV thrombosis and VTOS, this approach may delay or eliminate the potential use of thrombolytic therapy, resulting in propagation of thrombus from a focal lesion to a long-segment axillary-SCV occlusion that cannot be readily treated at the time of surgery. Indeed, in this study the incidence of long-segment SCV occlusion at the time of surgery was nearly twofold higher in patients that had a false-negative ultrasound at initial evaluation. Unfortunately, in this study, only 11% of the reports describing false-negative ultrasound studies had included a statement of limitations. We therefore recommend that vascular laboratory reports and IAC guidelines reflect these concerns by more clearly stating the limitations of ultrasound in assessing the central SCV, especially when studies are otherwise negative for DVT in the distal subclavian, axillary, basilic, and brachial veins.

One of the main limitations of this study is that it is retrospective in nature and the type of data collected do not allow determination of the overall sensitivity, specificity, or accuracy of upper extremity ultrasound for UE-DVT. The incidence of false-negative ultrasound studies was thereby higher than would be observed in a broader screening study of all patients presenting with arm swelling. Another limitation is that the initial clinical presentation and diagnosis of SCV thrombosis took place at diverse locations and practice settings and by a variety of different physicians; thus, it was not always clear if the initial ultrasound examination was done in an IAC-certified vascular laboratory or if each patient was evaluated by a vascular specialist. We also did not have access to complete descriptions of the methodology used in the initial ultrasound examinations, being limited to the information obtained from the printed ultrasound reports. Nonetheless, one of the main strengths of this study is that it reflects real-world clinical practice regarding the presentation of patients with possible UE-DVT and VTOS. Additional strengths are that all patients underwent treatment with a standardized protocol involving complete thoracic outlet decompression and flexible SCV reconstruction, depending on operative findings, and that there were a large number of study subjects for a relatively uncommon condition. We cannot expect to eliminate use of upper extremity ultrasound in the initial evaluation of suspected SCV thrombosis and possible VTOS, but hope our findings will bring more attention to this issue by vascular laboratories and specialists.

CONCLUSIONS

Duplex ultrasound is limited in the initial evaluation of patients with suspected SCV thrombosis, with false-negative results in 21% of patients with proven VTOS. This is rarely acknowledged in ultrasound reports, but false-negative ultrasound studies have the potential to delay definitive imaging, thrombolysis, and further treatment for VTOS. False-negative ultrasound results are associated with progressive thrombus extension and a more frequent need for SCV bypass reconstruction at the time of surgical treatment. Our findings suggest that one step toward improving the diagnosis and treatment of SCV thrombosis would be to only employ ultrasound with understanding that a negative study should not delay definitive imaging, thrombolysis, and surgical intervention.

AUTHOR CONTRIBUTIONS

Conception and design: EB, AA, BR, RT
Analysis and interpretation: EB, AA, WO, BR, RT
Data collection: EB, AA, RT
Writing the article: EB, RT
Critical revision of the article: EB, AA, WO, BR, RT
Final approval of the article: EB, AA, WO, BR, RT
REFERENCES


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