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Le RÔLE de la COMPRESSION dans la PRÉVENTION du SYNDROME POST-THROMBOTIQUE après THROMBOSE VEINEUSE AIGÜE : REVUE de la LITTÉRATURE

The ROLE of COMPRESSION THERAPY in the PREVENTION of the POSTTHROMBOTIC SYNDROME after ACUTE DVT: an UPDATE

H. PARTSCH, M.D.

RÉSUMÉ

Contexte : La compression dans la prévention et le traitement du syndrome post-thrombotique (SPT) est encore sous-utilisée et sous-estimée.
But : Faire une revue de la littérature concernant l'utilisation de la compression au stade aigu de la thrombose veineuse profonde (TVP) et durant les années suivantes comme un élément majeur du traitement.
Matériel et méthodes : Récapitulation des essais randomisés et contrôlés et des méta-analyses concernant la définition, l'incidence, les facteurs de risques et les méthodes de prévention et de traitement du SPT.
Résultats : Les bas de compression portés durant deux ans après une TVP permettent de réduire l'incidence d'un SPT de 50 %. Une recommandation pratique essentielle est de débuter les mesures anti-stase (compression et exercices de marche) dès que possible, chez les patients mobiles présentant une TVP, même à la phase aiguë. Une anticoagulation appropriée permet de réduire les récidives de TVP mais ne remplace pas la compression. Chez les patients présentant des signes évidents et les symptômes d'un SPT, la compression représente le geste thérapeutique de base. Cette attitude est largement basée sur l'expérience et sur les données de la littérature.
Conclusion : Dans le contexte de la triade de Virchow, la stase associée à une hypercoagulabilité et à des lésions vasculaires sont des éléments essentiels dans le déclenchement d'une thrombose. En plus d'une anticoagulation adéquate, des mesures anti-stase efficaces associant compression et marche active ne doivent pas être oubliées. Ces procédures peuvent diminuer la douleur et l'œdème à la phase aiguë d'une TVP et réduire le développement d'une TVP.

Mots-clefs : *compression, thrombose veineuse profonde, syndrome post-thrombotique, bas de contention.*

SUMMARY

Background: *Compression therapy for the prevention and the management of the postthrombotic syndrome (PTS) is still underused and underestimated.*
Aim: *To review available data from the literature concerning the use of compression in the acute stage of deep vein thrombosis and in the following years as an important part of treatment.*
Material and Methods: *A review concentrating on published randomized controlled trials and meta-analyses is given on definition, incidence, risk factors and methods for prevention and therapy of the PTS.*
Results: *Compression stockings worn for two years after deep vein thrombosis (DVT) are able to reduce the incidence of a PTS to about one half. A deciding practical recommendation is to start anti-stasis measures (compression and walking exercises) as early as possible, in mobile DVT patients already in the acute phase. Exact anticoagulation is able to reduce recurrent DVT but can not replace compression. In patients with manifest signs and symptoms of PTS compression is the basic treatment option. Up to now this proposal is mainly based on experience and should be endorsed by evidence based data.*
Conclusion: *Considering the triade of Virchow stasis together with hyper-coagulation and vessel-damage is one deciding triggering factor for (recurrent) thrombosis. Besides an adequate anti-coagulation effective anti-stasis measures using compression and exercise should not be forgotten. These procedures are able to reduce pain and edema in the acute phase of DVT and to reduce the development of a PTS.*

Keywords : compression therapy, deep vein thrombosis, post-thrombotic syndrome, medical compression stockings.

DEFINITION OF PTS

According to the recent definition proposed by an International study group post-thrombotic syndrome (PTS) may be defined by "chronic venous symptoms and/or signs secondary to previous deep vein thrombosis" [1]. The diagnosis of PTS is based on clinical grounds only if patients report a history of documented DVT; otherwise, objective testing is required [2].

CLINICAL SIGNS AND SYMPTOMS

A very valuable scoring system for assessing the severity of a PTS considering both, subjective symptoms and objective signs has been proposed by Villalta and Prandoni [3]. *Table I* summarizes the deciding criteria.

This scoring system describes the clinical picture in a patient who suffered from a documented DVT and is

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Scores cliniques du SPT (0 = absent, 1 = léger, 2 = modéré, 3 = sévère)	
5 symptômes • Douleurs • Crampes • Lourdeurs • Prurit • Paresthesies Léger = 5-14, sévère ≥ 15 Villalta S. et al. Haemostasis 1994; 24 (suppl. 1): 158a	**6 signes** • Œdème • Induration • Pigmentation • Ectasie veineuse • Rougeur • Tension des mollets

Table I. – Clinical scores for the evaluation of a PTS.

very useful for studies following the fate of patients after DVT. However, there are a large proportion of patients suffering from PTS in whom episodes of DVT may have stayed unrecognized. Some decades ago most venous ulcers have been attributed to a post-thrombotic syndrome. Based on Duplex investigations in different series of patients with venous leg ulcers we know now that nearly half of them show isolated superficial reflux, the other half present superficial and deep reflux. The proportion of purely deep refluxes is about 10% *(Fig. 1)* [4]. Among 71 legs with extended deep axial reflux and the clinical manifestation of C3-C6 Gillet et al. identified a primary etiology in 11 (15,5%) and a postthrombotic etiology in 60 limbs (84,5%). In the latter group, all but four patients were aware that they had had a previous deep venous thrombosis [5].

Different studies show that venous reflux namely in the popliteal vein, the lower leg veins and in superficial veins are more important for the development of skin changes and ulceration than proximal venous obstruction which may play a "permissive role" in promoting distal reflux [6].

INCIDENCE

About one third to half of DVT patients will develop PTS, in most cases within 1-2 years of acute DVT. The prevalence of severe post-thrombotic syndrome after

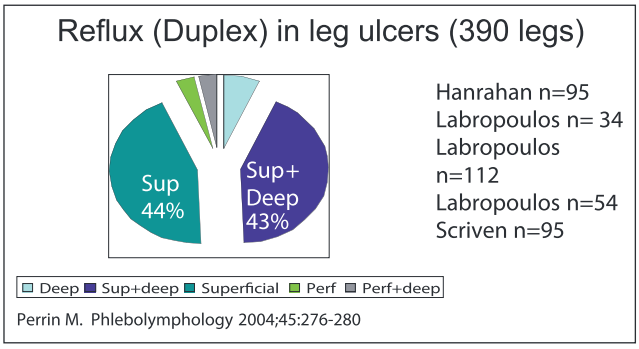


Fig. 1. – Distribution of venous reflux in leg ulcers reported in 5 studies [4].

that time is 4% [7]. In a 12-year follow-up study Franzeck and cookers found among 58 patients with DVT mild skin changes in 28%, marked trophic changes in 5%, and only one venous ulcer [8].

Asymptomatic DVT seems to be associated with a lower incidence of PTS. Patients who develop postoperative proximal or distal DVT and who receive 6 to 12 weeks of anticoagulant therapy are not predisposed to PTS [9]. However, it was shown that the overall relative risk of developing PTS was 1.58 (95% confidence intervals: 1.24-2.02) in patients suffering from asymptomatic DVT as compared to patients without DVT ($p < 0.0005$) [10].

RISK FACTORS

Important risk factors for PTS are older age, ipsilateral recurrence of DVT, and increased body mass index [11, 12]. Proximal DVT, male gender, and high D-dimer levels are independently associated with the development of PTS in patients with a first DVT. Patients with PTS have an increased risk of recurrent venous thromboembolism [13].

Poor quality of initial anticoagulation for the treatment of DVT as a risk factor for PTS is still under dispute. While intensity and duration of anticoagulation have been shown not to influence the risk of developing a post-thrombotic syndrome [14, 15], van Dongen and cookers have demonstrated that patients who spend more than 50% of their time beneath an INR level of 2.0 are at higher risk for PTS [odds ratio (OR): 2.71, 95% CI: 1.44-5.10] [16].

Whether the extent and location of the initial thrombosis are associated with the development of PTS is controversial. The lack of vein recanalization within the first 6 months appears to be an important predictor of PTS, whereas the development of transpopliteal venous reflux seems to be of minor importance [12]. These findings are endorsed by the experiences of Meissner showing that early recanalization is important in preserving valve integrity [17]. Immediate mobilization with compression in the acute stage of DVT may prevent thrombus growth and promote recanalization [18, 19, 20].

A multiple regression analysis based on follow-up investigations by Duplex and plethysmography found that the most important risk factor for early clinical signs of PTS was superficial reflux in months 3, 6, and 12 [21].

PREVENTION

Two randomized controlled trials have clearly shown that the long term use of compression stockings after an acute deep vein thrombosis (DVT) is able to reduce the incidence of PTS to about one half *(Table II)*. While custom-made garments were used in the study from Brandjes ad co-workers [22], similar beneficial results could been obtained by Prandoni et

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Auteur	N	Années après TVP	SPT total	SPT sévère	ulcère
Brandjes 97 chaussettes	96	6	20%	11%	1%
Pas de chaussettes	98	6	47%	23%	3%
Prandoni 04 Chaussettes*	90	2-5	25,6%	3,3%	
Pas de chaussettes	90	2-5	48,9%	11,1%	

* Chaussettes sous le genou.
Compression initiée à 1-2 semaines après TVP.

Table II. – Incidence of PTS after proximal DVT reported by two randomized controlled trials [22, 23].

al using ready-made stockings [23]. The indicated pressure range for the knee length stockings used in both trials was 30-40 mm Hg. No serious adverse effects were mentioned in both studies.

Recent systematic reviews and meta-analyses have endorsed the routine use of compression stockings during the following years after DVT [24, 25]. The review from Kakkos and co-workers has clearly shown that wearing compression stockings is able to reduce the incidence of PTS but not of new episodes of recurrent DVT [24].

Following these evidence medicine based facts it would be unethical to withhold medical compression stockings to patients after DVT. Prandoni et al recommend that stockings must be applied quickly after the thrombotic episode since venous hypertension and valve damage occur soon [23]. In fact compression was started only before hospital discharge, in average one week after the acute event. It may be hypothesized that immediate compression and walking could even further improve the positive outcome.

Starting compression in the acute stage of DVT

The timing of compression and walking in the acute stage of DVT seems to have a considerable impact on the development of a PTS. In a questionnaire sent to 38 Canadian thrombosis physicians who had prescribed elastic compression stockings in their practices 26% recommended compression as soon as DVT was diagnosed, 3% 1-2 days after DVT treatment was initiated, 26% within the month after DVT was diagnosed, 3% three months after DVT, 24% when acute symptoms of DVT improved or resolved and 18% when symptoms developed or became chronic [26]. With the kind allowance of the Canadian authors we have sent out the same questionnaire to a group of international phlebologists in different countries using a fax-service edited by the Sigvaris-company (Compression Bulletin). One of the interesting results of this review is presented in *Fig. 2*.

As can be seen the majority of the colleagues who corresponded to our questionnaire usually recommend compression stockings already in the acute stage of DVT. In Austria showing some slight aberration from the international trend compression bandages are mostly used in the acute phase of DVT replaced by compression garment only later [27]. Even considering that the selection criteria of the interviewed doctors in our review were certainly biased, the difference compared with the Canadian routine is remarkable.

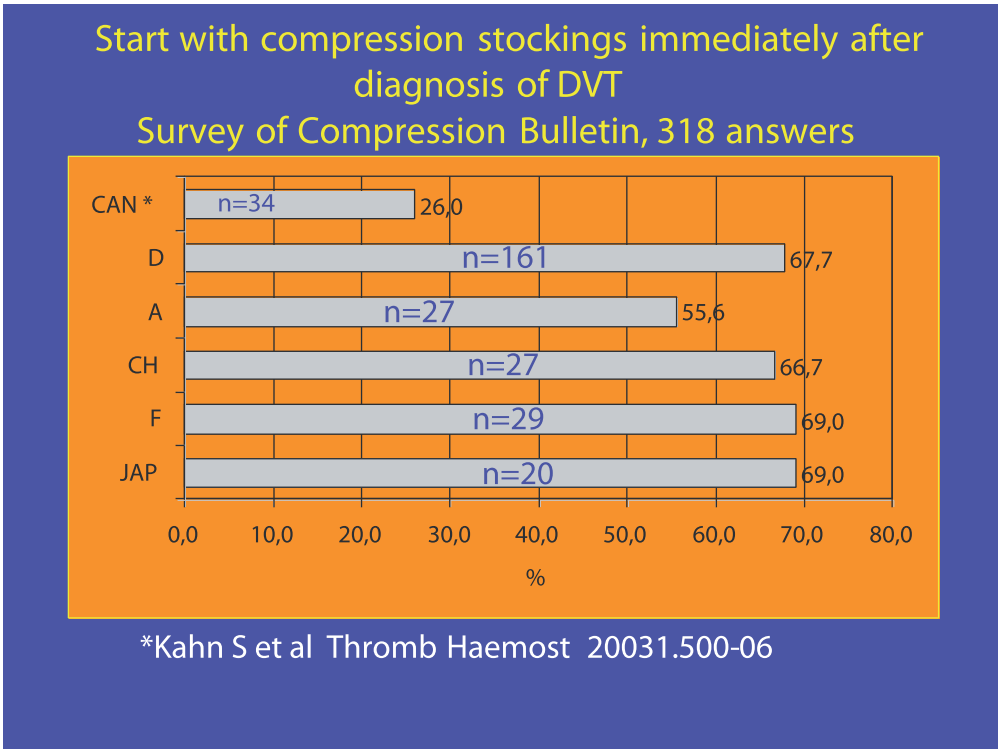


Fig. 2. – The columns represent the percentage of colleagues who declared to start with compression stockings in the acute phase of DVT. (318 answers returned).

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Benefits from immediate compression in the acute stage of DVT

Only few data are available concerning this practically important point.

As we know today bed rest promotes venous stasis and has obviously more risks concerning thrombus propagation and endangering complications, especially in older patients.

In a retrospective analysis of phlebographic studies comparing the thrombus extension in the initial stage with the result several days later thrombus propagation was demonstrated in 26% if patients were kept at bed-rest for more than 5 days, but only in 1% if mobilisation was started between day 0 and 2 [28].

A similar trend can be seen in an own randomized controlled trial in a total of 53 patients with proximal DVT in which bed rest without compression was compared with walking exercises either using compression stockings or bandages. All patients were treated with low-molecular weight heparin and the thrombus size was assessed by Duplex examination on day 0 and day 9. A progression of thrombus length in the femoral vein was seen in 40% after bed rest and in 28 % with walking and compression (n.s.). Taking also into account the length of the thrombus the difference between bed rest and walking with compression was statistically significant ($p < 0,01$) [18, 19]. In this study pain and swelling was significantly less in the compression groups. Repeat lung scans did not show a significant difference concerning new pulmonary emboli compared to bed-rest.

In a recent randomized controlled trial Arpaia and co-workers were able to demonstrate

that compression applied early was more effective than when started 2 weeks after DVT. Seventy-three patients with DVT were randomly assigned to elastic compression hosiery starting either immediately after diagnosis or 2 weeks later. After 14 and 90 days the residual thrombus was measured by compression ultrasonography, and venous patency and any pathological reflux were recorded. There were significantly more recanalized venous segments in the group treated with early compression [20].

In the last ACCP Guidelines "ambulation as tolerated" is recommended for patients with acute DVT [29].

Immediate mobilisation and compression reduces post-thrombotic syndrome

In order to investigate the influence of immediate mobilisation with adequate compression on the development of postthrombotic syndrome we have followed our patients of the above mentioned randomised controlled trial for an average period of two years. As we know from other studies the development of a PTS beyond this time interval is rare [11, 12] Judged by the Villalta-Prandoni scale [3] *(Table I)* a significantly better outcome could be found in the mobile group (median score 5,0) than in the bed rest group (median score 8,0) ($p < 0,01$). ("Mild PTS" = score 5-14, "severe PTS" score $\geq$ 15) *(Fig. 3)* [30]. A total score less than 5 meaning "no postthrombotic syndrome" was found in 12 from 26 (46%) mobile patients, but only in 2 from 11 (18%) patients treated with bed rest.

54% of the patients in both groups still wore their medical compression stockings at the time of the follow-up.

Figure 4 shows the course of the leg swelling from the acute stage of proximal DVT up to 2 years. After that time the previously thrombosed leg is in average still larger than the contra lateral leg.

Compliance to wear compression garment longer than one year after DVT will likely influence the severity of PTS. At least in those patients kept mobile with compression in the acute phase of DVT we were able to show that in half of those who wore the stockings

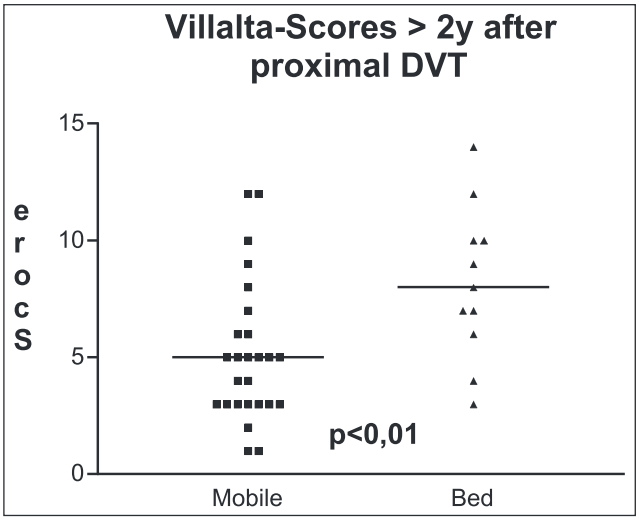


Fig. 3. – Severity of PTS assessed by the Villalta-score is significantly more pronounced in patients with proximal DVT who were kept in bed compared to those mobilized with compression in the acute stage.

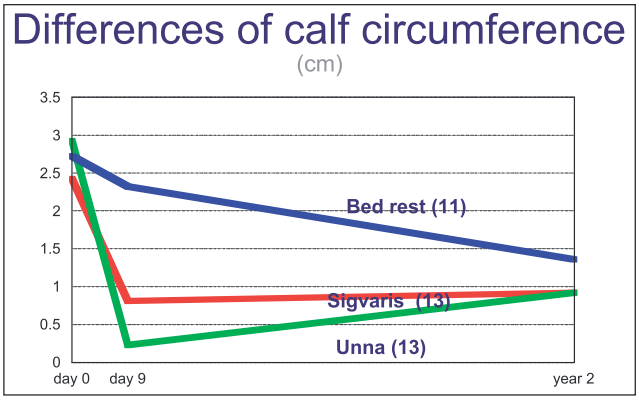


Fig. 4. – Swelling of the leg with proximal DVT is characterized by the difference of calf-circumferences between the thrombosed and the contralateral leg. In the acute stage of DVT (day 0) the difference was in average between 2,5 and 3 cm. Starting compression and walking exercises immediately the oedema reduction is more pronounced after inelastic Unna boot bandages than with compression stockings, in contrast to bed-rest. The follow up after more than 2 years shows an average difference of the calf circumference of 1 cm for the mobile DVT groups, and of 1,5 cm for the former bed rest group 54% of all patients wore still compression stockings after 2 years.

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longer than one year the calf circumference was even smaller compared to the contra lateral leg *(Fig. 5)*. In contrast all patients treated initially by bed-rest had considerable leg swelling, also if they had continued to wear the stockings for longer than one year.

THERAPY OF PTS

To abate the prevalence of PTS, the best policy is to prevent recurrent thrombosis and to use stockings.

It is an amazing fact that only very few evidence based medicine data are available concerning the treatment of a manifest postthrombotic syndrome. Kolbach et al have shown in a Cochrane review that there are only two trials, both from the same group of investigators that addressed physical treatment of postthrombotic syndrome. One crossover study lasting two months compared low and high pressure with intermittent compression units for severe post-thrombotic syndrome showing a beneficial effect of higher pressures. The second study, in patients with mild to moderate post-thrombotic symptoms, showed no effect of elastic compression stockings (30-40 mm Hg at the ankle region) when compared to so-called 'placebo' stockings that actually were one to two sizes too large. [31]. The conclusion of the authors that "the use of elastic compression stockings to treat post-thrombotic syndrome cannot be supported on the basis of the currently available data" clearly demonstrates that future research will be needed to endorse the usual everyday practice to prescribe compression stockings in such instances. The example of *Fig. 6* nicely illustrates that a lot of educational work has still to be done in order to convince our colleagues about the effectiveness of good compression in PTS.

Walking exercises seem to be beneficial in combination with compression stockings. A 6-month exercise-training program improved calf muscle strength and pump function, and high levels of physical activity at one month tended to be associated with reduced severity of postthrombotic symptoms during the subsequent 3 months [32].

Despite several surgical options, conservative treatment is preferable because half of the patients improve or remain stable during follow-up, provided they wear elastic stockings [2]. Based on the findings that patients with superficial reflux have an increased risk of development of the first clinical signs of PTS as early as after the third month [21] abolishment of reflux could theoretically considered. Practically the main concern in the first 3 months after DVT will concentrate on the anticoagulation treatment, not to forget well-fitted compression stockings and walking exercises. However, the point of superficial reflux correction in order to prevent severe PTS could be taken as one of the positive arguments for active treatment before (recurrent) DVT or after the cessation of anticoagulation.



Photo. – Postthrombotic syndrome of the right leg.

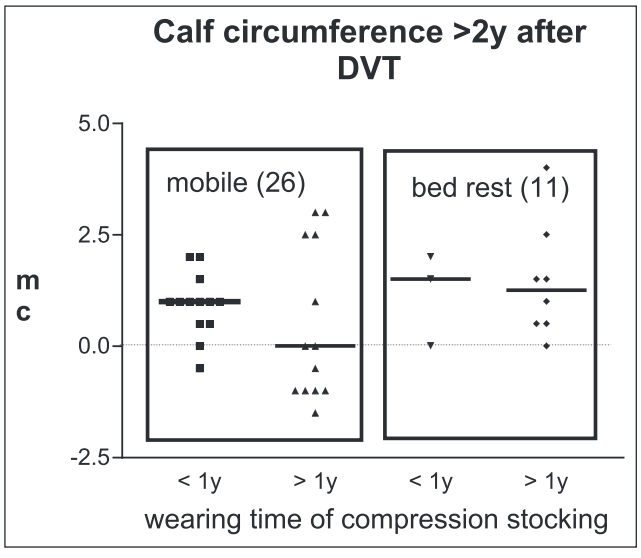


Fig. 5. – Differences of the largest calf-diameter between the thrombosed and the contralateral leg more than 2 years after DVT. Wearing the compression stockings more than 1 year leads to less swelling in the group which was kept mobile in the acute phase of DVT.

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A relatively new field for abolishment of superficial reflux by surgery, sclerotherapy or endovenous procedures was opened by reports demonstrating accelerated healing of venous leg ulcers, even in the presence of deep reflux due to a PTS [33-35]. A reduction of ulcer-recurrence by such interventions has been clearly demonstrated [36].

PTS surgery for deep reflux has a relatively high failure rate, especially in patients with PTS, and should only be performed in highly specialized and well-trained centers. When significant obstruction above the inguinal ligament is associated with reflux; most authors agree that obstruction should be treated first. Secondary deep venous reflux, mainly post-thrombotic syndrome may be treated only after failure of conservative treatment [37].

Adjunctive prescription of so-called venotropic drugs may be of value especially in patients with subjective symptoms [38].

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