

## Randomized study on the effects of different strategies of intermittent pneumatic compression for lower limb claudication

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**SUMMARY:** Randomized study on the effects of different strategies of intermittent pneumatic compression for lower limb claudication.

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**Background.** *The aim of the present study was to evaluate the efficacy of different strategies of intermittent pneumatic compression (IPC) for the treatment of lower limb claudication.*

**Methods.** *Five study groups were prospectively studied. Group 1: 9 patients not undergoing IPC; Group 2: six patients undergoing IPC 1 hour/thrice-a-day/4 months; Group 3: six patients undergoing IPC 2 hours/once-a-day/4 months; Group 4: six patients undergoing IPC 1 hour/thrice-a-day/2 months; Group 5: six patients undergoing IPC 2 hours/once-a-day/2 months.*

**Results.** *All patients completed the planned treatment schedule and stated a compliance of 33% in group 2, 83% in group 3, 66% in group 4 and 100% in group 5. Peak systolic velocity of the popliteal artery blood flow increased over baseline values particularly when IPC lasted 4 months (group 2: 85%, group 3: 81% vs. group 4: 76%, group 5: 73%). These beneficial effects lasted 10 months and vanished 14 months after the end of IPC treatment. The absolute claudication distance increased at the end of the treatment of 101% in group 2, 94% in group 3, 86% in group 4, and 83% in group 5, and it was still increased over the baseline values 14 months after the end of the treatment. No differences have been observed whether the treatment was performed once or thrice-a-day.*

**Conclusions.** *ICP treatment performed two hours once-a-day for four months provide excellent results with satisfactory treatment compliance. However, these effects are not durable and vanish about one year after the end of IPC treatment.*

**RIASSUNTO:** Studio randomizzato sugli effetti delle differenti strategie della compressione pneumatica intermittente per il trattamento della claudicatio degli arti inferiori.

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**Introduzione.** *Lo scopo di questo studio è di valutare l'efficacia di differenti strategie di compressione pneumatica intermittente (IPC) per il trattamento della claudicatio degli arti inferiori.*

**Metodi.** *Sono stati analizzati in prospettiva cinque gruppi di studio. Gruppo 1: 9 pz non sottoposti ad IPC; gruppo 2: sei pazienti sottoposti ad IPC per un'ora tre volte al giorno per quattro mesi; gruppo 3: sei pazienti sottoposti ad IPC per due ore una volta al giorno per quattro mesi; gruppo 4: sei pazienti sottoposti ad IPC per un'ora tre volte al giorno per due mesi; gruppo 5: sei pazienti sottoposti ad IPC per due ore una volta al giorno per due mesi.*

**Risultati.** *Tutti i pazienti hanno completato il programma di trattamento e hanno dichiarato una compliance del 33% nel gruppo 2, dell'83% nel gruppo 3, del 66% nel gruppo 4 e del 100% nel gruppo 5. Il picco di velocità sistolica del flusso dell'arteria poplitea è cresciuto oltre i valori base in particolare laddove la durata della terapia è stata di 4 mesi (gruppo 2: 85%, gruppo 3: 81% vs gruppo 4: 76%; gruppo 5: 73%). Questi effetti benefici si sono protratti per circa 14 mesi e sono svaniti dopo 14 mesi dalla fine del trattamento con IPC. La distanza assoluta di percorrenza senza claudicatio è cresciuta alla fine del trattamento oltre il 101% nel gruppo 2, del 94% nel gruppo 3, dell'86% nel gruppo 4 e dell'83% nel gruppo 5 ed inoltre è aumentata oltre il valore di base dopo 14 mesi dalla fine della terapia. Nessuna differenza è stata osservata se il trattamento IPC è stato fatto una o tre volte al giorno.*

**Conclusioni.** *La terapia compressiva pneumatica intermittente effettuata due volte al giorno per quattro mesi ha fornito risultati eccellenti con soddisfacente compliance. Tuttavia questi benefici effetti non sono durevoli e svaniscono a distanza di circa un anno dalla fine del trattamento.*

**KEY WORDS:** Limb critic ischaemia - Intermittent pneumatic compression - Claudicatio intermittens.  
Ischemia critica degli arti - Compressione pneumatica intermittente - Claudicatio intermittens.

### Introduction

Intermittent pneumatic compression (IPC) for the treatment of lower limb ischemia has been introduced in the Thirties (1, 2). Later on this method has been

abandoned because of poor results, until Gaskell and Parrot (3) demonstrated the increased blood flow related with the clinical use of IPC, which has been largely confirmed by more recent studies. A burden of evidence exists also on the superiority of simultaneous calf and foot IPC over isolated calf as well as foot IPC in improving the blood flow, ankle-brachial index (ABI), initial claudication distance, absolute claudication distance (ACD), and quality of life (4-17).

The aim of the present study was to evaluate the efficacy of different strategies of simultaneous calf and foot IPC in order to identify the most effective as well as the most tolerable and compliant with the patient's daily activities. In fact, correct application of IPC and patient compliance are essential to achieve its effectiveness.

## Patients and methods

This is a prospective study performed at the Division of General and Vascular Surgery Methodology, Department of Surgical Sciences, "Sapienza" University of Rome, Italy. The inclusion criteria were lower limb claudication of 100 to 300 meters as estimated at the treadmill test, occlusion of the superficial femoral artery without significant stenoses of the popliteal and crural arteries as estimated by Duplex ultrasound examination and/or angiography. Patients with a recent ipsilateral lower limb vein thrombosis, heart failure or any other condition preventing the treadmill test and the use of IPC device have been excluded from the study. Thirty-three patients fulfilling these criteria have been enrolled in this study after a detailed description of the study methods, the use of IPC device and of the follow-up controls. This study was approved by the Ethics Committee and all patients gave their consent to participate to the study.

Patients' characteristics are summarized in Tabella 1. Patients accepted to control for their risk factors, as otherwise suggested to all patients with coronary and peripheral artery disease referred to our clinic.

Patients have been randomized to five different study groups: Group 1: 9 patients not undergoing IPC treatment and considered as control group; Group 2; six patients undergoing IPC for 1 hour thrice-a-day for four months; Group 3: six patients undergoing IPC for 2 hours once-a-day for four months; Group 4; six patients undergoing IPC for 1 hour thrice-a-day for two months; Group 5: six patients undergoing IPC for 2 hours once-a-day for two months.

During and after the end of the study, all patients received clopidogrel 75 mg/day.

The study included 5 intervals: baseline, at the end of the treatment, and 6, 10 and 14 months after the end of the IPC treatment. Patients of group 1, the control group, have been evaluated at baseline, and 4, 10, 14, and 18 months later. At each control, an examiner blinded to patient's group assignment estimated the peak systolic velocity (PSV), the pulsatility index (PI) and the flow volume (FV) of the popliteal artery, and the ABI as well as the ACD. Ultrasound examinations have been performed with an AU5 Idea (Esaote Biomedica, Italy), and an PLIO XV (Toshiba, Japan) with 7.5 MHz linear probes, and with a Doppler Continuous Wave Multi\_DopT (DWL, Esaote, France-Italy) and DOPTEC 2000 (France) with 4 to 8 MHz probes.

ABI was measured by dividing the ankle blood pressure (obtained from the highest value obtained from the posterior tibial or dorsalis pedis arteries) with the highest of both brachial artery pressure values according to the TASK II guidelines (18).

ACD has been estimated with a standard treadmill test (3.2 km/h - 2 mph, 10% grade).

IPC of the calf and foot has been performed in the seated position with an Art Assist® AA-1000 (ACI Medical inc., San Marcos, CA). Two inflatable pads (foot and calf) have been inflated at a pressure of 120 mmHg, with a delay of 1 second for calf compression, inflation time 4 sec., deflation time 16 sec., 3 impulses per minute.

Patient compliance was defined as the extent to which the compression system was worn and the extent to which treatment regimen was followed. Treatment compliance was self-reported by the patient.

## Results

No complication occurred during ICP treatment. Three patients (two of group 2 and one of group 4) had slight calf pain during compression which disappeared within two weeks after the start of treatment. In no case this has led to discontinuation of the treatment. No relevant significant changes occurred in the control group in terms of hemodynamic parameters as well as ACD (Fig. 1). All patients completed the planned treatment schedule. At the end of the study, patients stated on a compliance of 33% in group 2, 83% in group 3, 66% in group 4 and 100% in group 5, thus, indicating a better compliance for a longer, but once-a-day treatment.

PSV was increased over baseline values at the end of the treatment. Such an increase was larger when IPC la-

TABLE 1 - CLINICAL CHARACTERISTICS OF THE PATIENTS AT BASELINE ACCORDING TO THE STUDY GROUPS.

	Group 1 (9 pts)	Group 2 (6 pts)	Group 3 (6 pts)	Group 4 (6 pts)	Group 5 (6 pts)
Age (years)*	64±5	67±6	66±5	63±7	65±8
Females	3	2	1	2	1
Smoking	4	2	2	2	3
Hypercholesterolemia	3	2	1	2	2
Diabetes	3	2	1	2	1
Hypertension	3	0	1	0	1

\* Age is reported as the mean±standard deviation.

sted 4 months (group 2: 85%, group 3; 81% vs. group 4: 76%, group 5: 73%). These beneficial effects lasted 10 months after the end of the IPC treatment and vanished 14 months after the end of the treatment (Fig. 1). No differences in terms of PSV have been observed whether the treatment was performed once- or thrice-a-day.

The changes in terms of PI were similar to the PSV ones (Fig. 1). The FV of the popliteal artery also increased at the end of the IPC treatment (group 2: 58%, group 3: 51%, group 3: 50%, group 5: 42%). Also the increase of VF was larger when the treatment lasted 4 months, independently of the daily treatment schedule. Resting ABI values increased 26% in group 2, 25% in group 3, 21% in group 4 and 18% in group 5.

The ACD increased at the end of the treatment of 101% in group 2, 94% in group 3, 86% in group 4, and 83% in group 5. The ACD was still increased over the baseline values 14 months after the end of the treatment (Fig. 1).

## Discussion

During the last decade several studies have confirmed the hemodynamic and clinical benefits of IPC treatment in patients with lower limb ischemia (4-17). This method acts through various mechanisms. At 120 mmHg, the lower limb superficial and deep veins are completely empty and the venous pressure drops from 60-80 mmHg almost to zero, thus the arterio-venous gradient increases. Venous pressure requires more than 15 seconds to return from zero to the baseline value, so the favourable effect of the increased arterio-venous gradient lasts for the entire rest time, except in case of chronic venous disease where the time need for veins to refill is a direct function of the severity of venous incompetence or outflow obstruction. As the rest period (15 seconds) is 75% of the whole cycle (20 seconds), it follows that the blood flow is increased for 75% of the machine's operation time.

To empty the venous compartment requires only 60 mmHg, however 120 mmHg are necessary to act on the arterial flow. If the systolic pressure at the ankle is less than 120 mmHg the blood flow is interrupted; if it is above 120 mmHg the blood flow is slowed. This interruption or deceleration, even over a brief time (4 seconds), triggers a second mechanism of action of endothelial origin. The endothelium is able to secrete a powerful vasodilator, nitric oxide, as well as other vasoactive, antiplatelet, antithrombotic substances such as tissue factor pathway inhibitor and plasminogen activator inhibitor (19-24). These inhibit platelet and macrophage adhesion to the endothelium and inhibit platelet thrombus and the inflammatory reaction, which

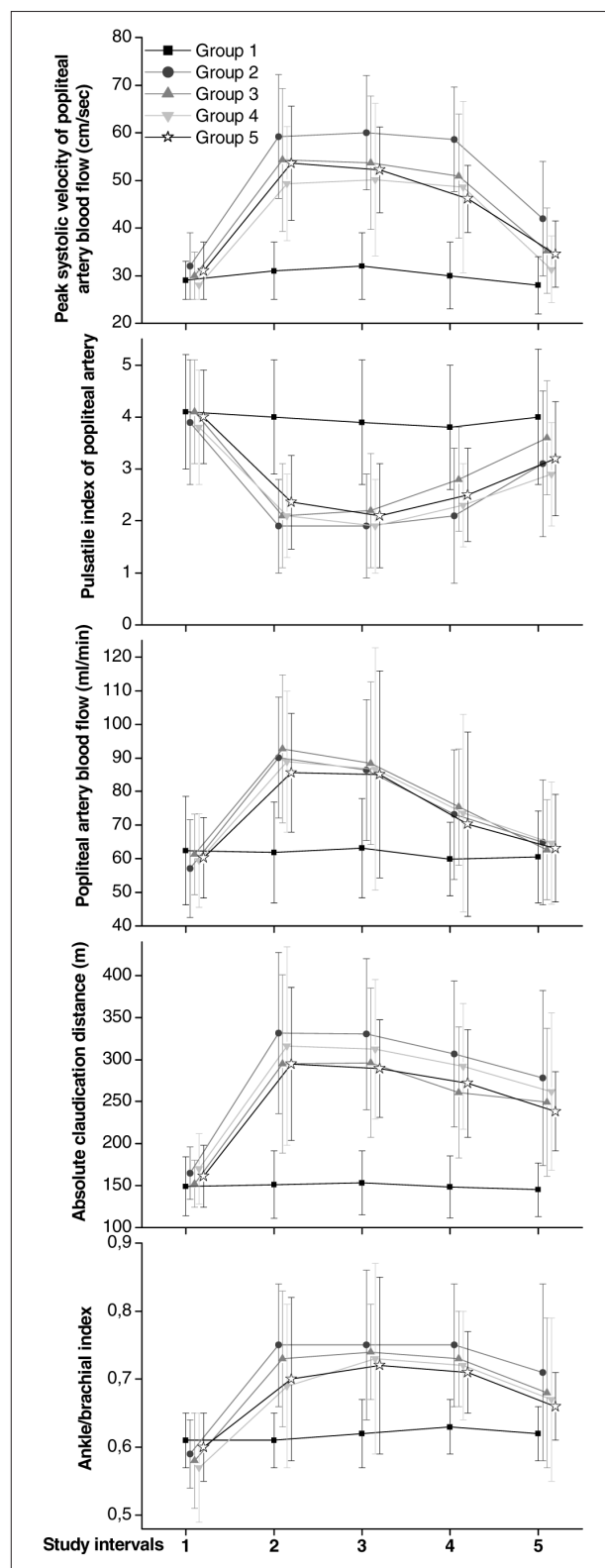


Fig. 1 - Outcome end-points after IPC treatment in different study groups. Group 1: no IPC treatment; Group 2: IPC for 1 hour thrice-a-day for four months; Group 3: IPC for 2 hours once-a-day for four months; Group 4: IPC for 1 hour thrice-a-day for two months; Group 5: IPC for 2 hours once-a-day for two months. For time intervals, please, refer to text.

is responsible for further endothelial damage. The endothelial paracrine action is stimulated by the blood flow velocity and the compression/decompression rate (19,25,26). In the resting phase, increased flow velocity and pulsatility increase the shear stress on the endothelium, which is a further stimulant for nitric oxide secretion. For this reason, the flow increases in the rest period, due to the effect of the endothelium and arteriovenous gradient. The stable resistances reduction and the high flow favour the development of the collateral circulation and an increased ABI.

We observed in the popliteal artery a first arterial flow wave, appearing at the end of compression, which does not always have the same morphology. In peripheral arterial disease, the ascending branch of the flow wave is sometime slow with a rounded apex, whereas sometime acceleration is very fast, the ascending branch almost vertical, the height greater and the apex pointed (fast acceleration waves). Normal subjects always have fast acceleration waves, which after two-three systoles return to their initial morphology. We had already observed this phenomenon in the medial cerebral artery upon sudden interruption of ipsilateral common carotid compression (11). In the peripheral arteries, fast acceleration wave is due to the sudden return of blood to arteries with a reduced caliber and to dilated microcirculation.

This study confirmed that ICP treatment is associated with significantly improved hemodynamics and ACD compared with the control group. However, these be-

neficial effects seem to decay after the 10-month interval. At 14 months after the end of ICP treatment, hemodynamic parameters having been similar to the control group's values, while the ACD having been still higher than the control group (Fig. 1). These effects were more pronounced in patients who underwent treatment for 4 months compared with those who underwent the ICP treatment for 2 months.

## Conclusions

ICP treatment seems to be associated with evident improvements in terms of hemodynamic and walking capacity changes. This study suggests that ICP treatment as performed two hours once-a-day for four months provide excellent results with satisfactory treatment compliance: This treatment schedule resulted in a relevant increase of ACD without interfering with patients' daily activities, compared with thrice-a-day schedule.

### List of abbreviations used

IPC	intermittent pneumatic compression
ABI	ankle-brachial index
ACD	absolute claudication distance
PSV	peak systolic velocity
PI	pulsatility index
FV	flow volume

### Competing interest

The authors declare that they have no competing interests.

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