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Below-Knee Elastic Compression Stockings To Prevent the Post-Thrombotic Syndrome

A Randomized, Controlled Trial

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Background: **Because only limited evidence suggests that elastic stockings prevent the post-thrombotic syndrome in patients with symptomatic deep venous thrombosis (DVT), these stockings are not widely used.**

Objective: **To evaluate the efficacy of compression elastic stockings for prevention of the post-thrombotic syndrome in patients with proximal DVT.**

Design: **Randomized, controlled clinical trial.**

Setting: **University hospital.**

Patients: **180 consecutive patients with a first episode of symptomatic proximal DVT who received conventional anticoagulant treatment.**

Interventions: **Before discharge, patients were randomly assigned to wear or not wear below-knee compression elastic stockings (30 to 40 mm Hg at the ankle) for 2 years. Follow-up was performed for up to 5 years.**

Measurements: **The presence and severity of the post-thrombotic syndrome were scored by using a standardized scale.**

Results: **Post-thrombotic sequelae developed in 44 of 90 controls (severe in 10) and in 23 of 90 patients wearing elastic stockings (severe in 3). All but 1 event developed in the first 2 years. The cumulative incidence of the post-thrombotic syndrome in the control group versus the elastic stockings group was 40.0% (95% CI, 29.9% to 50.1%) versus 21.1% (CI, 12.7% to 29.5%) after 6 months, 46.7% (CI, 36.4% to 57.0%) versus 22.2% (CI, 13.8% to 30.7%) after 1 year, and 49.1% (CI, 38.7% to 59.4%) versus 24.5% (CI, 15.6% to 33.4%) after 2 years. After adjustment for baseline characteristics, the hazard ratio for the post-thrombotic syndrome in the elastic stockings group compared with controls was 0.49 (CI, 0.29 to 0.84; $P = 0.011$).**

Limitations: **This study lacked a double-blind design.**

Conclusions: **Post-thrombotic sequelae develop in almost half of patients with proximal DVT. Below-knee compression elastic stockings reduce this rate by approximately 50%.**

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See editorial comment on pp 314-315.

One of every 3 to 4 patients with symptomatic proximal deep venous thrombosis (DVT) of the lower extremities will develop post-thrombotic sequelae (1–5). The incidence of the post-thrombotic syndrome is highest in elderly patients and after recurrent episodes of ipsilateral thrombosis (1, 3, 4, 6). This syndrome usually appears within 1 year after the index thrombosis (1, 2). Clinical presentation may vary from minor signs, including skin discoloration, venous ectasia, discomfort, and swelling, to severe manifestations, such as chronic pain, intractable edema, or leg ulcer (7, 8). Post-thrombotic sequelae have a substantial negative impact on quality of life (9) and have considerable socioeconomic consequences for both the individual patient and the health care system (10). There is indirect evidence that the incidence of the post-thrombotic syndrome is reduced when anticoagulation for the index episode of DVT is adequate in intensity and duration (1).

Graduated elastic compression stockings assist the calf muscle pump and reduce venous hypertension and reflux, thereby reducing edema and improving tissue microcirculation (11–14). However, evidence supporting the effectiveness of elastic stockings comes primarily from the results of a single randomized study conducted in patients with proximal DVT, which assessed the post-thrombotic syndrome by using a nonvalidated scale (2). Use of tailor-made and sized-to-fit elastic stockings decreased the incidence of mild or moderate sequelae from 47% to 20% and decreased the incidence of severe sequelae from 23% to 11% (2). In practice, however, such stockings are difficult to use because they are not widely available and are relatively expensive.

The limitations of the available evidence have hindered widespread implementation of compression elastic stockings for prevention of the post-thrombotic syndrome after DVT (15).We performed a randomized study to evaluate the efficacy of off-the-rack elastic compression stockings for prevention of post-thrombotic sequelae in patients with a first episode of acute symptomatic proximal DVT.

METHODS

Study Design and Outcomes

Our randomized, controlled trial evaluated the efficacy of below-knee compression elastic stockings, worn for 2 years, in preventing the post-thrombotic syndrome in patients with a first episode of proximal DVT. The main aim of the study was to compare the 5-year cumulative incidence of the post-thrombotic syndrome in patients who were assigned to the elastic stockings group and those who were not. We also assessed risk factors for the development of late sequelae.

Context

Although physicians often recommend elastic stockings to help prevent the post-thrombotic syndrome, few studies have evaluated the stockings' effectiveness.

Contribution

One hundred eighty patients with proximal deep venous thrombosis (DVT) were randomly assigned to wear or not wear below-knee elastic compression stockings for 2 years. More than 90% of the patients assigned to elastic stockings wore them daily during the 2-year period, but 5 of 90 patients stopped using them because of itching, redness, or discomfort. Twenty-six percent of the patients in the elastic stockings group developed the post-thrombotic syndrome compared with 49% of controls.

Implications

Below-knee elastic compression stockings reduce post-thrombotic sequelae in patients with proximal DVT.

–The Editors

Patients

Consecutive patients referred to the 2nd Division of Internal Medicine of the University of Padua, Padua, Italy, between January 1997 and March 2000 with clinically symptomatic proximal DVT, as confirmed by compression ultrasonography, were considered for the study. One of the trial physicians assessed eligibility criteria. Patients were excluded if they had recurrent ipsilateral DVT, preexisting leg ulcers or signs of chronic venous insufficiency, bilateral thrombosis, a short life expectancy, or a contraindication for use of stockings (for example, advanced-stage peripheral arterial insufficiency).

Patients who met the inclusion criteria and had no exclusion criteria received detailed written information about the study hypotheses and procedures and were asked to participate. In detail, they were informed that the value of elastic stockings for prevention of post-thrombotic sequelae was uncertain and that they would be randomly assigned to wear or not wear a supplied elastic stocking during the daytime. Patients had to give written informed consent to participate in the study. The Institutional Review Board of the University of Padua approved the study protocol.

Anticoagulant Treatment

Patients were treated with unfractionated or low-molecular-weight heparin, followed by at least 3 months of vitamin K antagonist therapy (target international normalized ratio, 2.0 to 3.0). Heparin treatment was discontinued when the international normalized ratio remained above 2.0 for 2 consecutive days and patients had received heparin for at least 5 days. All patients received initial treatment and began taking vitamin K antagonists while in the hospital.

Patients with transient risk factors were scheduled to receive up to 3 months of oral anticoagulant therapy, while patients with idiopathic thrombosis received at least 6 months of treatment. Patients with permanent risk factors, such as active cancer, were treated for the entire study period. The duration of anticoagulant treatment followed international guidelines and was adapted to conform to each patient's preferences and risk profile. The individual quality of oral anticoagulation was considered satisfactory if the international normalized ratio was within or above the therapeutic range in more than 70% of measurements.

Study Procedures

At hospital discharge, an average of 1 week after admission (range, 5 to 10 days), patients were randomly assigned in blocks of 20 to the elastic stockings group (that is, to wear a below-knee, graded compression stocking on the affected leg) or to the control group. Study group assignment was based on a computer-generated list that was accessible only to a trial nurse, who informed study physicians about treatment allocation after patients had provided informed consent.

New Medical Service, Linea Flebologica Flebysan, Rovigo, Italy, supplied the elastic stockings. The stockings, which were flat-knitted, applied 30 to 40 mm Hg of pressure at the ankle; they were made of cotton, latex, and rubber–polyamide and were available in 5 sizes. Patients received 2 stockings, which were replaced by identical stockings every 6 months. The stockings had to be used during the day or longer for a period of 2 years. The elastic stockings used in this study are currently sold in Europe for approximately 35.00 euros ($42 U.S.) each.

At baseline, a clinical history was taken detailing risk factors for venous thrombosis: malignant disease, recent trauma or surgery (within 3 months), prolonged immobilization (>7 days) due to medical illnesses, pregnancy or puerperium, ongoing hormonal therapy, and previous contralateral venous thrombosis. In all patients, we searched for a thrombophilic abnormality (that is, antithrombin, protein C or S deficiency, factor V Leiden mutation, prothrombin G20210 gene mutation, and lupus-like anticoagulants) before anticoagulation was started or at least 2 weeks after anticoagulation was completed, according to standard procedures (16). Patients were discharged with a letter for their family physician indicating that they had agreed to participate in a randomized study assessing the value of elastic stockings and specifying treatment allocation. Patients and their family physicians were given a card that listed the telephone numbers of the thrombosis clinic.

Follow-up and Assessment of Recurrent Thromboembolism

All patients were followed for a maximum of 5 years. The study was to be stopped when the last recruited patient reached 3 years of follow-up. All patients were asked to attend regular examinations at the study center at 3 and 6 months from the index event and every 6 months there-

after. In the interval between scheduled visits, patients were asked to report to the study center if symptoms or signs worsened. Patients who could not attend follow-up examinations at the study center were visited at home.

Patients were asked to return to the center if they developed symptoms suggestive of recurrent venous thromboembolism. Recurrent thromboembolic events were diagnosed as described elsewhere (17–19). Date and cause of death were documented for all patients who died during follow-up.

Assessment of the Post-Thrombotic Syndrome

Patients were instructed not to wear their stockings on the day of assessment and not to reveal their treatment allocation to the assessor. Therefore, each assessment was performed by an investigator who was aware of the side of the index DVT but did not know the treatment allocation or the results of previous measurements. Only the side of the index DVT was considered for development of the post-thrombotic syndrome.

The presence and severity of post-thrombotic signs and symptoms were scored by using a standardized scale, the same as that used in our previous investigations (1, 20, 21). The presence of 5 leg symptoms (pain, cramps, heaviness, pruritus, and paresthesia) and 6 objective signs (pretibial edema, induration of the skin, hyperpigmentation, new venous ectasia, and redness and pain during calf compression) was scored. For each item, a score of 0 to 3 was assigned by using the contralateral unaffected leg as the denominator for all evaluations. A lower-limb venous ulcer indicated severe post-thrombotic syndrome regardless of the sum of the remaining signs and symptoms. In the absence of a venous ulcer, patients were classified as having severe post-thrombotic syndrome if they had a score of 15 or more on 2 consecutive visits at least 3 months apart. A total score of 5 to 14 on 2 consecutive visits at least 3 months apart indicated mild post-thrombotic syndrome. All other patients, including those who had a score higher than 4 on a single examination, were classified as not having the post-thrombotic syndrome.

This scale was developed in a separate series of patients with overt post-thrombotic syndrome and patients without any signs or symptoms of the syndrome after an episode of DVT (20). It was subsequently demonstrated to have high interobserver agreement (21) and high sensitivity and specificity for discriminating between patients with and those without the post-thrombotic syndrome and patients with mild versus severe sequelae (9, 21). In addition, the scale correlated well with patients' perceptions about the interference of their leg symptoms with their daily lives (9, 21). An independent adjudication committee evaluated the scoring forms at the end of follow-up. Committee members were not involved in the clinical assessments and were unaware of treatment allocation.

Adherence, Adverse Effects, and Co-Interventions

Patients were instructed to use a notebook each day to record the length of time that they wore the assigned stocking, the use of unapproved stockings, the occurrence of possible adverse effects (such as itching, erythema, or other forms of allergic reaction), and the use of agents such as nonsteroidal anti-inflammatory drugs or aspirin. They were asked to bring the notebooks to their visits with the study physicians. Adherence was defined as satisfactory if stockings were reportedly used for at least 80% of daytime hours.

Statistical Analysis

Assuming that the 2-year rate of the post-thrombotic syndrome would be approximately 50% in controls, we calculated that approximately 85 patients would be required in each group to yield a power of 0.90 and a 2-sided significance level of 0.05 in detecting a 50% risk reduction with the use of compression stockings. The analysis was conducted on an intention-to-treat basis. Cumulative incidences of the post-thrombotic syndrome were calculated according to Kaplan–Meier. Patients who were lost to follow-up or died were censored after their last visit. Hazard ratios and 95% CIs for the effects of elastic stockings were calculated by using Cox regression models. Hazard ratios were also adjusted for age, sex, clinical presentation of DVT, thrombophilic status, extent of the index thrombotic episode, and use of unfractionated or low-molecular-weight heparin for initial treatment of thrombosis. To identify risk factors, these variables were included in a Cox regression model in which ipsilateral recurrent venous thrombosis was introduced as a time-dependent variable. In addition, the average and individual scores over time were calculated in all patients, including those who had developed the post-thrombotic syndrome.

Role of the Funding Source

The funding source had no role in the collection, analysis, or interpretation of the data or in the decision to submit the manuscript for publication. All investigators had full access to all of the study's data files.

RESULTS

Patients

Of 268 eligible patients with an episode of acute proximal DVT, 81 were excluded because of poor life expectancy ($n = 34$), previous ipsilateral DVT ($n = 20$), preexisting leg ulcers or venous insufficiency ($n = 12$), current use of elastic stockings ($n = 10$), bilateral thrombosis ($n = 3$), or known skin allergy to elastic stockings ($n = 2$). Of the remaining 187 patients, 180 agreed to participate and were randomly assigned to the elastic stockings group ($n = 90$) or to the control group ($n = 90$). The baseline characteristics of the patients in the 2 treatment groups were similar (**Table 1**). **Figure 1** shows the inclusion and progress of study participants.

Table 1. **Main Characteristics of the Study Patients***

Characteristic	Elastic Stockings Group (*n* = 90)	Control Group (*n* = 90)
Mean age ± SD, *y*	60.1 ± 18.5	63.0 ± 18.9
Men, *n (%)*	42 (46.7)	35 (38.9)
Type of clinical presentation, *n (%)*		
Idiopathic	36 (40.0)	37 (41.1)
Secondary	54 (60.0)	53 (58.9)
Risk factors for DVT		
Cancer, *n (%)*	15 (16.7)	10 (11.1)
Recent trauma, *n (%)*	15 (16.7)	20 (22.2)
Recent surgery, *n (%)*	26 (28.9)	19 (21.1)
Prolonged immobilization, *n (%)*	4 (4.4)	5 (5.6)
Hormonal therapy, *n/n*†	11/48	9/55
Pregnancy or puerperium, *n/n*†	4/48	2/55
Thrombophilia, *n (%)*	16 (17.8)‡	17 (18.9)§
Previous contralateral DVT, *n (%)*	4 (4.4)	8 (8.9)
Main clinical symptoms or signs, *n (%)*		
Tenderness	82 (91.1)	84 (93.3)
Edema	73 (81.1)	75 (83.3)
Pain	43 (47.7)	38 (42.2)
Redness	15 (16.6)	14 (15.5)
Collateral veins	12 (13.3)	11 (12.2)
Phlegmasia alba dolens	5 (5.5)	3 (3.3)
Location of DVT, *n (%)*		
Popliteal	41 (45.5)	41 (45.5)
Femoral	20 (22.2)	14 (15.6)
Popliteal and femoral	29 (32.2)	35 (38.9)
DVT treatment, *n (%)*		
Unfractionated heparin	73 (81.1)	66 (73.3)
Low-molecular-weight heparin	17 (18.9)	24 (26.7)
Median duration of vitamin K antagonist treatment (range), *d*	180 (45–1800)	180 (30–1800)

* DVT = deep venous thrombosis.
† In women only.
‡ Eleven patients had factor V Leiden mutation, 1 had prothrombin mutation, 2 had deficiency of protein S, 1 had deficiency of protein C, and 1 had lupus-like anticoagulants.
§ Three patients had factor V Leiden mutation, 5 had prothrombin mutation, 2 had deficiency of protein S, 1 had deficiency of protein C, and 6 had lupus-like anticoagulants.

During the study period, 3 patients were lost to follow-up (2 in the control group and 1 in the elastic stockings group) and 19 died (12 in the control group and 7 in the elastic stockings group), all in the first 3 years. Causes of death were cancer ($n = 7$), ischemic stroke ($n = 4$), pulmonary embolism ($n = 3$), myocardial infarction ($n = 2$), heart failure ($n = 2$), and other ($n = 1$). The average duration of follow-up was 50.5 months (median, 54 months [range, 7 to 60 months]) in the elastic stockings group and 47.5 months (median, 52 months [range, 6 to 60 months]) in the control group.

During the study period, 75 patients (38 in the elastic stockings group and 37 controls) developed symptoms or signs suggestive of recurrent venous thromboembolic complications. Complications were confirmed in 12 patients in the elastic stockings group (13.3%) and in 13 controls (14.4%). Of the 25 recurrences, 7 were ipsilateral DVT, 11 involved the contralateral leg, and 7 were episodes of pulmonary embolism (fatal in 3 patients). Six ipsilateral recurrences were observed during the first 2 years.

Adverse Effects, Adherence, and Co-Interventions

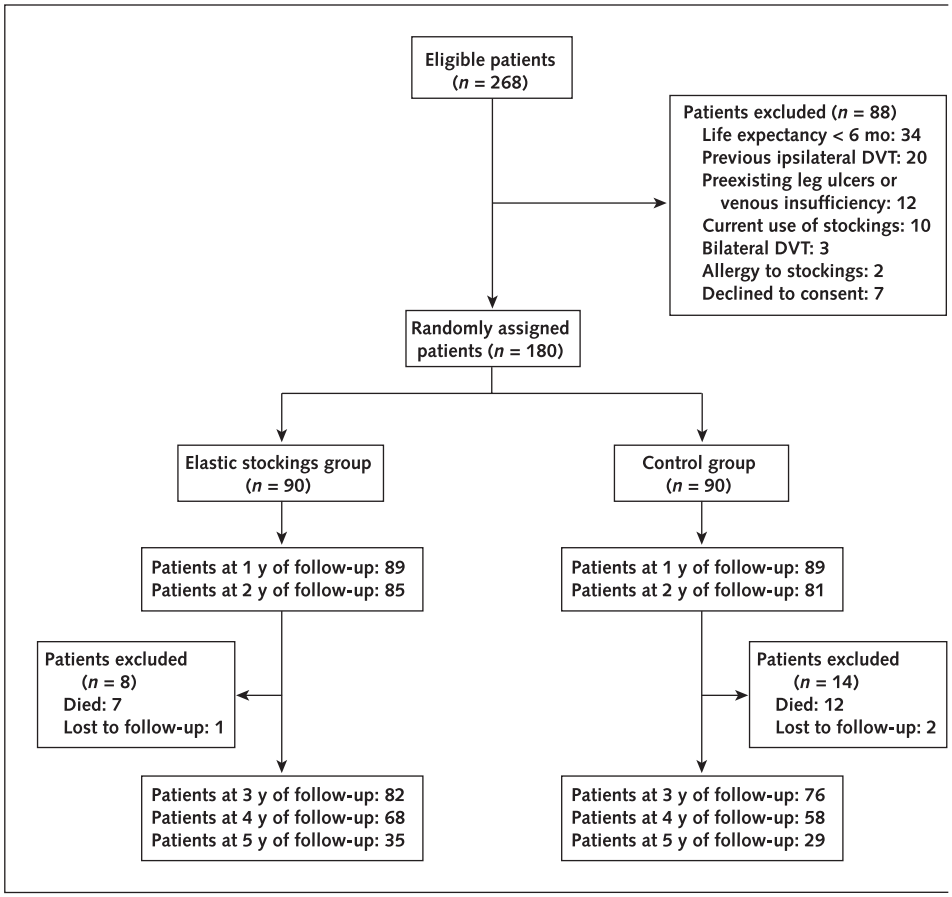
Six of the 90 patients assigned to receive elastic stockings withdrew from the study early, 5 because of intolerance to the stockings (itching alone or associated with erythema in 3 patients and discomfort in the remaining 2) and 1 because of difficulty putting the stocking on. Of the remaining 84 patients, 78 wore their stockings for at least 80% of daytime hours during the 2-year period. Most patients reported wearing their stockings after 2 years. No patients in the elastic stockings group wore stockings other than those provided for the study.

Of the 90 controls, 12 wore various types of elastic stockings (most providing 12 to 18 mm Hg of pressure at the ankle) for varying periods ranging from 6 weeks to 6 months, by self-prescription or prescription of their attending physicians (**Table 2**). Fifteen controls and 6 patients in the elastic stockings group used agents such as nonsteroidal anti-inflammatory drugs or aspirin for varying periods (ranging from a few days to 3 weeks) (**Table 2**). Oral anticoagulants were administered for up to 6 months in 55 of 90 patients in the elastic stockings group and for longer periods in the remaining 35 patients; the corresponding figures in the control group were 59 and 31 patients, respectively (**Table 2**). The quality of oral anticoagulant treatment was similar in both groups: Sixty-three patients in the elastic stockings group and 65 controls achieved an international normalized ratio within or above the targeted therapeutic range of 2.0 to 3.0 on at least 70% of measurements.

The Post-Thrombotic Syndrome

Forty-four of 90 controls and 23 of 90 patients in the elastic stockings group developed post-thrombotic sequelae. The sequelae were severe in 10 controls and in 3 patients in the elastic stockings group. All but 1 event developed in the first 2 years. The cumulative incidence of the post-thrombotic syndrome in the control group was 40% (95% CI, 29.9% to 50.1%) after 6 months, 46.7% (CI, 36.4% to 57.0%) after 1 year, and 49.1% (CI, 38.7% to 59.4%) after 2 years, remaining stable thereafter. In the elastic stockings group, the corresponding figures were 21.1% (CI, 12.7% to 29.5%), 22.2% (CI, 13.8% to 30.7%), and 24.5% (CI, 15.6% to 33.4%), respectively; the incidence increased to 25.7% (CI, 16.6% to 34.7%) after 3 years and then remained stable (**Figure 2**). The hazard ratio for the post-thrombotic syndrome in the elastic stockings group compared with the control group was 0.47 (CI, 0.28 to 0.79; $P = 0.004$). After adjustment for baseline characteristics, the hazard ratio remained unchanged (0.49 [CI, 0.29 to 0.84]; $P = 0.011$). These findings indicate that 4.3 patients (CI, 2.8 to 10.8 patients) need to be treated with elastic compression stockings to prevent 1 additional case of the post-thrombotic syndrome.

Figure 1. **Flow diagram of the study.**



DVT = deep venous thrombosis.

Of the 13 patients with severe post-thrombotic syndrome, 6 developed it rapidly, that is, within 3 months of follow-up, while 7 progressed to this stage after a longer period of mild symptoms. The cumulative incidences of severe post-thrombotic syndrome at the end of follow-up were 3.5% (CI, 0% to 7.3%) in the elastic stockings group and 11.7% (CI, 4.8% to 18.6%) in the control group.

Table 2. **Co-Interventions and Cotreatments***

Variable	Elastic Stockings Group (*n* = 90), *n*	Control Group (*n* = 90), *n*
Use of elastic stockings other than those provided		
6 wk	0	4
7–12 wk	0	4
13–16 wk	0	2
17–20 wk	0	1
21–24 wk	0	1
Use of agents such as NSAIDs or aspirin		
<1 wk	3	7
8–14 d	2	5
15–21 d	1	3
Use of oral anticoagulants		
Up to 3 mo	30	32
4–6 mo	25	27
7–12 mo	12	12
13–24 mo	10	8
>2 y	13	11

* NSAID = nonsteroidal anti-inflammatory drug.

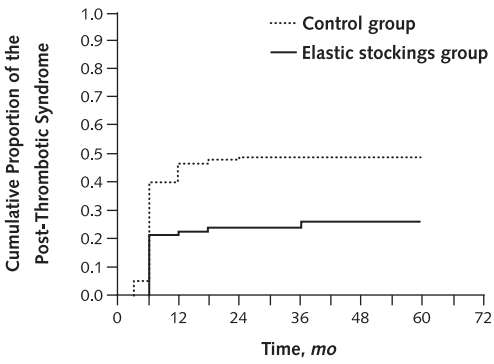
Additional Observations

The average and individual scores of the post-thrombotic syndrome over time in the 2 study groups are shown in **Tables 3** and **4**, respectively. **Table 5** shows symptoms and signs leading to the diagnosis of the post-thrombotic syndrome in the 2 study groups.

Risk Factors for the Post-Thrombotic Syndrome

Of the tested variables, only recurrent ipsilateral DVT and age were associated with the post-thrombotic syndrome. The hazard ratios were 3.32 (CI, 1.04 to 10.62; $P = 0.04$) for recurrent ipsilateral DVT and 1.36 (CI, 1.15 to 1.60; $P = 0.003$) for every 10-year increase in age. Of the 67 cases of the post-thrombotic syndrome, 2 occurred in the 32 patients who were younger than 40 years of age at the time of the index thrombosis. Sex, extent of the index thrombosis, clinical presentation, thrombophilic status, and type of initial treatment were not associated with development of the post-thrombotic syndrome.

Figure 2. **Cumulative incidence of the post-thrombotic syndrome in patients wearing elastic stockings and those in the control group.**



Patients at risk, *n*

Control group	90	54	47	43	41	40	40	33	26	20 16
Elastic stockings group	90	71	69	66	64	63	62	59	48	31 24

DISCUSSION

The results of this randomized study show that elastic stockings are well tolerated and that their use reduces the overall incidence of the post-thrombotic syndrome from 49% to 26% and the overall incidence of severe sequelae from 12% to 3.5%. Only approximately 4 patients need to be treated with elastic compression stockings to prevent 1 additional case of the post-thrombotic syndrome. Increasing age and ipsilateral recurrent thrombosis were the only risk factors for the post-thrombotic syndrome.

Our results are fully consistent with those of a previous randomized trial conducted in a similar patient sample (2). However, that study used a more complicated strategy based on the use of tailor-made elastic compression stockings. In both studies, as well as in other observational studies (1, 4, 5), the great majority of post-thrombotic sequelae occurred during the first year after the index thrombosis. At first glance, the findings of a more recent study, reporting that most patients do not have post-thrombotic sequelae 1 year after an episode of proximal DVT and do not require elastic compression stockings, seem to conflict with these observations (22). However, that study also enrolled patients with asymptomatic thrombosis, who are at low risk for the post-thrombotic syndrome (23). In fact, in the subpopulation of patients with symptomatic thrombosis, the prevalence of the post-thrombotic syndrome as assessed with a different, nonvalidated (and probably less sensitive) scale was 27%, which is certainly not negligible and not distinctly different from our findings. Moreover, because stockings in that study were provided only 1 year after the index thrombosis, that is, when most patients have already developed post-thrombotic sequelae, a large preventive effect was unlikely.

We believe that substantial evidence endorses the high efficacy of elastic compression stockings for prevention of the post-thrombotic syndrome after symptomatic proximal DVT. In addition, a recent survey found that patients with DVT are willing to purchase elastic compression stockings despite the cost, tolerate them well, and are usually willing to wear them daily (14). Since widely available ready-made below-knee stockings have been shown to be effective, there should be no more barriers to widespread implementation.

Some methodologic aspects of our study require comment. We included only patients with proven symptomatic proximal DVT, except those with previous ipsilateral thrombosis or manifestations of severe venous insufficiency. The diagnosis of the post-thrombotic syndrome was based on a validated scale, which has been shown to have high reproducibility as well as good correspondence with patients' perceptions of quality of life (9, 21). Because of the open design of our study, we took care to avoid bias in the assessment of the post-thrombotic syndrome. An investigator who was not involved in patient care and who was unaware of previous findings applied the pertinent scale. In addition, patients were instructed not to wear their stockings on the day of assessment and not to disclose information on treatment allocation to the assessor. Another physician independently collected information on protocol adherence at each follow-up visit. Finally, a blinded adjudication committee evaluated the scoring forms at the end of follow-up. Therefore, we believe that the size of the observed treatment effect is accurate and thus applicable to the large majority of patients with symptomatic proximal DVT.

Table 3. **Scores of the Severity of Symptoms and Signs of the Post-Thrombotic Syndrome over Time***

Time	Elastic Stockings Group			Control Group		
	Patients, *n*	Symptom Score	Sign Score	Patients, *n*	Symptom Score	Sign Score
3 mo	90	0.78 ± 1.05	3.14 ± 2.25	90	2.16 ± 2.14	3.37 ± 1.96
6 mo	90	0.96 ± 1.21	2.81 ± 2.21	90	2.54 ± 2.12	3.02 ± 2.22
1 y	89	0.79 ± 1.29	2.45 ± 2.27	89	2.28 ± 2.09	3.02 ± 2.22
2 y	85	1.00 ± 1.35	2.29 ± 2.18	81	2.51 ± 2.28	2.52 ± 2.11
3 y	82	0.63 ± 0.96	1.84 ± 2.13	76	2.11 ± 2.00	2.43 ± 2.29
4 y	68	0.63 ± 0.96	1.78 ± 1.92	58	2.48 ± 1.96	2.47 ± 1.96
5 y	35	0.54 ± 0.82	1.83 ± 2.08	29	2.34 ± 1.84	2.45 ± 1.53

* Scores are based on the standardized scale described in the Methods section. Values presented with a plus/minus sign are means ± SD.

Table 4. **Individual Post-Thrombotic Syndrome Scores in the 2 Study Groups***

Time	Elastic Stockings Group, *n*				Control Group, *n*			
	Patients	Score			Patients	Score		
		0–4	5–14	≥15		0–4	5–14	≥15
3 mo	90	59	31	0	90	36	52	2
6 mo	90	54	36	0	90	38	50	2
1 y	89	65	23	1	89	43	42	4
2 y	85	62	22	1	81	39	38	4
3 y	82	68	14	0	76	40	33	3
4 y	68	57	10	1	58	25	30	3
5 y	35	31	4	0	29	14	14	1

* Scores are based on the standardized scale described in the Methods section. Scores higher than 4 were observed occasionally (that is, at 1 but not 2 consecutive follow-up evaluations) in 14 patients treated with elastic stockings and in 26 controls. Venous ulcer not associated with a score higher than 14 was observed in 2 patients treated with elastic stockings and in 6 controls.

In this study, the incidence of the post-thrombotic syndrome in the elastic stockings group did not differ from that observed in a large series of patients reported previously (1). Those patients received only 3 months of oral anticoagulant therapy and used elastic stockings for 2 years after their thrombotic episode. Anticoagulation in our study was generally given for much longer periods, according to current guidelines, and considerably reduced recurrent thromboembolism. However, the incidence of the post-thrombotic syndrome remained unchanged, suggesting that further refinement of anticoagulant treatment alone is unlikely to affect the development of late post-thrombotic sequelae. On the other hand, since the frequency of recurrent thrombotic events did not differ between our 2 study groups, the effect of elastic stockings on the development of the post-thrombotic syndrome may not be mediated through reduction of recurrent ipsilateral venous thromboembolism. Although the precise mechanism by which stockings reduce the risk for the post-thrombotic syndrome is unknown, they seem to affect clinical symptoms more than objective signs. It is hypothesized that elastic stockings counterbalance the effects of venous hypertension resulting from persistent venous obstruction, valve damage, or both and assist the muscle pump (11–14). Since venous hypertension and valve damage occur soon after a thrombotic episode, this suggests that stockings must be applied quickly. It is unclear whether elastic stockings are beneficial after the first 2 years; this issue warrants further investigation.

In conclusion, patients with proximal DVT are at high risk for post-thrombotic sequelae in the first year after the acute episode. Early use of ready-made elastic stockings, which are relatively inexpensive, safe to use, and well tolerated, can substantially reduce this risk. This treatment has the potential to be systematically adopted beside conventional anticoagulation in all patients presenting with DVT of the legs.

From University Hospital of Padua, Padua, Italy; and Academic Medical Center, Amsterdam, and Academic Hospital, Maastricht, the Netherlands.

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Table 5. **Symptoms and Signs Leading to the Diagnosis of the Post-Thrombotic Syndrome in the 2 Study Groups**

Manifestations	Mild Post-Thrombotic Syndrome, *n (%)*		Severe Post-Thrombotic Syndrome, *n (%)*	
	Elastic Stockings Group (*n* = 20)	Control Group (*n* = 34)	Elastic Stockings Group (*n* = 3)	Control Group (*n* = 10)
Heaviness	13 (65.0)	25 (73.5)	3 (100)	7 (70.0)
Pain	9 (45.0)	15 (44.1)	1 (33.3)	6 (60.0)
Cramps	5 (25.0)	5 (14.7)	2 (66.6)	6 (60.0)
Pruritus	6 (30.0)	9 (26.5)	1 (33.3)	5 (50.0)
Paresthesia	12 (60.0)	19 (55.8)	2 (66.6)	7 (70.0)
Pretibial edema	19 (95.0)	32 (94.1)	2 (66.6)	8 (80.0)
Skin induration	14 (70.0)	20 (58.8)	2 (66.6)	7 (70.0)
Hyperpigmentation	14 (70.0)	23 (67.6)	3 (100)	6 (60.0)
Venous ectasia	14 (70.0)	26 (76.4)	2 (66.6)	7 (70.0)
Redness	13 (65.0)	24 (70.6)	2 (66.6)	8 (80.0)
Compression pain	2 (10.0)	3 (8.8)	1 (33.3)	2 (20.0)
Venous ulcer	–	–	2 (66.6)	6 (60.0)

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