Deep Venous Thrombosis of the Upper Extremity: A Reappraisal

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SUMMARY Deep venous thrombosis (DVT) of the upper extremity is an unusual thrombotic event (1–2% of all DVT) which can be conveniently divided into two categories, traumatic (including “stress”) and spontaneous. The spontaneous form is not reported as often in the literature, but occurs more commonly than the traumatic form. There is an increased left-sided predominance in spontaneous DVT compared with the traumatic form, where a right-sided predominance exists. Possible anatomical and physiological explanations are offered for the left-sided predominance in spontaneous DVT of the upper extremity. The thrombogenesis of DVT of the upper extremity is compared with DVT of the lower extremity. An analysis of responses to therapy and considerations for other therapeutic approaches are offered.

DEEP VENOUS THROMBOSIS (DVT) of the lower extremity is widely recognized as a leading cause of morbidity and mortality in adult patients.1,2 DVT of the upper extremity is much less common, occurring with an incidence estimated at 1–2% of that of DVT of the lower extremity.3,4 We were interested in this disparity and the possibility that study of DVT of the upper extremity might provide some insights into the broader problem of venous thromboembolism. We were struck by significant differences between our series of patients and patients reported previously,5–7 and therefore reviewed our experience with DVT of the upper extremity and the available literature. Our analysis suggests that:

1) There is no agreement regarding the best terminology for the subgroups of this disorder. We use a scheme (table 1) similar to that of Coon and Willis,4 which divides thrombosis into traumatic and spontaneous (nontraumatic). Stress, or effort, thromboses are a subset of the traumatic category,4 as their pathogenesis and clinical importance seem closely similar to those of a thrombosis due to clavicular fracture. In contrast, we feel that other “secondary” forms of thromboses (i.e., congestive heart failure, malignancy) have different characteristics (and perhaps pathogenesis) from those resulting from clavicular fracture or “stress.”

2) The relative incidence of the two groups is different from that frequently suggested by the literature, as selection bias in favor of stress thromboses exists in a number of review articles. Preferential lateralization occurs toward the left side in the spontaneous thromboses in contrast to the usual right-sided predominance in “stress” thromboses. Plausible anatomical and physiological reasons explain this preferential localization.

3) Differences and similarities exist between thrombogenesis in the deep veins of the lower and upper extremities.

4) Prompt administration of anticoagulants is the preferred therapy, and anatomical localization of DVT of the upper extremity may be useful in predicting the late outcome of therapy.

Materials and Methods

We studied 12 patients with 14 clinical episodes of DVT of the upper extremity. Most of them were referred to us by the physicians at hospitals affiliated with the University of Utah, but were otherwise unselected. Bias can be inherent in any referral population, but we feel that our patients are at least as representative of the disorder as patients reported...
from vascular surgery services. The diagnosis was made in all cases by typical physical findings and confirmed in 10 episodes by venography and in another two by Doppler ultrasound examination. Long-term outcome was assessed by direct patient exam, chart review, or interview with the patient.

Results

Five patients (one episode each) had a traumatic etiology, including three cases of stress thrombosis. There were seven patients (nine episodes) with spontaneous thrombosis. The age, sex, involved side, dominant hand, and accompanying clinical diagnoses are listed in tables 2 and 3. The group with traumatic thrombosis had a lower mean age (30 years vs 41 years) and the location of the stress thromboses, of which we had very few, indicates a right-sided predominance (3 of 3), as has been commonly reported, particularly in right-handed people. However, in the thromboses related to or associated with another illness, there were more thromboses on the left side than on the right (six of nine).

No associated illness predominated in our spontaneous group but, as is indicated in the literature, plausible predisposing factors included polycythemia, thrombocytosis, quadriplegia, probable antithrombin III deficiency, malignancy, intravenous pyelography, and systemic venous hypertension (specifically, congestive heart failure). In three patients, two or more risk factors existed.

The therapy, duration of therapy, and both short- and long-term outcome are described in table 4. All of the patients had resolution of their pain and edema during the initial hospitalization and therefore had good short-term outcome. One episode of pulmonary embolism occurred during the acute stage of the illness but that patient had simultaneous acute DVT of his lower extremity. All patients were treated with elevation of the arm and all but one received anticoagulants, usually intravenous heparin for 7-10 days, followed by variable periods of oral anticoagulant therapy. Long-term outcome was assessed at an average of 21 months after the thrombosis (range 3-43 months). Six patients were completely without symptoms in the affected arm at follow-up, four had minimal residual symptoms, none had significant residual symptoms and two could not be contacted.

Discussion

Descriptions of DVT of the upper extremity in the past have usually emphasized "stress thrombosis," which is most frequent in healthy young men and typically follows unusual arm exertion. Such series have noted a predominance in the right arm, presumably because most people are right-handed and therefore use it for unusual or difficult tasks. Few reports have dealt with spontaneous DVT of the upper extremity but most of those that have supplied sufficient data support our observation of an equal or increased incidence in the left arm. Loring reviewed 83 reported cases (and added four of his own) of patients with congestive heart failure who developed DVT of the upper extremity. The clinical diagnosis was confirmed by autopsy in 49 cases (85 of the 87 were New York Heart Association functional class IV) and by venography in nine. There was a marked predilection for the left side, with 58.6% of the thromboses on the left only, 14.9% bilateral, and only 26.4% exclusively on the right. Several mechanisms may be responsible.

First, there is a significant difference between the right and left sides in the anatomy of the venous system of the upper thorax (fig. 1). The two brachiocephalic (innominate) veins are asymmetrical, the left being 6 cm compared with 2.5 cm on the right.

Second, the left brachiocephalic vein is bounded anteriorly by the clavicle and upper sternum and posteriorly by the right brachiocephalic, left common carotid, and left subclavian arteries. This cir-
cumstance may be analogous to that of the left common iliac vein which is usually crossed and occasionally compressed by the right common iliac artery, which may explain the increased incidence of iliofemoral venous thrombosis in the left lower extremity compared with the right. \(^{12,13}\) The validity of applying this explanation to the left brachiocephalic vein is supported by the occasional finding of unilateral left jugular venous distension in type I dissection of the aorta as the vein is compressed by the enlarging aorta;\(^{14}\) in fact, upper extremity thrombosis has been reported\(^{16}\) as a forerunner of an aortic arch aneurysm. Accordingly, such anatomic confines might represent a latent or partial obstruction which could be converted to a high-grade obstruction when an increased central venous pressure, resulting from heart failure, leads to dilatation of the great veins.

Third, it is possible that obstruction to flow might occur even without clear anatomical obstruction if flow patterns were disrupted:

1) While the importance of flow patterns in veins isn't known, areas of eddy current formation and stasis might increase the risk of thrombosis in veins as they do in arteries. If so, the left brachiocephalic vein should be at greater risk as several of its tributaries (internal jugular, inferior thyroidal, internal thoracic) enter at nearly right angles (fig. 1), a situation known to create eddy currents in high flow systems. The tributaries of the right brachiocephalic vein enter at more acute angles and should be less disruptive to flow. This point is admittedly speculative.

2) In the erect subject the relatively horizontal course of the left brachiocephalic vein could lead to a decreased flow rate compared with the more vertical and direct route of the right brachiocephalic vein.

3) The entrance of the veins from the upper ex-

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**Table 3. Spontaneous DVT of the Upper Extremity**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Involved arm</th>
<th>Dominant hand</th>
<th>Underlying illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>59</td>
<td>M</td>
<td>Left</td>
<td>Unknown</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>G</td>
<td>57</td>
<td>M</td>
<td>Left</td>
<td>Right</td>
<td>Chronic bronchitis; cor pulmonale, polycythemia</td>
</tr>
<tr>
<td>H</td>
<td>28</td>
<td>M</td>
<td>Left</td>
<td>Right</td>
<td>Probable antithrombin III deficiency, IVP</td>
</tr>
<tr>
<td>I</td>
<td>22</td>
<td>M</td>
<td>Right</td>
<td>Right</td>
<td>Uncategorized coagulation abnormality</td>
</tr>
<tr>
<td>J</td>
<td>53</td>
<td>M</td>
<td>Right</td>
<td>Unknown</td>
<td>Chronic bronchitis; cor pulmonale</td>
</tr>
<tr>
<td>K</td>
<td>34</td>
<td>M</td>
<td>Right</td>
<td>Left</td>
<td>Mediastinal lymphoma; after surgery and irradiation</td>
</tr>
<tr>
<td>L</td>
<td>48</td>
<td>M</td>
<td>Left</td>
<td>Right</td>
<td>Quadriplegia; polycythemia rubra ver with thrombocytosis</td>
</tr>
<tr>
<td></td>
<td>49</td>
<td></td>
<td></td>
<td>Left</td>
<td></td>
</tr>
</tbody>
</table>

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**Table 4. Thrombus Location and Treatment Results**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Proximal extent of thrombus</th>
<th>Anticoagulant therapy</th>
<th>Follow-up results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traumatic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Subclavian</td>
<td>None</td>
<td>Normal - 5 mos.*</td>
</tr>
<tr>
<td>B</td>
<td>Axillary</td>
<td>Heparin/warfarin</td>
<td>Mild pain after exercise - 10 mos.</td>
</tr>
<tr>
<td>C</td>
<td>No venogram</td>
<td>Heparin/warfarin</td>
<td>Normal - 1 mos.; lost to follow-up</td>
</tr>
<tr>
<td>D</td>
<td>Axillary</td>
<td>Heparin/warfarin</td>
<td>Occasional mild pain after exercise - 3 mos.</td>
</tr>
<tr>
<td>E</td>
<td>Subclavian</td>
<td>Heparin/warfarin</td>
<td>Normal - 17 mos. (pain after exercise for initial 6 mos.)</td>
</tr>
</tbody>
</table>

| Spontaneous |                                  |                       |                   |
| F           | Subclavian                     | Heparin/warfarin      | Normal - 12 mos.* |
| G           | Subclavian                     | Heparin/warfarin      | Normal - 30 mos.* |
| H           | No venogram                    | Heparin/warfarin      | Lost to follow-up |
| I           | Axillary                       | Heparin/warfarin      | Normal - 37 mos.  |
| J           | Axillary                       | Heparin/warfarin      | Normal - 27 mos.  |
| K           | Subclavian                     | Heparin/warfarin      | Mild pain after exercise - 10 mos. |
| L           | Subclavian                     | Heparin/warfarin      | No pain or edema - 43 mos. (recurrence at 5 mos.) |
| Subclavian  | Heparin/warfarin              | No pain or edema - 38 mos. |

*Deceased.
tremity into the thorax and the collapsible nature of venous walls combine to create a situation in which segments of the veins may collapse and potentially lead to some obstruction to flow. Strandness and Sumner have elaborated upon earlier observations which describe this phenomenon (vascular waterfall), including the differences which occur during flow through horizontal versus vertical collapsible tubes. The differences include resistance to flow in horizontal tubes. This facet of the phenomenon may help to explain the increased incidence of thromboses on the left side, as the left brachiocephalic vein would have resistance to flow while the subject is either supine or erect since its path is largely horizontal in either position. In contrast, the right side would have an increased resistance only when the subject is supine since its path is largely vertical in an erect subject (fig. 1).

4) Changes in intrapleural pressure significantly affect flow rates in the inferior vena cava and might logically be expected to do the same in the superior vena cava and its tributaries. Studies which have sought to define the importance of such pressure changes have shown significant changes in superior vena caval flow rates with coughing. Deep breathing and the Valsalva and Müller maneuvers, all of which have marked effects in the inferior vena cava, have less effect in the superior vena cava. We do not know whether the right and left brachiocephalic veins are equally influenced by such maneuvers, so we cannot implicate pleural pressure changes in thrombus localization.

Finally, Loring reports that more than half of the thromboses he studied were at the confluence of the left internal jugular and subclavian veins. In most people the thoracic duct enters at the same point, raising the possibility that the inflow of lymph might include a thromboplastic substance. For example, an elevated concentration of low-density lipoprotein might increase the tendency for platelet aggregation as has been shown in patients with type II hyperlipoproteinemia. The rise in serum free fatty acid concentration, which appears several hours postprandially, results at least in part from lymph flow via the thoracic duct. The highest serum concentration of free fatty acids would be expected to occur in the portion of the left brachiocephalic vein just proximal to the ductal entrance before complete admixture of lymph with venous blood has occurred. The significance of such a localized rise in serum concentration of free fatty acids rests on the demonstration that thrombosis can be induced by an increased free fatty acid concentration, particularly with long chain saturated fatty acids.

Why does DVT of the upper extremity occur with an incidence estimated at only 1–2% of that of DVT of the lower extremity? There is no analog to the soleal venous network of the lower extremity in the upper extremity. These veins, which become progressively more patulous with age, are believed to be the initiating site of most DVT in the lower extremity, at least partly because of stagnation when the patient is recumbent. Even in patients confined to bed, cessation of arm motion and stagnation are less likely to occur than cessation of leg motion, as long as the patient is conscious; if there is less hydrostatic pressure in the arms than in the lower extremity;
increased fibrinolytic activity has been reported in the venous endothelium of the upper extremity compared with the lower extremity. 30, 34

When managing a patient with DVT of the upper extremity, the clinician must decide on the optimal treatment. As we reviewed our own experience and the literature, we noted several points.

1) Several authors stressed the high incidence (up to 95%) of residual deficit in those patients treated "conservatively" 5, 6, 9 and used this as a basis for recommending a more aggressive approach using thrombectomy. 5, 6, 9, 30, 36

2) “Conservative” management means different things to different investigators, including a variable mixture of heat, elevation, and anticoagulants. Details of the anticoagulant therapy are frequently absent but in many instances it was clearly inadequate. In those studies in which the patients were promptly treated with heparin, the incidence of residual disability seems to have been significantly less. 4, 37 Thus, the higher incidence of residual disability after “conservative management” may reflect one or both of two possibilities. First, since these reports are primarily from surgical groups, there might be a selection bias toward more severe disease. Second, the anticoagulant therapy in many settings was suboptimal, particularly where only oral agents were used since it takes 4–7 days to get an antithrombotic (in contrast to an anticoagulant) effect. 38, 39 We are unaware of a well-designed surgical trial and would argue against routine thrombectomy on the basis of the experience with iliofemoral thrombectomy where it has been shown that thrombi recur quickly after operation. 40–42

3) Tilney et al. have suggested that recanalization, as judged by venography, is less likely to occur in DVT of the upper extremity than of the lower extremity. 9 This is surprising, since fibrinolytic activity is reported to be higher in arm veins than in veins of the lower extremity. 30, 34 If conservatively treated thrombi of the upper extremity are less likely to recanalize, then the application of fibrinolytic therapy might offer some advantage. The few reported instances of streptokinase therapy in DVT of the upper extremity 44–46 offer inconclusive results.

4) The data of Adams et al. 4 suggest that the location of the thrombus may be important in the long-term outcome, although our series does not show such a relationship, probably because of the favorable outcome, even in the cases of subclavian involvement. When the cases of Adams et al. are analyzed by site of involvement, virtually all patients with long-term disability had involvement of the subclavian vein (10 of 11 patients with poor outcome in whom the extent of the thrombus was given). Conversely, in their two patients with a good long-term result in whom the extent was given, involvement was limited to the axillary vein. Such a correlation is plausible, since potential collateral pathways are less plentiful as the site of thrombosis becomes more proximal. Caution should be applied in interpreting this analysis, since we excluded almost half of their patients because they had no venograms to define the extent of the thrombus.

We are using the following therapeutic approach:

1) Treatment is instituted with a loading dose of heparin to provide an immediate antithrombotic effect following which the heparin dose is adjusted to maintain the partial thromboplastin time at 1.5–2 times control. 57 Oral anticoagulants are begun simultaneously and then used solely after a minimum of 7 days of heparin therapy. The aim is twofold: to prevent the further proximal propagation of the thrombus and occlusion of potential collateral pathways and to minimize the incidence of pulmonary embolism which in some series of patients has been estimated to be as high as 12%. 6

2) The arm is elevated to allow gravity and the resultant hydrostatic pressure to work for the patient. Presumably, this increases flow through the high resistance venous collaterals and the inherent partial collateral circulation of any venous bed, i.e., the lymphatic circulation. 48

3) Heat is applied only for symptomatic relief.

4) After the acute episode is treated, the patient is evaluated for predisposing factors, either local anatomic abnormalities or systemic disease which would predispose to DVT.

Acknowledgement
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