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# Effects of Intermittent Pneumatic Compression on Reduction of Postoperative Lower Extremity Edema and Normalization of Foot Microcirculation Flow in Patients Undergoing Arterial Revascularization

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

BCE 1 **Katarzyna Pawlaczyk**  
ABD 2 **Marcin Gabriel**  
CD 3 **Tomasz Urbanek**  
BF 2 **Łukasz Dzieciuchowicz**  
CDF 2 **Zbigniew Krasieński**  
EF 2 **Zofia Gabriel**  
CG 4 **Małgorzata Olejniczak-Nowakowska**  
BE 2 **Michał Stanisic**

1 Department of Hypertensiology, Angiology and Internal Diseases, Medical University, Poznań, Poland  
2 Department of General and Vascular Surgery, Medical University, Poznań, Poland  
3 Department of General and Vascular Surgery, Medical University of Silesia, Katowice, Poland  
4 Department of Cancer Prevention, Medical University of Silesia, Katowice, Poland

**Corresponding Author:** Katarzyna Pawlaczyk, e-mail: [kati2911@poczta.onet.eu](mailto:kati2911@poczta.onet.eu)  
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**Background:** In patients with chronic leg ischemia, the beneficial effect of arterial revascularization can be significantly decreased due to postoperative leg swelling. The aim of this study was to assess the effects of intermittent pneumatic compression (IPC) on skin flow normalization in patients undergoing revascularization procedures due to chronic leg ischemia.





**Material/Methods:** We evaluated 116 patients with chronic leg ischemia. The patients were divided into groups according to the performed treatment (endovascular or surgical) and implementation of IPC postoperatively. The leg edema assessment and microcirculation flow assessment were performed pre- and postoperatively, using percutaneous O<sub>2</sub> pressure (T<sub>cp</sub>O<sub>2</sub>), cutaneous blood perfusion (CBP) measurements, and skin flow motion assessment.

**Results:** In patients who did not receive IPC, a decrease in CBP value was observed in the 1<sup>st</sup> postoperative assessment. Among patients receiving IPC, the CBD value increased at the 1<sup>st</sup> and 2<sup>nd</sup> postoperative measurements, especially in the surgical group. The lowest T<sub>cp</sub>O<sub>2</sub> values were observed in by-pass surgery group without IPC postoperatively.

**Conclusions:** The benefits of the by-pass procedure in patients with leg ischemia can be significantly reduced by postoperative edema. Among patients with postoperative leg edema, local tissue blood perfusion can be improved by the use of IPC, which can result in decreased local leg swelling, as well as improved skin blood perfusion and T<sub>cp</sub>O<sub>2</sub>.

**MeSH Keywords:** **Brain Edema • Intermittent Pneumatic Compression Devices • Ischemia • Microcirculation • Vascular Surgical Procedures**

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 3160  3  2  18



## Background

Microcirculation injury related to pre- and perioperative leg ischemia or to revascularization-related reperfusion can affect arterial revascularization. As previously shown, the beneficial effect of revascularization procedures can be significantly decreased or delayed due to postoperative leg swelling [1]. In turn, this can negatively affect the wound healing process, including the healing of ulcers or other soft tissue injuries.

Despite the theoretical potential for negative effects of postoperative edema on healing of wounds and trophic changes, as well as on the progress of postoperative rehabilitation and ambulation, few studies have been dedicated to this topic. One proposed option to decrease postoperative swelling complications is to avoid making surgical incisions in the groin and popliteal regions and, if necessary, to make a more lateral groin incision and perform lateral surgical lymph node dissection [2,3].

Compression therapy is one of the most commonly used treatment modalities in patients with leg edema. In contrast to venous and lymphatic diseases, the presence of the arterial insufficiency remains an important contraindication to compression therapy, which is especially important in the setting of an ankle – brachial index (ABI) of less than 0.6. Previous studies have shown that among patients with significant leg ischemia who are not candidates for surgical or endovascular treatment, intermittent pneumatic compression (IPC) can improve the local circulatory conditions [4–6]. Despite some promising reports confirming the beneficial effect of this treatment for non-reconstructive critical leg ischemia, the use of IPC for this indication remains still experimental. Additionally, we do not know whether compression therapy, and especially IPC, can improve the soft tissue blood supply disturbances related to the postoperative leg swelling among patients

undergoing arterial peripheral by-pass surgery. Taking into account the potential role of postoperative leg swelling on microcirculation flow depletion, the aim of the study was to assess the effects of intermittent pneumatic compression on skin flow normalization in patients undergoing revascularization procedures due to chronic leg ischemia.

## Material and Methods

One hundred sixteen patients with chronic leg ischemia at stages 3 and 4 according to the Rutherford classification were evaluated. In all patients, an isolated occlusion of the femoral superficial artery was diagnosed. The following exclusion criteria were established: the presence of true or false arterial aneurysms; cancer; chronic venous disease; chronic or acute kidney failure; inflammatory arterial disease; uncontrolled hypertension; trophic skin changes; use of steroids, immunosuppressive or phlebotrophic drugs; and previous arterial, venous or lymphatic surgery of the affected extremity. All patients received acetylsalicylic acid (100–150 mg o.d.) and statin (atorvastatin 20–40 mg o.d.) in the postoperative period. The TASC II criteria were used to choose the optimal revascularization method [6].

According to the projected treatment, the patients were divided into 5 groups (Table 1). In 48 patients, PTA of the superficial femoral artery was performed; 12 patients required additional stenting of the femoral artery. Unfractionated heparin (UFH) was administered (5 000 U i.v.) during the procedure, and a therapeutic dose of low molecular weight heparin was continued on the first post-operative day. For further treatment, only antiplatelet drugs were continued. In 30 patients from the endovascular group (group 1), no compression therapy treatment was applied, and in the further 18 cases, IPC

**Table 1.** Group characteristics.

	Group				
	1 (angioplasty/ stent)	2 (by-pass surgery)	3 (angioplasty/ stent + IPC)	4 (by-pass surgery + IPC)	5 (conservative + IPC)
No. of patients	30	29	18	19	20
Age – mean ±SD	64.6±11.2	66.5±9.7	64.7±10.2	66.6±10.9	63.3±11.4
BMI – mean ±SD	26.5±4.3	25.5±5.5	27.3±3.7	27.2±4.7	25.6±3.6
Dyslipidemia No. (%)	24 (80)	25 (86.2)	14 (77.8)	12 (63.1)	18 (90)
Arteria hypertension No. (%)	18 (60)	19 (65.5)	12 (66.7)	12 (63.1)	15 (75)
Smoking No. (%)	22 (73.3)	21 (72.4)	11 (61.1)	12 (63.1)	13 (65)
Diabetes No. (%)	8 (26.7)	10 (34.5)	6 (33.3)	6 (31.6)	5 (25)
Ischemic hart disease No. (%)	23 (76.7)	20 (69)	16 (88.9)	15 (78.9)	9 (45)

was used postoperatively (group 3). Forty-eight patients underwent femoral-popliteal by-pass implantation. In all cases, a 6-mm PTFE prosthesis was implanted. In all cases, 100 U/kg of UFH was administered intraoperatively, and low molecular weight heparin was continued postoperatively until hospital discharge. Twenty-nine patients from this group received no postoperative compression therapy (group 2), and 19 patients received IPC therapy (group 4). Group 5 consisted of 20 patients who were treated conservatively; in all cases, IPC was applied during the same treatment period as that of the groups treated invasively.

### Compression therapy

Intermittent pneumatic foot compression began on postoperative day 1 and continued to postoperative day 14. IPC was applied to patients in the supine position and with slight leg elevation. Single-chamber cuffs (Kendall SCD Express Foot Cuff) were used and in all patients foot compression was applied. The compression cycles (Kendall 7325 Response SCD pump) consisted of 4 s of cuff inflation, a 1 s pressure plateau and 15 s of cuff deflation. The maximum pressure was individualized to reach a value that was 10 mmHg lower than the diastolic pressure measured on the toe arteries (the pressure values ranged from 50 to 72 mmHg; mean 59 mmHg). IPC was applied for one hour daily, and the treatment continued for two weeks following the revascularization procedure.

### Microcirculation flow assessment

All measurements were performed in the morning during a non-fasting state and using the same temperature settings (21°C). The assessment was performed in the supine position after 15 min of rest. All measurements were performed at the following 4 times: 1 day before surgery or endovascular procedure and 15, 30 and 90 days after the procedure. The ankle-brachial index and the pole test index were measured in all patients prior to microcirculation flow assessment.

Microcirculation flow assessment was performed using the Periflux System 5000 (Perimed, Sweden) with the PF 5010 LDPM Unit and the PF 5020 Temp Unit (Perimed, Sweden). The measurements were performed using the bifunctional heating probe (Angled Small Thermostatic Laser Doppler Probe 457, Perimed, Sweden). PeriSoft for Windows 2.50 software was used for the signal analysis. The probe was applied to the skin in the dorsal region of the foot (in the middle between the second and third metatarsals).

For the skin blood flow assessment, *Cutaneous Blood Perfusion* (CBP) was estimated in perfusion units [1 PU=10 mV]. The evaluation was performed at the following 3 times during each measurement: in the resting condition, during the thermal

stimulation test (44°C) and after post-ischemic hyperemia (3 min of ischemia followed by reactive hyperemia – *leg skin post-occlusive hyperemia – POH*) [7]. The skin flow motion assessment was performed using spectral analysis and generalized wavelet analysis. In the frequency range from 0.01 Hz to 1.6 Hz, 5 bands of the flow motion compounds were selected: endothelial (0.01–0.02 Hz), neurogenic (0.02–0.06 Hz), muscular (0.06–0.2 Hz), respiratory (0.2–0.6 Hz) and cardiac (0.6–1.6 Hz) bands. The results of the skin flow motion assessment are presented in Power Density Units [PU/Hz] [8].

Percutaneous O<sub>2</sub> pressure measurement (*transcutaneous pressure of oxygen – TcpO<sub>2</sub>*) was performed using a Clark electrode (tc electrode REF 945-605, E 5250-TcpO<sub>2</sub>, Radiometer Medicals Aps, Denmark) and the PF 5040 TcpO<sub>2</sub>/pCO<sub>2</sub> module of the Periflux System 5000.

An assessment of leg edema was based on volumetric assessment by a specially calibrated basket filled with water at 37°C.

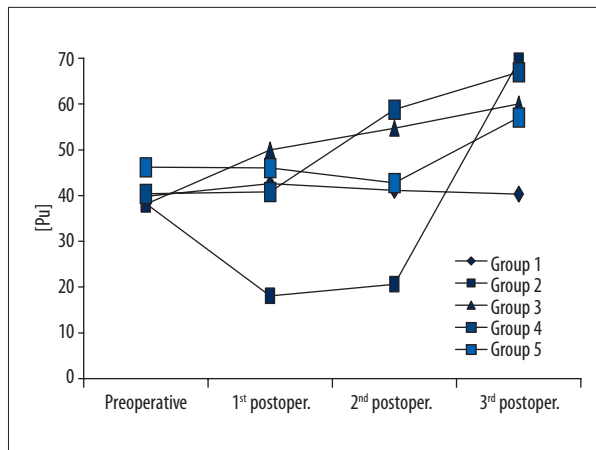
Before the study, approval was obtained from the local bioethics committee of the Medical University of Poznań (no 1071/07 and 1083/08). STATISTICA v.9 from StatSoft was used for statistical analysis. The Mann-Whitney test for group comparisons and the Wilcoxon test for measurement comparisons within groups were used. Additionally, the Spearman correlation index was used, and values of p<0.05 were considered statistically significant.

## Results

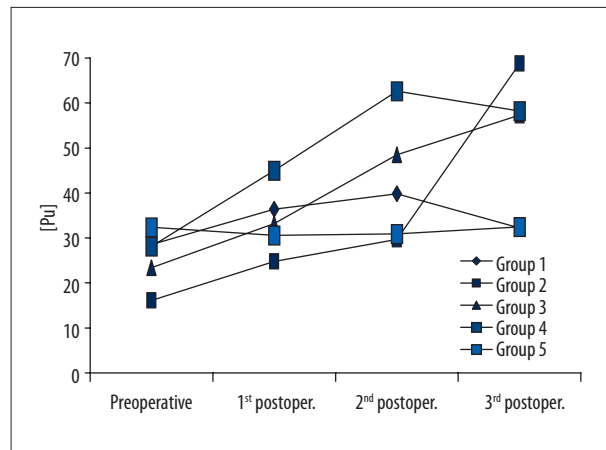
The mean ABI value in groups 1–4 increased from 0.53±0.06 preoperatively to 0.75±0.03 at the first postoperative assessment (p<0,001). There were no significant differences between the groups treated invasively (groups 1–4), and there was no statistically significant difference in the ABI values measured before the start of the treatment and after 14 days of therapy in the group 5 (treated conservatively).

The differences in the skin flow measurements are presented in Figures 1 and 2.

In groups 1, 3 and 4, a significant increase in TcpO<sub>2</sub> was observed at the first postoperative measurement (similar values were observed at the following measurement) (Table 2). In group 2, the results of the pre- and 1<sup>st</sup> postoperative TcpO<sub>2</sub> measurement did not differ significantly; however, a significant increase was noticed at the 2<sup>nd</sup> and 3<sup>rd</sup> postoperative measurement in group 2 (after postoperative edema decrease). In group 5, there were no differences in TcpO<sub>2</sub> value. Compared to patients in other groups, those in group 2 had the lowest TcpO<sub>2</sub> value at the 1<sup>st</sup> and 2<sup>nd</sup> postoperative assessments. At



**Figure 1.** Changes in the CBP median in the thermal stimulation test.



**Figure 2.** Changes in the CBP median in the ischemic stimulation test.

**Table 2.** Statistically significant differences in TcPO<sub>2</sub> measurements between the groups and between measurements (Wilcoxon test).

Group	The level of significance between measurements					
	0–1	0–2	0–3	1–2	1–3	2–3
1	<0.001	<0.001	<0.001	0.027	0.016	1.000
2	0.053	<0.001	<0.001	0.079	<0.001	<0.001
3	0.001	0.001	0.001	0.983	0.528	0.349
4	0.001	<0.001	<0.001	0.520	0.171	0.136
5	0.058	0.279	0.218	0.681	0.204	0.940

the last evaluation, TcPO<sub>2</sub> was highest among patients who underwent bypass implantation (groups 2 and 4).

To assess the potential influence of IPC on microcirculation changes, two patient groups were compared. Group C(–) consisted of 59 patients who underwent vascular reconstruction (endovascular and surgical) from groups 1 and 2 and who had no postoperative IPC treatment. Group C(+) consisted of 58 patients from groups 3 and 4 who underwent revascularization procedures and who received IPC in the early postoperative period. The percent of the patients with low grade, moderate or advanced post-procedure swelling in the groups selected according to the way of the vascular reconstruction as well as to the IPC implementation was presented in the Table 3. The statistically significant differences between groups C(+) and C(–) were as follows:

Resting skin blood flow (CBP – cutaneous blood perfusion)

In patients who did not receive IPC, a decrease in CBP value was observed in the 1<sup>st</sup> and 2<sup>nd</sup> postoperative assessments (–8.1% and –3.6%, respectively). Among patients receiving IPC, the CBD value increased at the 1<sup>st</sup> and 2<sup>nd</sup> postoperative measurements (+4.2% and +8.6%, respectively). There were

no significant differences between the preoperative measurement and the CBD value measured 60 and 90 days after the procedure.

#### Power density of the endothelial bond

A significant postoperative decrease in the power density value of the endothelial bond (in the 1<sup>st</sup> postoperative assessment) in the C(–) group and a significant increase in the C(+) group were observed (–3% and +2.9%, respectively). In the further assessments there were no statistically significant differences.

#### Cutaneous blood flow perfusion in the thermal stimulations test (CBP<sub>H</sub>)

Compared to the preoperative value, the CBP<sub>H</sub> value increased 17.4% and 30% in the 1<sup>st</sup> and 2<sup>nd</sup> postoperative assessments, respectively. In the C(+) group, the respective values increased 34.5% and 89.7% (p<0.049).

#### Power density of the endothelial bond

The power density of the endothelial bond in the thermal stimulation test differed between the preoperative and postoperative

**Table 3.** Percent of the patients with post-procedure leg swelling in the 1<sup>st</sup> and 3<sup>rd</sup> postoperative assessment (in comparison to the preoperative assessment).

Group	Postoperative control	No swelling	Small swelling (leg volume increase <10%)	Moderate swelling (leg volume increase + 10–20%)	Advanced swelling (leg volume increase >20%)
Endovascular treatment	1 <sup>st</sup> (15days)	46.7%	30.0%	16.6%	6.7%
	3 <sup>rd</sup> (90 days)	73.4%	23.3%	3.3%	0.0%
By-pass implantation	1 <sup>st</sup> (15days)	13.8%	27.6%	31%	27.6%
	3 <sup>rd</sup> (90 days)	34.6%	51.7%	10.3%	3.4%
Endovascular treatment + IPC	1 <sup>st</sup> (15days)	38.9%	38.9%	22.2%	0.0%
	3 <sup>rd</sup> (90 days)	77.8%	22.2%	0.0%	%
By-pass implantation + IPC	1 <sup>st</sup> (15days)	26.3%	47.4%	26.3%	0.0%
	3 <sup>rd</sup> (90 days)	84.4%	10.4%	5.2%	0.0%

assessments in the C(–) group. The differences between the preoperative measurement and the 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> postoperative assessments were as follows: –4.2%, 18.8% and 45.8%, respectively. In the C(+) group, the respective values were: +15.1%, +23.6% and +72.9% (all statistically significant;  $p < 0.05$ ).

#### Cutaneous blood perfusion in the ischemia stimulation test

In the C(–) group, the CBP value increased at the 3<sup>rd</sup> postoperative assessment compared to the preoperative evaluation and also differed between the 1<sup>st</sup> and 3<sup>rd</sup> postoperative evaluations (+82% and +25.6%, respectively). In the C(+) group, the CBP increases in the same intervals were higher (+224% and +96.9%, respectively;  $p < 0.048$ ). Comparing to the preoperative evaluation in the C(–) group, there were only small changes in the power density of the endothelial bond during ischemia stimulation test at the 1<sup>st</sup> and 2<sup>nd</sup> postoperative assessment (0.3% and 8.7%, respectively). In the group C(+) power density of the endothelial bond during ischemia stimulation significantly increased (+10.1% and +23.6% at the 1<sup>st</sup> and 2<sup>nd</sup> postoperative assessments, respectively;  $p < 0.049$ ). Similar observations concerning the neurogenic bond power density were observed among patients from the C(+) group (+26.7% and +55.6% in the 1<sup>st</sup> and 2<sup>nd</sup> postoperative assessments, respectively;  $p < 0.038$ ). In the C(–) group, a slight reduction in this parameter was observed postoperatively (–5.6% and –2.2%, respectively). The index of the ischemia stimulation test increased 53.5% in the C(–) group and 120% in the C(+) group between the preoperative and 1<sup>st</sup> postoperative assessment. At the 3<sup>rd</sup> postoperative evaluation, these values increased from 78.9% in the C(–) group and 231.5% in the C(+) group ( $p < 0.017$ ).

IPC use was also associated with changes in the microcirculation flow among patients treated conservatively. 2 weeks of IPC treatment among group 5 resulted in an increase in some evaluated parameters. These included basic skin flow (resting as well as following ischemic stimulation), thermal stimulation index, power density of the neurogenic and muscular bonds and pole test index. Other parameters, including the ABI value, did not differ significantly.

#### Discussion

A delay and a decrease in improvement in microcirculation blood flow among patients who underwent surgical femoral – popliteal by-pass suggest a negative influence of surgery-related edema on microcirculation flow modulation. The postoperative use of IPC among these patients resulted in a reduction of edema as well as in an increase in skin blood perfusion with the multiplication of the thermal and ischemic index values in the second and third postoperative measurements. Simultaneously, these patients experienced a reduction in CBP in the early postoperative period (edema-related), and use of IPC led to a significant increase in CBP (in course of edema decrease).

There were no significant effects of compression therapy on the perfusion parameters in patients who underwent endovascular procedures. In both groups (with and without IPC) following PTA of the femoral artery, an increase in the microcirculation flow was observed at the first postoperative evaluation. It should be emphasized that in patients undergoing endovascular treatment, relatively few cases of postoperative edema were observed.

An increase in  $TcpO_2$  was observed in all patients. In patients treated postoperatively with IPC (after surgery or endovascular procedures), a significant increase in  $TcpO_2$  on the 1<sup>st</sup> postoperative day was reported. In contrast to these observations, among patients who underwent femoral-popliteal bypass without postoperative IPC, a delayed increase in the  $TcpO_2$  was observed (noticed in the second postoperative assessment but not in the first). This observation suggests the potential role of surgery-related swelling on impairment of microcirculation skin flow. Accordingly, the use of above mentioned compression has a significant effect not only on the reduction of edema but also on the skin flow parameters.

The decrease in postoperative swelling seems to be the most important mechanism influencing skin flow modification and its disturbances after femoral-popliteal bypass, though other mechanisms should also be considered following observations in patients treated conservatively with IPC. This group of patients experienced an increase in the pole test index (without a significant increase in ABI value) two weeks after initiating IPC therapy. Previous investigators have also suggested that there is a positive effect of IPC on ABI. A study by de Haro et al. found no differences in the resting ABI after 1 and 3 months of IPC therapy [4]. However, another study utilizing 4 hr IPC sessions over a 5-month period found an increase in the mean ABI of 17% [9]. More obvious changes following IPC implementation were observed in the post-exercise ankle-brachial pressure index. Compared to baseline, post-exercise ABI increased 97% after 3 months and 110% after 5 months of therapy. It seems (limited changes in the resting ABI and significant post exercise ABI increase) that IPC does not stimulate anatomical changes in the circulation or in the development of collateral circulation [10]. These observed changes suggest the role of IPC in improving the reactive vessel dilatation in response to exercise [4]. Some studies suggest that IPC mediates NO and prostaglandin release from the endothelial cells, which would lead to an increase in the shear stress of the blood in the affected vessels [11].

Another important effect of IPC is its potential influence on peripheral blood flow due to the repeated compression of the sympathetic nerves receptors (which are also responsible for the precapillary sphincter tension) [12]. Under normal conditions, the *veno-arteriolar reflex* (VAR) is related to the precapillary sphincter stricture, which is related to the increase in venous pressure. The increase in peripheral resistance that decreases the peripheral arterial flow plays a significant role in the standing position and for the patients with PAOD and concomitant edema [13]. Both, hemodynamically successful revascularization as well as IPC therapy can significantly increase the veno-arterial reflex index [4]. This can be a result of an increase in the neurogenic bond flow motion amplitude documented among patients treated conservatively with IPC

only. Additionally, the veno-arterial reflex can be modified due to reduction of the vein system reservoir blood volume (which is related to the positive influence of IPC on the venous outflow) [14].

The results of our study suggest that in patients undergoing arterial revascularization, IPC has a positive effect when proper compression pressure is applied. In our investigation, foot cuff pressures of 45 to 60 mmHg were applied. The reduction of pressures to the abovementioned values were adjusted to the increased sensitivity of the affected extremities (related to the presence of leg ischemia and surgery related complains). When using IPC for patients with ischemia, other investigators have used pressures from 65 to 180 mmHg (mostly 120 mmHg) simultaneously with longer and more frequent sessions [4,10]. Unfortunately, as has been reported by some authors, the higher pressure can significantly affect patient quality of life, especially with regard to pain [4]. According to some studies, only 35–80% of patients treated with IPC were satisfied with the results and the method of therapy [10,15]. In the described study, all patients accepted IPC treatment when the proposed pressures in the study protocol were used. Another important modification was the use of the foot pump IPC as opposed to the calf-length cuffs used by others. In previous papers, a relationship between increased popliteal artery flow and compression cuff placement was suggested. The smallest changes were observed when IPC was applied to the foot only. However, an increase in flow was observed when calf compression was applied, particularly when foot compression and calf compression were applied simultaneously [15–18]. In our study protocol the foot IPC was applied – in the further studies, the calf length IPC in the same treatment model should be evaluated. On the other hand the choice of IPC restricted to the foot can be the optimal option for the patients with popliteal distal or crural by-pass anastomosis.

Another important factor influencing the efficacy of IPC in patients with leg ischemia may be the initial ABI value and degree of ischemia [5]. In our study the patients with class 3 and 4 according to the Rutherford classification were evaluated. According to the previous suggestions, the effect of IPC on the hemodynamic parameters may be related to an increase of the NO release from the endothelial cells. In patients with critical leg ischemia, the dysfunction of the endothelial cell can be observed, which can result in NO synthesis and release depletion. In this clinical situation, the limited efficacy of the IPC on the flow parameters should be suspected.

## Conclusions

The benefits of the by-pass procedure in patients with leg ischemia can be significantly reduced by the presence of

postoperative edema. Among patients with postoperative leg edema, local tissue blood perfusion can be improved by the use of IPC, which can result not only in a decrease in local leg swelling, but also in improved skin blood perfusion and TcPO<sub>2</sub> improvement.

The healing of skin trophic changes and ulcerations is potentially related to the improvement in microcirculation. In this context, the positive role of endovascular revascularization can be explained not only by the minimal invasiveness of the procedure and successful reperfusion, but also by the potential lack of local postoperative edema and impairment of tissue blood perfusion (in contrast to the open surgical procedures).

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