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Does the Location of Deep Venous Thrombosis of the Leg Determine the Risk of the Post-thrombotic Syndrome?

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Abstract

Post-thrombotic syndrome (PTS) is an often disabling long-term complication of deep venous thrombosis (DVT). There is increasing evidence suggesting that location of the thrombotic lesion could be of clinical importance. Therefore, patients with flebographic proven DVT who have not used compression stockings were studied in order to investigate whether locations of DVT are related to risk for PTS.

Fifty-nine percent of all patients developed PTS, mostly within 18 months of follow up. The incidence rate of PTS in patients with a popliteal vein thrombosis was 4.8% (2.4-8.6) per month of follow up, while these rates were 3.0% (2.1-4.2) and 5.5% (2.5-10.5) for femoral, resp. iliofemoral location. Risk for PTS was not different at various locations (p=0.276), indicating that location of DVT is not an important risk factor for PTS.
Introduction
In the past three decades the diagnostic and therapeutic management of patients with deep venous thrombosis of the legs (DVT) have improved substantially. However, the management of an often disabling long-term complication of DVT, the post-thrombotic syndrome (PTS), has not been optimised. PTS develops in about 50% of patients with a first episode of DVT, and the use of elastic stockings is so far the only known effective preventive option. Although the precise mechanism of development of PTS remains unclear, a combination of factors is thought to cause this complication. Damage to venous valves and outflow obstruction are presumed to be the most important determinants.

As has been shown for risk of venous insufficiency, location of DVT might also play a role in the development of PTS, although data are conflicting. For example, Johnson et al. found that both popliteal and tibial thrombosis are associated with an increased risk for PTS. An other study however stated that DVT extending above the knee joint into the femoral or iliac vein leaded in about 75% of patients to mild to severe symptoms of PTS. However, when compared to a reference group, this finding showed not to be of any statistical significance.

More knowledge about an association between location of DVT and PTS, if any, might contribute to our understanding of this disease and be of use for the management of patients with DVT. Therefore, we performed a subanalysis of data from an earlier reported prospective cohort study which evaluated the effect of compression stockings, to examine whether the location of DVT is related to the risk for PTS.

Methods
The design of the earlier reported study on the usefulness of stockings in patients with acute DVT in the prevention of PTS has been described in detail elsewhere. Briefly, ninety consecutive patients, treated for acute venographic proven DVT, but not randomised to the use of compression stockings, were eligible for inclusion in this analysis. All patients were treated with unfractionated heparin for at least 5 days, and vitamin K antagonist therapy was continued for three months (INR was maintained between 2.0 and 3.0). They were followed up for at least 5 years.

PTS was classified by an independent adjudication committee by the only clinical scale that has been validated for this purpose. PTS was considered present if a score of 3 or higher plus at least one objective symptom was recorded on two
consecutive follow-up visits. Symptoms during the first 3 months of treatment were not labelled as post-thrombotic.

Three categories were used to classify the location of the thrombosis, according to the most proximal vein segment involved: 1. vena poplitea; 2. vena femoralis (superficial or common femoral veins); 3. iliofemoral (iliac and femoral veins). Incidence rates with 95% confidence intervals were calculated for the occurrence of post-thrombotic syndrome. Observation months were defined as all months since date of inclusion or until the date of establishment of PTS.

Results
Flebographic results of 50 men and 40 women were evaluated. Their mean age was 59 (standard deviation: 17) years. All individuals except two that were lost to follow-up, and 12 who died during the study, completed follow up. Five patients died because of complications of malignant disease, three patients because of cardiac disease and four with other, non-cardio-vascular, causes.

Sixty-nine percent of patients had a thrombus involving the femoral vein, while 18% had a thrombus at the popliteal location, and in 13% the iliofemoral site was involved. Of all of our studied individuals, 55 (59%) developed mild to severe PTS, mostly within 18 months of follow-up.

There were 228 months of follow up in individuals with the popliteal area involved, 1098 and 163 for the femoral, respectively iliofemoral location. In the popliteal group 11 (69%) patients developed PTS, in the femoral and the iliofemoral group 33 (53%) and 9 (7.5%), respectively. The incidence rate of PTS in patients with a popliteal thrombosis was 1.8% (95%CI: 2.1-8.6) per month of follow-up, while these rates were 3.0% (2.1-4.2) for femoral thrombosis and 5.5% (2.5-10.5) for the iliofemoral location (p= 0.276). None of the patients lost to follow-up had PTS at last visit.

Discussion
Our analysis of various locations of venous abnormalities in patients presenting with symptomatic proximal DVT did not reveal differences in risk for PTS. This is in accordance to the results of another prospective study on thrombotic parameters and their association with PTS, using also venography for the diagnosis of DVT. Furthermore, our data are in accordance to the findings of another study showing that more than two thirds of patients with vena poplitea thrombosis
Nevertheless, in contrast to our study, Johnson et al. found that popliteal thrombosis increased risk for PTS more than 3-fold as compared to other locations. Differences in significance of risks between both studies are likely explained by methods used for diagnosis of DVT (venography vs. duplex ultrasonography), because duplex ultrasonography is less accurate in the diagnosis of DVT. However, this difference may also have been caused by the lack of statistical power of our study. Nevertheless, none of the individuals studied was using compression stockings or bandages, the so far only known intervention for prevention of PTS.

Although this study has not brought possible new determinants that may be used for the prevention of PTS, it is clear that monthly incidence of PTS is high in patients with DVT who do not use stockings. So, counseling of patients on possibility of PTS with the intention to optimise compliance of the use of elastic stockings remains so far the only possible option.

References
