Prospective Randomized Controlled Trial to Analyze the Effects of Intermittent Pneumatic Compression on Edema Following Autologous Femoropopliteal Bypass Surgery

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Abstract

Background Patients who undergo autologous femoropopliteal bypass surgery develop postoperative edema in the revascularized leg. The effects of intermittent pneumatic compression (IPC) to treat and to prevent postreconstructive edema were examined in this study.

Methods In a prospective randomized trial, patients were assigned to one of two groups. All patients suffered from peripheral arterial disease, and all were subjected to autologous femoropopliteal bypass reconstruction. Patients in group 1 used a compression stocking (CS) above the knee exerting 18 mmHg (class I) on the leg postoperatively for 1 week (day and night). Patients in group 2 used IPC on the foot postoperatively at night for 1 week. The lower leg circumference was measured preoperatively and at five postoperative time points. A multivariate analysis was done using a mixed model analysis of variance.

Results A total of 57 patients were analyzed (CS 28; IPC 29). Indications for operation were severe claudication (CS 13; IPC 13), rest pain (10/5), or tissue loss (7/11). Revascularization was performed with either a supragenicular (CS 13; IPC10) or an infragenicular (CS 15; IPC 19) autologous bypass. Leg circumference increased on day 1 (CS/IPC): 0.4%/2.7%, day 4 (2.1%/6.1%), day 7 (2.5%/7.9%), day 14 (4.7%/7.3%), and day 90 (1.0%/3.3%) from baseline (preoperative situation). On days 1, 4, and 7 there was a significant difference in leg circumference between the two treatment groups.

Conclusions Edema following femoropopliteal bypass surgery occurs in all patients. For the prevention and treatment of that edema the use of a class I CS proved superior to treatment with IPC. The use of CS remains the recommended practice following femoropopliteal bypass surgery.

Introduction

Patients experiencing disabling claudication, rest pain, or tissue loss may be treated with a femoropopliteal bypass. In general, an autologous bypass graft is preferred to an artificial graft [1]. Edema occurs postoperatively in most patients who are revascularized with a femoropopliteal bypass [2–6] and causes discomfort to the patient and may delay rehabilitation and wound healing. Also, edema is known to impair macrovascular and microvascular circulation [7]. The pathophysiology of postreconstruction edema is thought to be a combination of hyperemia [8–11], increased capillary permeability [7, 12], and lymphatic [3, 4, 13–16] and venous [4, 17] disruption. Reperfusion of ischemic tissue leads to up-regulation of inflammatory processes as well [18, 19]. Edema typically emerges during the first postoperative week and lasts up to 3 months, although cases of chronic edema are also reported [20].

Treatment of lower limb edema is mostly based on leg elevation, external compression with stockings [21], or lymph massage [13]. The use of external compression is mostly based on clinical experience as there are no reported prospective studies on the effect of compression stockings on

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postoperative edema. The use of intermittent pneumatic compression (IPC) is an alternative concept in edema reduction following surgical procedures on a limb. IPC on the foot has been proven effective for reducing edema in the lower limb after orthopedic and trauma surgery [22, 23]. IPC is also known to increase arterial flow and pressure in the lower limb in patients suffering from peripheral arterial disease (PAD) [24–26]. An effective treatment of postoperative edema may reduce inflammatory processes and improve wound healing.

The aim of this trial was to compare the effect of IPC on leg edema and changes in inflammatory parameters with that of class I compression stockings (delivering 18 mmHg) above the knee following autologous femoropopliteal bypass surgery.

Methods

Study design

A nationally recognized medical ethics review committee and the hospital's medical ethics review committee granted approval for a single center randomized controlled trial. Due to a lack of information about the magnitude of a differential treatment effect on lower limb circumference, a power analysis performed prior to the trial was based on a Cohen's $d = 0.75$, representing a medium to large treatment effect [27]. This effect should be detectable with 80% power in 30 patients eligible per group and a test size of 0.05 (two-sided). Using sealed envelopes, each patient was allocated to one of two groups according to randomly permuted blocks of 10 each. Vascular assessment included an ankle-brachial pressure index (ABI), a walking test, a venous and arterial duplex ultrasonography (US) assessment, and either digital subtraction angiography (DSA) or magnetic resonance angiography (MRA) scans. All patients gave their written informed consent.

Inclusion criteria

All patients suffered from peripheral vascular disease of Rutherford category 3, 4, 5, or 6 in the principal lower limb vessels or crural vessels as defined by the Intersociety Consensus for the Management of Peripheral Arterial Disease (TASC II) [28]. There was unobstructed iliac inflow and sufficient outflow through at least one crural vessel based on arterial duplex US, DSA, and/or MRA findings gathered preoperatively. In addition, we tested the iliac inflow clinically prior to revascularization.

Exclusion criteria

Patients suffering from severe cardiac failure [New York Heart Association (NYHA) classes III and IV] were excluded owing to hemodynamic effects of IPC that are not completely understood. Patients with known deep vein thrombosis or pulmonary embolism on admission were not included for the same reason. Patients who required hemodialysis because of severe renal impairment were excluded, as were patients who experienced preexisting limb edema due to severe liver impairment (Child-Pugh score B and C), venous insufficiency, or endocrinologic diseases or who manifested edema caused by medication. Patients with large ulcers (>3 cm^2) on the plantar aspect of the foot or who had undergone amputations that would compromise the fit of the IPC pad were excluded. A greater saphenous vein that was occluded, calcified, or varicose or had a minimal caliber of <2.0 mm was considered unsuitable to be used as an autologous bypass graft [29, 30]. Further exclusion criteria were known malignant diseases, enrollment in other trials, and mental inability to understand the contents of the trial.

Surgical procedure

Surgery was performed under general and/or spinal anesthesia. A deep-tunneled reversed or in situ supragenicular or infragenicular femoropopliteal bypass was constructed. A standardized medial incision was made in the groin at the site of the bifurcation of the femoral artery. The popliteal dissection was made above or below the knee. Small lymphatic structures were coagulated, and large lymphatic structures were ligated using Vicryl (Ethicon, Somerville, NJ, USA). The grafts were implanted end-to-side. A routine Doppler assessment was performed before closure of the surgical wounds. Patients underwent systemic heparinization (5000 IE) during the operation. Oral anticoagulant administration (acenocoumarol) was initiated for a 2-year period or was resumed postoperatively [31].

Treatment groups

Group 1 patients were fitted with a compression stocking (Brevet tx; Mölnlycke, Göteborg, Sweden) postoperatively. The stocking delivers graduated pressure up to 18 mmHg (class I) on the lower and upper leg and features low-pressure areas on the heel and over the popliteal vein. During hospitalization, the patients wore the stocking on the affected limb day and night. After discharge from hospital, the patients continued using the stocking during the day until the eighth week after surgery. Group 2 patients received IPC (A-V impulse technology; Orthofix Vascular Novamedix, Andover, UK) on the affected limb during the night, 2000–0800 h (8:00 p.m.–8:00 a.m.), for 7 days postoperatively in hospital. After discharge from hospital, patients continued using a compression stocking during the day (as mentioned for group 1) until the eighth week after surgery.

IPC

The A-V impulse technology is an IPC device. It works by intermittently pumping compressed air into a pad that fits the foot. The pad flattens the plantar arch of the foot on inflation, thereby deflating the venous plexus. The pad is inflated in 0.4 s in which a pressure is built up to 130 mmHg. Deflation occurs through perforations in the pad. A cycle of 20 s allows efficient priming of the venous pump [22, 23]. A sudden inflation impulse reproduces a physiological ratchet-like flow pattern of venous return.

Measurements

Lower limb circumference measurements were performed at six time points: the day prior to surgery and postoperatively at 1, 4, and 7 days; 2 weeks; and 3 months. Three circumferential marker lines that were applied preoperatively were assessed using a tape measure [32]. The first marker line was 10 cm medial below the knee joint; the second marker line was 10 cm above the medial malleolus; and the third marker line was between the two lines mentioned. At each time point, each marker line was measured three times and the wound condition was assessed.

Administration of antibiotics and diuretics were registered. Leukocyte counts and C-reactive protein (CRP) concentrations were measured at four time points: the day prior to surgery and postoperatively at 1, 7, and 14 days. Patients were hospitalized during the first week after surgery. The ABI was obtained at day 4 and at 3 months. A duplex US assessment was repeated at 3 months.

Intention to treat

This study was carried out on an "intention-to-treat" basis. Patients were encouraged to carefully mobilize beginning on the first postoperative day if possible. No restrictions were laid down regarding early rehabilitation schedules. Group 1 patients who used the compression stocking mobilized while wearing their stockings. Group 2 patients used IPC only at night as they were not able to mobilize when the device was active. Patients who did not tolerate or experienced discomfort from the IPC device were offered a compression stocking and vice versa. Patients experiencing postoperative complications were treated according to common medical practice. The complications that occurred did not result in exclusion from analysis unless the patient was lost to follow-up during the first two postoperative weeks. A duplex US assessment was performed if an in-graft stenosis or obstruction was suspected. The original groups were maintained for the data analysis.

Statistical analysis

Statistical analysis was performed with SPSS 15.0 software (SPSS, Chicago, IL, USA). The nine circumferences measured at each time point in each patient were averaged after logarithmic transformation. The choice of a natural logarithmic transformation of the circumference measurements before analysis was made for a practical reason: A change or difference on the log scale can be back-transformed to a percentage as a common effect measure in this field. Leukocyte counts and CRP concentrations were logarithmically transformed as well because of the positive skewness of their distribution. The data were analyzed using a mixed-model analysis of variance (ANOVA). A restricted maximum likelihood method was used for estimating the various effects. This method is known to be able to deal correctly with missing observations. The dependent variable is the average logarithmically transformed circumference, as just defined. The following independent variables were entered in the model: a between-subject factor group (two levels); a within-subject factor measurement beyond baseline (five levels: days 1, 4, 7, 14, and 90); the group-by-measurement interaction factor; and the baseline value of the average logarithmically transformed circumference as a continuous between-subjects covariate. The following effects were tested and estimated with their 95% confidence intervals (CIs): the difference in circumference between the two groups at each time point beyond baseline; an overall test (across all five measurements simultaneously) of this difference; and the within-subject changes from baseline per time point in either group. These effects were back-transformed by exponentiation to obtain percent differences and changes in circumference with their 95% CIs. In the analysis, no structure was imposed on the (co)variances of the five repeated measurements.

Similar analyses were done per level (10 cm below the knee, 10 cm above the malleolus, and between the two sites) and for leukocyte counts and CRP concentrations, where the dependent variable was the averaged logarithmically transformed circumference.

To test the contribution of the position of the distal anastomosis (supragenicular/infragenicular) to the explanation of the outcome variable considered, we compared the original statistical model (as described above) with an extended model containing all additional effects of the position of the distal anastomosis (main effects and treatment interactions) by means of the likelihood ratio test.

Categoric variables were compared between two groups using Fisher's exact test. A value of $P < 0.05$ denotes statistical significance.

Results

Between 2006 and 2009, a total of 62 autologous femoropopliteal bypass reconstructions using the ipsilateral saphenous vein were performed. In all, 31 patients were randomized to each arm: Group 1 patients used the compression stocking, and group 2 patients used IPC. Altogether, 57 patients were analyzed in this trial (Fig. 1). Five patients were excluded: Three died before the 14th day after the operation—one from pneumonia (compression stocking group); one from a myocardial infarct (compression stocking group); one from sepsis (IPC group); one underwent an amputation before the 14th day after surgery (compression stocking group); and one refused to continue participation in the trial (IPC group). The resulting maximum number of data points is 1026, of which 15 are missing (1.46%). Baseline characteristics and surgical characteristics are given in Tables 1 and 2, respectively. The randomized groups appear to be in balance for baseline characteristics as judged by the uniform distribution of the P values over the interval (0.1).

Leg circumference

There was an increase in leg circumference in both groups after surgery. The increase in the IPC group was significantly larger than in the compression stocking group as shown in Fig 2. The differences between the treatment groups were significant on days 1, 4, and 7. However, there were no significant differences between the groups on days 14 and 90. Table 3 shows the original leg circumferences and the magnitude of the increase in the two treatment groups. All effects indicate a larger rate of increase in circumference in the IPC group than in the compression stocking group. Percent differences in circumference between groups (at each level) are presented in Table 4. At each level there was an overall (across all measurements) significant difference between the treatment groups. On days 1 and 4 this was particularly so at the highest level measured (10 cm below the knee joint). The position of the distal anastomosis made no significant contribution to the amount of edema ($P = 0.82$). Four patients did not tolerate the IPC device. These patients were further treated with the compression stockings. All patients tolerated the compression stockings.

Laboratory results

Leukocyte counts and CRP concentrations were increased compared to those of the preoperative levels at all time points in both groups, except for the leukocyte counts on day 7 in group 1. Changes in CRP concentration and the

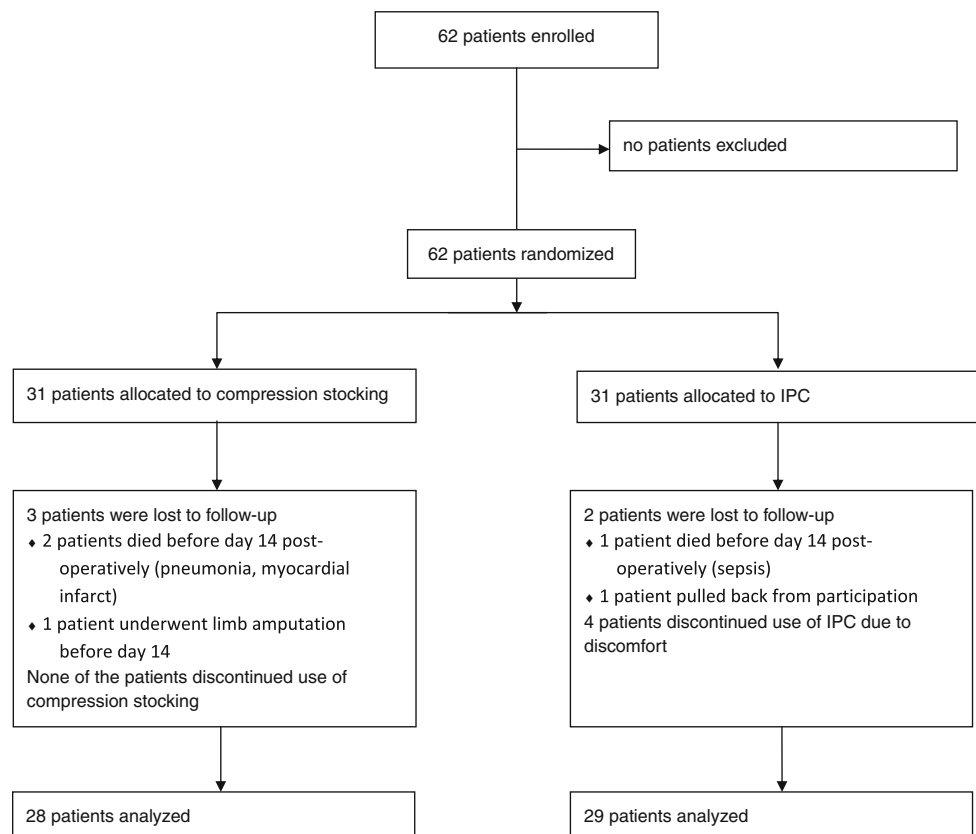**Fig. 1** Trial profile. *IPC* intermittent pneumatic compression

Table 1 Baseline characteristics

Variable	Compression stocking	IPC
No.	28	29
Age (years), mean and range	69 (57–84)	67 (39–88)
Sex (male/female)	23/5	22/7
Rutherford stage 3/4/5–6	11/10/7	13/5/11
ABI[a]	0.49 (0.14)	0.45 (0.21)
ABP[a]	150 (21)	148 (24)
Risk factors		
Diabetes	10	15
Serum cholesterol (mmol/L)[a]	4.9 (1.3)	5.0 (1.3)
Positive family history for cardiovascular disease	13	12
Smoking, current or recent	13	16

ABI ankle-brachial pressure index, *ABP* ankle-brachial pressure

[a] Mean and SD

Table 2 Bypass graft characteristics

Reconstruction characteristic	Compression stocking	IPC	P
Distal anastomosis			0.42
Supragenicular	13	10	
Infragenicular	15	19	
Graft			0.19
In situ	4	1	
Reversed deep tunneled	24	28	

Table 3 Raw summary of absolute circumferences per session absolute circumference (cm)

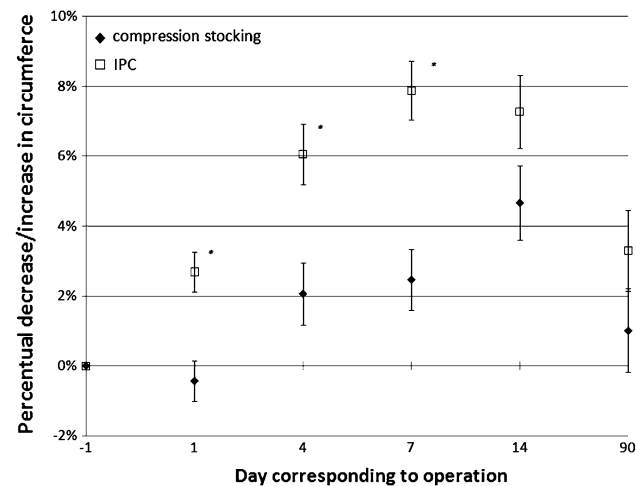| Day	Group	No.	Mean	SD
−1	compression stocking	28	29.5	2.9
	IPC	29	31.1	3.7
1	compression stocking	28	29.4	2.9
	IPC	29	31.9	3.6
4	compression stocking	28	30.1	2.8
	IPC	29	32.9	3.7
7	compression stocking	27	30.5	3.0
	IPC	29	33.4	3.7
14	compression stocking	28	30.9	3.3
	IPC	29	33.3	3.8
90	compression stocking	25	30.3	3.3
	IPC	27	31.9	3.8

Fig. 2 Percent increase of averaged lower limb circumference with standard error markers. Differences between groups are significant on postoperative days 1, 4, and 7. *Significant difference between groups

leukocyte counts are plotted in Figs. 3 and 4, respectively. Differences in leukocyte count and CRP concentration between the treatment groups were not significant in the overall model. The increase in the CRP concentration was significant in both treatment groups postoperatively on all days. There were no significant correlations between circumferential measurements and leukocyte counts or CRP concentrations at any time. The position of the distal anastomosis made no significant contribution ($P = 0.89$) to the increase in the CRP concentration. However, the position of the distal anastomosis showed a significant contribution ($P = 0.0008$) to the leukocyte counts. At postoperative day (POD) 1, patients who used IPC had 29% higher ($P = 0.004$) leukocyte counts than patients who used a compression stocking following supragenicular bypass surgery. However, following infragenicular bypass surgery we found a nearly significant ($P = 0.080$) reverse difference on POD 1: Patients who used IPC had 11% lower leukocyte counts than patients who used a compression stocking.

Complications

The postoperative courses and characteristics are listed in Table 5. There were no significant differences in the occurrence of complications between the groups. Wound infections occurred in eight patients (two patients in the

Table 4 Baseline adjusted mean percent differences in circumference between groups averaged over three levels and per height as estimated by a mixed model ANOVA

Day	Mean of three heights (%) (95% CI)	At 10 cm above the malleolus (%)	Middle (%)	At 10 cm below the knee (%)
1	3.1[a] (1.4–4.9)	1.7	4.0[a]	4.4[a]
4	3.9[a] (1.4–6.5)	3.5[a]	4.3[a]	4.6[a]
7	5.3[a] (2.8–7.9)	5.5[a]	6.6[a]	4.3[a]
14	2.5 (−0.5 to 5.6)	1.7	4.0[a]	2.3
90	2.3 (−1.1 to 5.7)	0.5	3.8	2.3
Overall P	0.0006	0.0074	0.0003	0.0175

A positive percentage means a larger increase in leg circumference in the IPC group compared to the compression stocking group
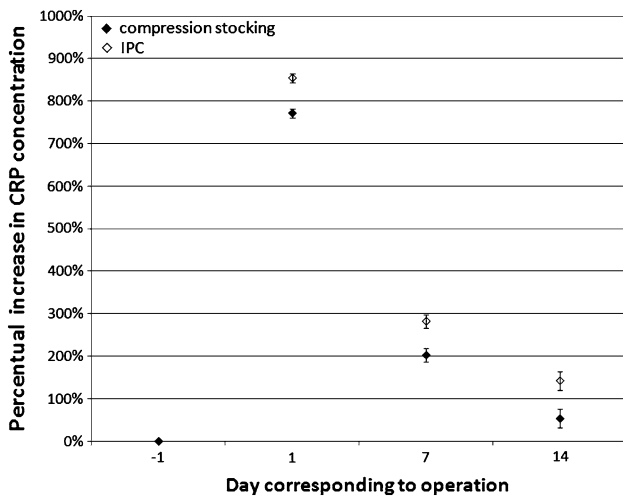
ANOVA analysis of variance

[a] $P < 0.05$

Fig. 3 Percent increase in C-reactive protein (*CRP*) concentration with standard error markers
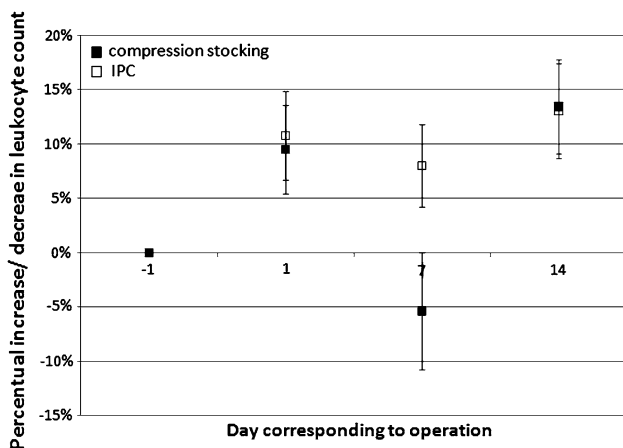

Fig. 4 Percent increase in leukocyte count with standard error markers

Table 5 Postoperative course and complications

Event/postoperative course	Compression stocking	IPC	P
Wound infection	2	6	0.25
Infection (other than wound)	1	1	1.00
Hematoma	3	4	1.00
Seroma	0	2	0.49
Occlusion	2	2	1.00
Myocardial infarct	1	0	0.49
Treatment device switch	0	4	0.12
Hospital stay (days)	7.9 (6–19)	9.7 (7–34)	0.16
Diuretic use	10	6	0.25

compression stocking group, six patients in the IPC group) and were treated with antibiotic therapy.

Discussion

Postoperative edema has been observed and quantified after revascularization surgery using an autologous femoropopliteal bypass in this randomized controlled trial. The patients who used IPC developed significantly more edema than the patients who used the compression stocking. The null hypothesis that there is no difference between treatment groups across all measurements could be significantly rejected. The position of the distal anastomosis did not affect the amount of postoperative edema. None of the previously performed studies compared the use of an IPC device versus a compression stocking. The difference in the amount of edema between the groups vanishes within a week after the use of IPC was discontinued. Starting on POD 8, all patients used a compression stocking during the day. The occurrence of postoperative edema in all revascularized patients with a femoropopliteal bypass is in accordance with findings in the literature [2–6].

We also observed increases in leukocyte counts and CRP concentrations following femoropopliteal surgery, but there were no significant differences in these two parameters between treatment groups. Patients who used IPC following a supragenicular femoropopliteal bypass had higher leukocyte counts immediately after the operation than patients who used a compression stocking.

Soong et al. [18] and Rabl et al. [19] hypothesized that reperfusion of ischemic tissue could lead to cell damage and result in up-regulating of inflammatory processes and edema formation. That the presence of edema is a contributing factor to increases in inflammatory parameters could not be proved. Significantly higher leukocyte counts in the IPC group were found only on POD 1 following a supragenicular bypass operation, whereas significantly more edema formation was seen in the IPC group as a whole and at most postoperative time points. These analyses concerning the explanatory contribution of the position of the distal anastomosis to the model were not prespecified as hypotheses in the protocol. Formally, then, these analyses are of an explorative nature. The inconclusive significant results concerning the leukocyte count must be considered as hypothesis-generating rather than hypothesis-testing.

The difference in leukocyte counts and CRP concentrations might be associated with wound infections, although a firm correlation was not found. A significant difference in the occurrence of wound infections between groups could not be detected. However, there seems to be a trend of more wound infections and a prolonged hospital stay in patients who had a larger amount of edema (i.e., the patients who used IPC). Based on this study, the evidence is not sufficient to associate the amount of edema with increases in inflammatory parameters or wound infections.

Edema following femoropopliteal surgery is likely to be multifactorial, with a large attribution of lymphatic disruption [3, 4], hyperemia [10, 33], and microvascular permeability [12, 18, 34]. The lymphatics can be damaged as a result of surgery, or their function can be impaired by inflammatory processes or adjacent tissue trauma [6]. Edema following arterial reconstruction undertaken because of a popliteal aneurysm is surprisingly of the same magnitude as edema following revascularizations for PAD, suggesting a large contribution of lymphatic disruption in the pathophysiology [6]. Studies on the effect of lymph-sparing approaches during femoropopliteal surgery have not been conclusive [4, 6]. Dysfunctional autoregulation mechanisms are also likely to contribute to hyperemia [8, 10]. Autoregulation mechanisms do maintain a constant perfusion pressure in the limbs, although this mechanism fails in patients with severe PAD. An increase in the arteriovenous pressure gradient may cause an increase in microvascular permeability for fluids and proteins [5, 9]

and inflammatory responses following revascularization, resulting in edema [10, 34]. However, the attribution of hyperemia is probably limited, as illustrated by the occurrence of only a small increase in limb volume following percutaneous revascularization because no lymphatics are damaged [35].

We used a graduated (class I) compression stocking that exerted 18 mmHg pressure to the limb. There have been no large, quality studies on the effect of compression stockings for the treatment and prevention of postreconstructive edema. We selected a class I stocking because class II stockings and above might exert too much pressure on the leg, possibly resulting in even more patient discomfort or graft failure. The working mechanism of the compression stocking is to increase pressure on the interstitial space [21] and to augment the peripheral circulation by lowering flow resistance at the arteriolar level [36].

The IPC devices do facilitate lymphatic and hemodynamic circulation in the lower limb. Among them, the A-V impulse technique has been tested successfully for edema reduction following orthopedic surgery on the lower limb [22, 23]. It is thought that when the IPC is active compression of the foot is followed by emptying of terminal lymphatics, allowing drainage of fluids from the interstitium. It may also assist in moving fluids from the interstitium to the lymphatics [37].

As mentioned, the A-V impulse system is an IPC on the foot only. This might be a shortcoming of the study because there are also IPC systems that fit the calf. However, we chose an IPC on the foot because of the satisfying results following orthopedic and trauma surgery [22, 23]. Another reason we chose IPC on the foot is to avoid subjecting surgical wounds on the calf to intermittent compression. Those surgical wounds were made in some patients when the superficial saphenous vein was (partly) harvested in the lower leg. IPC is also thought to attribute to arterial [25, 38] and venous [39, 40] blood flow. For patients suffering PAD and in healthy subjects, IPC combined on the foot and calf can double the arterial flow into the limb immediately after compression. This effect has been demonstrated in native arterial blood flow as well as in infragenicular femoropopliteal bypass grafts [38]. Venous flow velocity in the common femoral vein increases during compression by a factor of 2.5–3.0, which indicates that venous emptying is facilitated [39, 40]. In immobilized patients, the venous muscle pump function is not maintained and blood is no longer cleared from the veins, which results in venous hypertension. The use of IPC might prevent fluids from moving out of the capillaries [41].

In this trial, we chose to apply IPC on the foot in a controlled situation, while the patient was hospitalized. We decided not to introduce the system in an uncontrolled out-of-hospital situation because edema emerges mostly during

the first postoperative week [20] and knowledge of the effect of IPC on freshly revascularized patients was lacking. The results, however, did not encourage us to investigate the effect of IPC on the foot over a longer period.

The use of IPC on the foot resulted in significantly more edema than did the use of compression stockings following femoropopliteal bypass surgery. This was contrary to what could be expected based on orthopedic and trauma findings [22, 23]. However, in those studies, IPC was applied day and night. We choose to apply IPC only at night so a not to interfere with early rehabilitation schedules. Using IPC immediately postoperatively has probably resulted in amplification of the hyperemic effect. This hyperemic effect probably outweighed the enhancement of venous and lymphatic flow and was probably limited in the patients who used the compression stockings, as less edema developed in them. Patients who used IPC at night did not use compression stockings during the day. The absence of these stockings or IPC on the calf might also have contributed to increased edema. It cannot be ruled out that the application of IPC on the foot and the might result in another outcome.

Conclusion

In this study, the development of postoperative edema following autologous femoropopliteal bypass surgery was quantified at subsequent time points up to 3 months after surgery. The use of compression stockings postoperatively has been the standard practice. A study on the effect of IPC, which was expected to have a beneficial effect on edema, resulted in the conclusion that it leads to a short-term increase in edema. However, the amount of edema decreases to the same extent when using a compression stocking after the use of IPC is halted. The use of compression stockings following femoropopliteal surgery is thus the recommended practice.

References

1. Veith FJ, Gupta SK, Ascer E et al (1986) Six-year prospective multicenter randomized comparison of autologous saphenous vein and expanded polytetrafluoroethylene grafts in infrainguinal arterial reconstructions. J Vasc Surg 3:104–114

2. Eickhoff JH, Engell HC (1982) Local regulation of blood flow and the occurrence of edema after arterial reconstruction of the lower limbs. Ann Surg 195:474–478

3. Hannequin P, Clement C, Liehn JC et al (1988) Superficial and deep lymphoscintigraphic findings before and after femoropopliteal bypass. Eur J Nucl Med 14:141–146

4. AbuRahma AF, Woodruff BA, Lucente FC (1990) Edema after femoropopliteal bypass surgery: lymphatic and venous theories of causation. J Vasc Surg 11:461–467

5. Campbell H, Harris PL (1985) Albumin kinetics and oedema following reconstructive arterial surgery of the lower limb. J Cardiovasc Surg (Torino) 26:110–115

6. Haaverstad R, Johnsen H, Saether OD et al (1995) Lymph drainage and the development of post-reconstructive leg oedema is not influenced by the type of inguinal incision: a prospective randomised study in patients undergoing femoropopliteal bypass surgery. Eur J Vasc Endovasc Surg 10:316–322

7. Jacobs MJ, Beckers RC, Jorning PJ et al (1990) Microcirculatory haemodynamics before and after vascular surgery in severe limb ischaemia: the relation to post-operative oedema formation. Eur J Vasc Surg 4:525–529

8. Henriksen O (1974) Orthostatic changes of blood flow in subcutaneous tissue in patients with arterial insufficiency of the legs. Scand J Clin Lab Invest 34:103–109

9. Eickhoff JH (1980) Forefoot vasoconstrictor response to increased venous pressure in normal subjects and in arteriosclerotic patients. Acta Chir Scand Suppl 502:7–14

10. Sumner DS, Folse R (1968) Persistent hyperemia following prolonged arterial occlusion. Ann Surg 168:837–843

11. Henriksen O, Paaske WP (1980) Local regulation of blood flow in peripheral tissue. Acta Chir Scand Suppl 502:63–74

12. Junger M, Frey-Schnewlin G, Bollinger A (1989) Microvascular flow distribution and transcapillary diffusion at the forefoot in patients with peripheral ischemia. Int J Microcirc Clin Exp 8:3–24

13. Balzer K, Schonebeck I (1993) Edema after vascular surgery interventions and its therapy. Z Lymphol 17:41–47

14. Storen EJ, Myhre HO, Stiris G (1974) Lymphangiographic findings in patients with leg oedema after arterial reconstructions. Acta Chir Scand 140:385–387

15. Vaughan BF (1990) CT of swollen legs. Clin Radiol 41:24–30

16. Fernandez MJ, Davies WT, Tyler A et al (1984) Post-arterial reconstruction edema: are lymphatic channels to blame? Angiology 35:475–479

17. Sullivan WG, Thornton FH, Baker LH et al (1971) Early influence of popliteal vein repair in the treatment of popliteal vessel injuries. Am J Surg 122:528–531

18. Soong CV, Young IS, Lightbody JH et al (1994) Reduction of free radical generation minimises lower limb swelling following femoropopliteal bypass surgery. Eur J Vasc Surg 8:435–440

19. Rabl H, Khoschsorur G, Petek W (1995) Antioxidative vitamin treatment: effect on lipid peroxidation and limb swelling after revascularization operations. World J Surg 19:738–744

20. Vaughan BF, Slavotinek AH, Jepson RP (1970) Edema of the lower limb after vascular operations. Surg Gynecol Obstet 131:282–290

21. Pflug JJ, Calnan JS (1973) The relationship between the blood, lymphatic and interstitial circulation in the leg. Vasa 2:75–80

22. Stranks GJ, MacKenzie NA, Grover ML et al (1992) The A-V impulse system reduces deep-vein thrombosis and swelling after hemiarthroplasty for hip fracture. J Bone Joint Surg Br 74:775–778

23. Gardner AM, Fox RH, Lawrence C et al (1990) Reduction of post-traumatic swelling and compartment pressure by impulse compression of the foot. J Bone Joint Surg Br 72:810–815

24. Delis KT, Nicolaides AN, Wolfe JH et al (2000) Improving walking ability and ankle brachial pressure indices in

symptomatic peripheral vascular disease with intermittent pneumatic foot compression: a prospective controlled study with one-year follow-up. J Vasc Surg 31:650–661

25. Eze AR, Comerota AJ, Cisek PL et al (1996) Intermittent calf and foot compression increases lower extremity blood flow. Am J Surg 172:130–134 (discussion 135)

26. Van Bemmelen PS, Mattos MA, Faught WE et al (1994) Augmentation of blood flow in limbs with occlusive arterial disease by intermittent calf compression. J Vasc Surg 19:1052–1058

27. Cohen J (1988) Statistical power analysis for the behavioral sciences. Lawrence Erlbaum Associates, Hillsdale, NJ

28. Norgren L, Hiatt WR, Dormandy JA et al (2007) Inter-society consensus for the management of peripheral arterial disease (TASC II). Eur J Vasc Endovasc Surg 33(Suppl 1):S1–S75

29. Schanzer A, Hevelone N, Owens CD et al (2007) Technical factors affecting autogenous vein graft failure: observations from a large multicenter trial. J Vasc Surg 46:1180–1190 (discussion 1190)

30. Panetta TF, Marin ML, Veith FJ et al (1992) Unsuspected pre-existing saphenous vein disease: an unrecognized cause of vein bypass failure. J Vasc Surg 15:102–110 (discussion 110–112)

31. Anonymous (2000) Efficacy of oral anticoagulants compared with aspirin after infrainguinal bypass surgery (The Dutch bypass oral anticoagulants or aspirin study): a randomised trial. Lancet 355:346–351

32. Te Slaa A, Mulder P, Dolmans D, et al (2010) Reliability and reproducibility of a clinical application of a simple technique for repeated circumferential leg measurements. Phlebolgy [Epub ahead of print]

33. Simeone FA, Husni EA (1959) The hyperemia of reconstructive arterial surgery. Ann Surg 150:575–585

34. Husni EA (1967) The edema of arterial reconstruction. Circulation 35:I169–I173

35. Payne SP, Jones K, Painter D et al (1995) Does the limb swell after revascularisation by percutaneous transluminal angioplasty? Eur J Vasc Endovasc Surg 9:272–276

36. Schubart PJ, Porter JM (1986) Leg edema following bypass. In: Bergan JJ (ed) Reoperative arterial surgery. Grune & Stratton, Orlando, pp 328–329

37. McGeown JG, McHale NG, Thornbury KD (1988) Effects of varying patterns of external compression on lymph flow in the hindlimb of the anaesthetized sheep. J Physiol 397:449–457

38. Delis KT, Husmann MJ, Szendro G et al (2004) Haemodynamic effect of intermittent pneumatic compression of the leg after infrainguinal arterial bypass grafting. Br J Surg 91:429–434

39. Blackshear WM Jr, Prescott C, LePain F et al (1987) Influence of sequential pneumatic compression on postoperative venous function. J Vasc Surg 5:432–436

40. Griffin M, Kakkos SK, Geroulakos G et al (2007) Comparison of three intermittent pneumatic compression systems in patients with varicose veins: a hemodynamic study. Int Angiol 26:158–164

41. Coleridge Smith PD, Thomas P, Scurr JH et al (1988) Causes of venous ulceration: a new hypothesis. Br Med J (Clin Res Ed) 296:1726–1727