

Editorial Focus

Deep venous thrombosis of the upper extremity: Is thrombophilia a relevant clinical issue?

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Upper extremity deep-vein thrombosis (UE-DVT) usually refers to thrombosis of the axillary or subclavian veins. Thrombosis may develop spontaneously, as a complication of a central venous catheter (CVC) or in cancer. Historically, UE-DVT was regarded a self-limiting and rather benign disease. However, data from prospective cohort studies and registries demonstrated that significant complications such as pulmonary embolism, superior vena cava syndrome or postthrombotic syndrome may occur (1–3).

Spontaneous development of UE-DVT is relatively rare and accounts for less than 5% of all cases with DVT. Thrombosis of the veins draining the upper extremity was first postulated as a cause of acute pain and swelling of the arm by Sir James Paget in 1875 (4). Subsequently, von Schroetter in 1884 related the clinical syndrome to thrombotic occlusion of the axillary and/or the subclavian veins then named the Paget-von Schroetter syndrome (5). Since it was observed that thrombosis often occurred following unusual strenuous exercise of the affected arm or shoulder the term “effort” thrombosis (“thrombose par effort”) was used to describe UE-DVT in the often young and physically active individuals. It became evident, that a compressive anatomic anomaly at the thoracic outlet predisposed patients to the effort related development of UE-DVT (thoracic outlet syndrome).

Wider use of CVC in cancer or other severe medical conditions contributed to an increased clinical importance of UE-DVT in the past few decades. Actual population based data revealed that more than 60% of all UE-DVT patients had a history of recent CVC placement at the corresponding upper extremity (6). The presence of an indwelling CVC and cancer was found to be the most powerful independent predictor of UE-DVT. Recent large-scaled registries have also provided contemporary profiles of patients with UE-DVT underlining the paramount role of CVC placement and cancer for both development and outcome of UE-DVT (2).

Apart from the local and site-specific risk factors for UE-DVT mentioned above most of our knowledge about the role of other risk factors for venous thromboembolism (VTE) comes from studies with patients suffering from lower extremity deep-

vein thrombosis (LE-DVT), which is by far the most frequent localization of thrombotic disease. The specific impact of hereditary and acquired thrombophilia has been extensively studied in LE-DVT with consistent and reproducible prevalence and risk estimations. By contrast, prevalence data of thrombophilia in UE-DVT patients are sparse and limited to some few, mostly observational small studies with varying results ranging from prevalences not different from the general population up to values found in unselected LE-DVT cohorts.

In this issue of *Thrombosis and Haemostasis* Linnemann et al. present prevalence data of thrombophilia based on the currently largest series of 150 consecutive patients with UE-DVT (7). Patients were retrieved from the single center MAISTHRO-registry on thromboembolism and were compared to 300 age- and sex-matched control patients with LE-DVT. Similar to other registries the rate of CVC or cancer related UE-DVT was approximately 60%. Overall, Linnemann et al. (7) found at least one thrombophilic factor (factor V Leiden mutation, prothrombin G20210A mutation, antiphospholipid antibodies, high factor VIII levels, protein C, – S, -antithrombin deficiency) in 34% of all patients. Prevalence was considerably lower compared to the rate of 55.3% in the control group with LE-DVT. Meaningful differences in distribution of any single thrombophilia between the two localizations of venous thrombosis were not detected due to small numbers.

Although less prevalent than in LE-DVT, thrombophilia appears to be a rather frequent finding in UE-DVT. Do these observations implicate screening for thrombophilia in UE-DVT? Irrespective of the accepted role of thrombophilia as a risk factor for thromboembolism in general, the answer most probably is “no”. As repeatedly documented, CVC and cancer are the predominant risk factors for roughly two third of all UE-DVT patients, whereas in spontaneous UE-DVT arm position-dependent compression of the subclavian vein appears to be the most critical causative factor for development of UE-DVT. In both groups additional detection of thrombophilia is very unlikely to affect clinical management. In the remaining small group of patients with a primary UE-DVT, screening for thrombophilia might be poten-

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Received July 22, 2008
Accepted July 22, 2008

Prepublished online August 14, 2008
doi:10.1160/TH08-07-0463

tially advisable as data indicate a higher relative risk of recurrent thromboembolism in first episode spontaneous UE-DVT and thrombophilia (8). However, as absolute risk for recurrence is low, and data on the benefit of prolonged anticoagulation in pa-

tients with UE-DVT and thrombophilia are lacking, there is currently no sound scientific basis to recommend screening for thrombophilia in UE-DVT of any cause.

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