

# Intermittent compression units for severe post-phlebotic syndrome: a randomized crossover study

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## Abstract

**Background:** Although uncommon, severe post-phlebotic syndrome may be associated with persistent, intractable pain and swelling that interfere with work and leisure activities. This study was performed to determine whether intermittent compression therapy with an extremity pump benefits patients with this condition and, if so, whether the benefit is sustained.

**Methods:** The study was a randomized crossover trial. Over the period 1990 to 1996, all patients in the clinical thromboembolism program of an Ontario teaching hospital who had a history of deep vein thrombosis and intractable symptoms of post-phlebotic syndrome were recruited into the study. The study involved using an extremity pump twice daily for a total of 2 months (20 minutes per session). The patients were randomly assigned to use either a therapeutic pressure (50 mm Hg) or a placebo pressure (15 mm Hg) for the first month. For the second month, the patients used the other pressure. A questionnaire assessing symptoms and functional status served as the primary outcome measure and was administered at the end of each 1-month period. A symptom score was derived by summing the scores for individual questions. At the end of the 2-month study, patients were asked to indicate their treatment preference and to rate the importance of the difference between the 2 pressures. Treatment was considered successful if the patient preferred the therapeutic pressure *and* stated that he or she would continue using the extremity pump *and* that the difference between the therapeutic and placebo pressures was of at least slight importance. All other combinations of responses were considered to represent treatment failure. Patients whose treatment was classified as successful were offered the opportunity to keep the pump and to alter pressure, frequency and duration of pump use to optimize symptom management. In July 1996 the authors contacted all study participants whose treatment had been classified as successful to determine whether they were still using the pump and, if so, whether they were still deriving benefit.

**Results:** In total 15 consecutive patients (12 women and 3 men) were enrolled in the study. The symptom scores were significantly better with the therapeutic pressure (mean 16.5) than with the placebo pressure (mean 14.4) (paired *t*-test,  $p = 0.007$ ). The treatment for 12 of the patients (80%, 95% confidence interval 52% to 96%) was considered successful. Of these, 9 patients continued to use the pump beyond the crossover study and to derive benefit.

**Interpretation:** The authors conclude that a trial of pump therapy is worthwhile for patients with severe post-phlebotic syndrome and that a sustained beneficial response can be expected in most such patients.

Post-phlebotic syndrome is characterized by pain, swelling and, less commonly, ulceration of the leg.<sup>1</sup> It occurs in approximately 60% of patients after an episode of proximal deep vein thrombosis.<sup>2,3</sup> The mainstay of therapy for this syndrome is the use of graduated elastic compression stockings.<sup>4</sup> Although many patients benefit from stockings, some do not, and others find them unacceptable for cosmetic reasons or because they are uncomfortable and inconvenient. Thus, some patients experience chronic, intractable pain and swelling that interfere markedly with work and leisure activities.



## Evidence

## Études

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The Jobst extremity pump, an intermittent compression unit (Jobst, Inc., Toledo, Ohio), consists of an inflatable synthetic sleeve that fits over the extremity and a pump that intermittently inflates and deflates the sleeve. The pump pressure can be adjusted, and pressures of 30–60 mm Hg have been used therapeutically to relieve symptoms of leg swelling resulting from lymphedema<sup>5</sup> and in a small pilot study of patients with post-phlebotic syndrome,<sup>6</sup> described briefly below.

On the assumption that the discomfort and disability experienced by some patients with post-phlebotic syndrome are caused by extensive swelling and given the reported success of treatment of lymphedema with the extremity pump,<sup>5</sup> we performed a pilot study of pump therapy in 5 patients with severe post-phlebotic syndrome.<sup>6</sup> All 5 patients had been severely incapacitated, and all had excellent improvement with pump therapy, in terms of both symptoms and functioning. To evaluate pump therapy further in a methodologically rigorous study and to obtain a reasonable estimate of the true proportion of patients with severe post-phlebotic syndrome who might derive clinically important benefit from the pump, we conducted a randomized crossover study.

## Methods

The study was approved by the Institutional Review Board of Chedoke–McMaster Hospitals, Hamilton, Ont., and informed, written consent was obtained from all patients.

## Subjects

The study participants were recruited from the clinical thromboembolism program of McMaster University, Hamilton, Ont., between 1990 and 1996. To be eligible for the study, patients had to meet all of the following criteria:

- previous deep vein thrombosis documented venographically, by impedance plethysmography or by venous ultrasonography
- intractable symptoms of post-phlebotic syndrome causing significant limitation of lifestyle, significant morbidity or both, as indicated by any of the following:
  - loss of job or absenteeism from work because of post-phlebotic syndrome
  - interference with day-to-day activities, e.g., housework, sports
  - frequent loss of sleep
- failure of condition to improve with use of graduated compression stockings or patient's intolerance of or refusal to use such stockings.

Potential subjects were excluded from the study if they had had deep vein thrombosis within the past 3 months or if they were unable to travel to the clinic.

## Intervention

The eligible patients were all given an extremity pump, to be used twice daily (20-minute sessions) for a total of 2 months. The

patients were randomly assigned, by means of a computer-generated randomization schedule, to use the extremity pump at either 50 mm Hg (the therapeutic pressure) or 15 mm Hg (the placebo pressure) for the first month. The pressure level for the placebo was chosen because it was not expected to have a significant hemodynamic effect but was sufficient to inflate the sleeve and helped to reduce bias (see section "Avoidance of bias," below). The patients were encouraged to use the pump at noon and in the evening but to use their judgement regarding convenience and feasibility of the timing of sessions. After 1 month, the patients were instructed to use the other pressure for the second month, such that those who had been using the therapeutic pressure switched to the placebo pressure and vice versa.

## Measurement of outcome

At the end of each 1-month period a symptom score was derived from the answers to a questionnaire assessing symptoms and functional status. The patients were asked to identify the activity causing the greatest pain or swelling and the activity most limited by their symptoms. Information about degree and duration of pain and swelling in the legs and degree of limitation of activity over the 1-month period was also elicited. Each answer was associated with a numeric score, and individual scores were summed to obtain an overall symptom score. The primary analysis was based on a comparison of the symptom scores obtained for each pressure level. At the end of the 2-month study period, a global rating for each patient was obtained, also by questionnaire. For this rating, the patients were asked to identify whether they felt better during the first or second month of the study, whether they would continue using the compression device and, if they felt better using the therapeutic pressure, their perceived rating of the importance of the difference between the pressure levels. The patient's global rating was used to determine whether the treatment had been successful or not. The treatment was considered successful if the patient preferred the therapeutic pressure *and* stated that he or she would continue using the compression device *and* indicated that the difference between the therapeutic and placebo pressures was of at least slight importance. All other combinations of responses were considered to represent treatment failure.

## Avoidance of bias

Both the health care personnel and the patients were blinded to the randomization order of the compression pressures. Although the patients and the investigators were not blinded to the pump pressure itself, the possibility of bias was reduced by informing the patients that both the efficacy and the optimum pressure for symptom relief were unknown and that we were comparing the relative effects of a high pressure and a low pressure.

## Post-study follow-up

Patients whose treatment was classified as successful were given the opportunity to keep the pump after the study was completed and were encouraged to alter the pressure, frequency and duration of pump use to optimize symptom management. These patients were seen every 3 months. In addition, in July 1996 we contacted all of the study participants whose treatment had been classified as successful to determine whether they were still using the pump and, if so, whether they were still deriving benefit.



## Statistical analysis

The primary analysis consisted of a comparison of the symptom scores for the therapeutic and placebo treatment periods by means of paired *t*-tests. In addition, the proportion of successful treatments was expressed as a point estimate with its corresponding 95% confidence interval (CI). On the basis of our hypothesis that treatment would be successful for 80% of the patients, we planned to recruit 20 patients or to continue recruitment for 6 years (the duration of grant funding), whichever came first.

## Results

A total of 15 patients (12 women and 3 men, mean age 60 [range 38–81] years) were screened for eligibility; all were enrolled into the study (Table 1). Six of the patients used the pump on the right leg, 8 used the pump on the left leg, and 1 used the pump on both legs.

The mean symptom score was 14.4 for the period during which placebo pressure was used and 16.5 for the period during which therapeutic pressure was used. The minimum score (corresponding to the most severely affected patients) is 10, whereas the maximum score (corresponding to the least severely affected patients) is 70. The mean difference (2.1 [standard error of the mean 0.7]) was statistically significant ( $p = 0.007$ ). In general, a symptom score difference of 2.1 represents a clinically significant difference and qualitatively correlates with an improvement that ranges from "slight" (e.g., patient 10) to "very" (e.g., patient 2). (Table 1).

For 12 of the patients (80% of the sample, 95% CI 52% to 96%) the treatment was considered successful (Table 1). Of these, 9 (75%) continued to use the pump after the

crossover study, at pressures between 40 and 50 mm Hg and from once a day to 4 times a day. Of these 9 patients, 1 died of metastatic cancer and the others continued to use the pump regularly and to derive benefit 6 to 30 months after their enrollment in the original study.

## Interpretation

There is a critical need to evaluate potentially effective therapy for patients with post-phlebotic syndrome, because of the lack of therapeutic alternatives for patients who do not benefit from graduated compression stockings. In our pilot study,<sup>6</sup> 5 patients with severe post-phlebotic syndrome experienced immediate and sustained improvement in symptoms after using the Jobst compression unit, so we went on to evaluate the device in a formal trial. Our results indicate that for patients with severe post-phlebotic syndrome who do not benefit from or cannot tolerate stocking therapy, pump therapy is a reasonable option and that a beneficial response can be expected in about 80% of such patients. The benefits of the pump are seen within the first month of treatment and, in most patients, are sustained. Although the regimen tested (two 20-minute sessions daily at a pressure of 50 mm Hg) is beneficial for many patients and is a good starting point, we found it reasonable to ask patients to alter the pressure, frequency and timing of the therapy to suit their needs.

We chose to conduct a randomized crossover trial rather than a randomized between-patient trial so that each patient could compare the 2 regimens and indicate their preference. This is an efficient way to obtain valid findings, given that the sample size requirements for a randomized trial were

**Table 1: Patient characteristics and outcome for 15 patients in a randomized crossover trial of intermittent compression devices for the treatment of severe post-phlebotic syndrome**

Patient no.	Age, yr	Sex	Pressure level; symptom score*		Treatment outcome†	Perceived importance‡	Still using pump
			Placebo	Therapeutic			
1	68	F	24	27	Successful	Very	No
2	50	F	17	19	Successful	Very	Yes
3	59	F	17	22	Successful	Very	Yes
4	68	F	18	22	Successful	Moderate	Yes
5	64	M	9	10	Successful	Slight	No
6	38	F	5	9	Successful	Slight	No
7	43	F	24	25	Successful	Very	Yes
8	74	F	18	21	Successful	Very	Yes
9	81	F	13	15	Successful	Very	Yes
10	26	F	13	15	Successful	Slight	Yes
11	65	F	10	15	Successful	Very	Yes
12	50	F	10	15	Successful	Very	Yes
13	79	F	15	15	Failed	NA	No
14	71	M	12	7	Failed	NA	No
15	61	M	10	10	Failed	NA	No

Note: NA = not applicable.

\*Derived from answers to the questionnaire assessing symptoms and functional status, which was completed after each 1-month segment of the study. Placebo pressure was 15 mm Hg, and therapeutic pressure was 50 mm Hg.

†Derived from answers to the global patient profile questionnaire, which was completed after the 2-month study period. The perceived importance is the patient's perception of the importance of the difference between the 2 pressure levels.



too large to make such a study feasible. Because of the nature of the intervention, the patients could not be blinded to the treatments, but 2 mechanisms were used to minimize bias. First, the patients were informed that we were comparing a high-pressure regimen (50 mm Hg) with a low-pressure regimen (15 mm Hg) and that we were uncertain which (if either) was preferable. Second, we asked the patients not to inform the interviewer administering the questionnaires at the end of each 1-month period which pressure had been used during the preceding month. Although these manoeuvres could not have eliminated bias altogether, the fact that 75% of the patients whose treatment was considered successful continued to use pump therapy beyond the study period increases the likelihood that the therapy was associated with a clinically important benefit. A questionnaire was used as the primary outcome measure because a means of objectively evaluating post-phlebotic syndrome has not been validated. A questionnaire focusing on clinically relevant questions therefore seemed sensible. This approach appears to have been valid, because the symptom scores were better with the therapeutic pressure for all patients whose treatment was classified as successful, but not for those whose treatment was classified as having failed.

This study was not designed to determine the incidence of severe, intractable post-phlebotic syndrome, but our findings suggest that it is relatively uncommon, given that it took 6 years to recruit 15 patients. Moreover, in a parallel, 3-part study evaluating the use of graduated compression stockings 1 year after proximal deep vein thrombosis, we enrolled over 200 patients during the same period. However, the lack of effective therapy for this relatively small group of patients and the substantial morbidity associated with severe post-phlebotic syndrome underline the clinical importance of our results.

The mechanism of the therapeutic benefit of pump therapy is probably due to a reduction in edema, which relieves the symptoms caused by the presence of fluid in a closed compartment.

In summary, severe, intractable post-phlebotic syndrome is very difficult to treat. Our results suggest that the extremity pump has a role in reducing morbidity due to this condition.

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Competing interests: None declared.

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We're seeking articles of up to 1200 words, and illustrations are encouraged. Entries received before Oct. 1, 1999, are more likely to be published.

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