Effect of High-Pressure, Intermittent Pneumatic Compression for the Treatment of Peripheral Arterial Disease and Critical Limb Ischemia in Patients Without a Surgical Option

Oscar M. Alvarez, PhD[1,2]; Martin E. Wendelken, DPM, RN[1]; Lee Markowitz, DPM[1]; and Christopher Comfort, MD[1]

Wounds 2015;27(11):274-278

From the [1]Center for Curative & Palliative Wound Care, Calvary Hospital, Bronx, NY; and [2]Department of Medicine, New York Medical College, Valhalla, NY

Address correspondence to:
Oscar M. Alvarez, PhD
Center for Curative & Palliative Wound Care, Calvary Hospital
1740 Eastchester Road
Bronx, NY 10461
oalvarez@calvaryhospital.org

Disclosure: This study was funded in part by a grant from State of New York Department of Health for Palliative Care in Patients with Peripheral Arterial Disease, and by a grant from the RTS Family Foundation. BioCompression Systems, Inc, Moonachie, NJ, provided the high-pressure, intermittent pneumatic compression devices at no cost. Dr. Wendelken is a principal of BioVisual Technologies, LLC and was involved in the design and programming of PictZar CDM planimetry software used in this study.

Abstract: Thirty-four subjects with symptomatic peripheral arterial disease (PAD) or critical limb ischmeia (CLI) who were experiencing claudication pain, chronic resting pain, numbness and ischemic lower leg/foot ulceration were randomized into 2 treatment groups. *Materials and Methods.* Eighteen of these patients received treatment with high-pressure, intermittent pneumatic compression (HPIPC) 60 minutes twice daily for 16 weeks, and 16 subjects received standard care consisting of an exercise regimen of walking for 20 minutes twice daily for 16 weeks. The HPIPC device delivers bilateral pressures of 120 mm Hg. Cycle times provide sequential compression for 4 seconds (+/- 0.5 seconds) followed by a 16-second rest period (+/- 3.0 seconds), resulting in a 20-second cycle or 3 cycles per minute. The study was designed to measure patient-centered outcomes. The primary endpoint was peak walking time (PWT), defined as time to maximally tolerated claudication pain. Secondary endpoints included change in resting ankle brachial index, ulcer healing, relief of resting/wound pain, and quality of life (QoL) index. Age (73.7 years vs 72.7 years), baseline PWTs (1-6 minutes), and risk factors were similar in both treatment groups. *Results.* At 4 weeks, the percent change from baseline in PWT did not vary significantly between treatment groups (17.8% for HPIC and 17% for standard care). After 8 weeks, the percent change in PWT for the HPIPC group was 41% compared to 32% for the group receiving standard care ($P = 0.062$). At the 16-week time point the percent change from baseline in PWT was significantly different between treatment arms (35.5% for the standard care group and 54.7% for the group receiving HPIPC [$P = 0.043$]). The mean reduction in wound surface area was 57% and 71% at 12 weeks and 16 weeks, respectively, for the HPIPC group, compared to 45% and 56% for the control group. The HPIPC group reported significantly greater pain relief at the 12-week ($P = 0.044$) and 16-week ($P = 0.038$) time points. Compared to the control group, the HPIPC group reported improvement in patient-centered outcomes such as physical function and bodily pain. These differences were statistically significant ($P < 0.05$) at the 16-week evaluation period. *Conclusion.* High-pressure, intermittent pneumatic compression therapy consisting of 2 hours daily for a period of 16 weeks significantly improved PWT, reduced resting pain, and improved healing rates, physical function, and bodily pain. There were no device-related complications, allowing for long-term use. This study further supports that HPIPC is safe and effective and should be considered for patients who are not candidates for endovascular or surgical procedures. Furthermore, HPIPC offers an excellent alternative for the palliative care of patients suffering from the symptoms of PAD and CLI.

Key words: Peripheral arterial disease, critical limb ischemia, intermittent pneumatic compression

Lower extremity peripheral arterial disease (PAD) is estimated to affect 8-20 million Americans.[1,2] The most common presenting symptom of lower extremity PAD is ambulation-induced muscle pain, or claudication. Normally a nonsurgical, medically treated problem, claudication does not indicate the severity of disease, long-term limitation, or potential limb loss.[3] Patients with severe PAD or critical limb ischemia (CLI) usually require endovascular or surgical revascularization to prevent extremity loss.[2-4] Intermittent claudication may occur in 1 or both legs and often worsens over time. Symptoms and signs of PAD include walking impairment (eg, fatigue, aching, numbness, and pain). Critical limb ischmeia is the most advanced form of PAD[2,4] and is associated with chronic ischemic rest pain, ulcers, or gangrene attributable to objectively proven arterial occlusive disease. Mild to moderate PAD can be improved in many patients with medical treatments combined with supervised exercise.[4-6] Guidelines detail medical and surgical treatment recommendations for patients with lower extremity PAD showing early signs of claudication.[6] In the authors' experience, ischemic ulcers are among the most difficult to treat successfully because they are painful and frequently complicated with infection that can lead to wet or dry gangrene. Arterial ulcers are generally diagnosed clinically and are almost always associated with intermittent claudication, resting pain, pulselessness, and paresthesia. Treatment for ischemic ulcers should be guided by the severity of the PAD. In patients with mild to moderate PAD, wounds often improve if the patient is able to ambulate and tolerate light static compression.

High-pressure, rapid-sequence, intermittent pneumatic calf, and foot compression (HPIPC) devices apply compression to the foot, ankle, and calf using cuffs attached to the leg. This compression regimen simulates the beneficial effects of brisk walking, without pain or tissue trauma. The foot, ankle, and calf veins are almost completely emptied in the sitting position by using pressures that are more than twice those typically used in traditional intermittent pneumatic compression (IPC) devices designed for deep venous thrombus (DVT) prevention, chronic venous insufficiency, or lymphedema. By compressing all the tissues below the knee, a large volume of venous blood is emptied with venous pressure dropping to nearly 0. The increased arterial-venous pressure gradient results in greater arterial flow. Greater arterial flow alters the shear rate and may stimulate endothelial cell function, causing the release of nitric oxide along with tissue factor pathway inhibitors that cause dilation and anticoagulation.[7] Several studies using HPIPC have shown improvement in perfusion, claudication (resting) pain, and wound healing in patients with PAD and CLI.[8-10] Reimbursement for HPIPC devices has existed since 2004 under HCPCS code E0675. In spite of several published RCTs and numerous case series (referenced in this manuscript), the recently released future local coverage determination (effective on 12/01/2015) states "a pneumatic compression device coded E0675 to treat PAD is not eligible for reimbursement. There is insufficient evidence to demonstrate that reimbursement is justified. Claims for E0675 will be denied as not reasonable and necessary."[11]

This randomized, prospective, controlled study was designed to measure the effects of HPIPC therapy in patients with moderate to advanced PAD who were no longer candidates for an endovascular or surgical intervention.

Methods

From July 2009 to December 2012, the authors performed a randomized prospective parallel group longitudinal study in an outpatient wound care center setting. In total, 64 patients were evaluated and screened for eligibility and 34 were randomized. All but 1 (33/34) of the study subjects had been previously diagnosed with type 2 diabetes. All patients had claudication pain, resting pain, numbness, and lower leg/foot ulceration corresponding to stages III and IV of the Fontaine Classification of Peripheral Arterial Disease.[4] Critical limb ischemia was defined according to the Transatlantic Inter-Society Consensus (TASC II) document[4] as those patients whose arterial disease has resulted in breakdown of the skin or pain in the foot at rest. All study subjects were classified as inoperable by their vascular surgeon with agreement from the patient's primary care doctor. All patients were referred to the Center for Curative & Palliative Wound Care, Calvary Hospital, Bronx, NY.

Eighteen subjects received treatment with HPIPC 60 minutes twice daily for 16 weeks and 16 subjects received standard care consisting of an unsupervised exercise regimen as tolerated. The recommended exercise regimen was walking on a treadmill for 20 minutes twice daily. The HPIPC device used in this study was the BioArterial Plus (Bio Compression Systems Inc, Moonachie, NJ) (Figure 1). This HPIPC device delivers bilateral pressures of 120 mm Hg. Cycle times provide sequential compression for 4 seconds (+/-0.5 sec.) followed by a 16-second rest period (+/-3.0 sec.), resulting in a 20-second cycle or 3 cycles per minute. High-pressure, intermittent pneu-

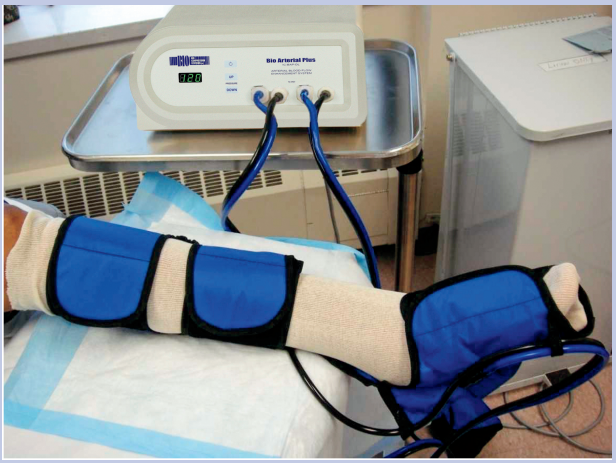

Figure 1. Photograph of study subject undergoing high-pressure, intermittent pneumatic compression therapy. Therapy was prescribed for 60 minutes twice daily for 16 weeks.

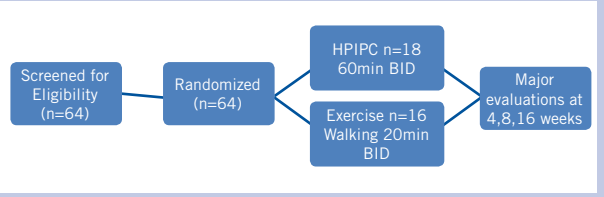

Figure 2. Study design. HPIPC: high-pressure, intermittent pneumatic compression

matic compression therapy was applied while patients were in the sitting position with legs dependent.

This study was designed to capture patient-centered outcomes with endpoints aimed at quality of life indicators. The primary endpoint was peak walking time (PWT), defined as time to maximally tolerated claudication pain. Secondary endpoints included ulcer healing, relief of resting/wound pain, quality of life index (QOL) and change in ankle brachial indices (ABI). A diagram depicting the study design is presented in Figure 2. The mean age was 72.5 with 45% of the subjects over 75 years. There were 26 males and 8 females and 97% (33/34) had been previously diagnosed with type 2 diabetes. The indication for treatment with HPIPC was nonreconstructable disease (82%, 28/34) and excessive surgical risk (18%, 6/34). Patients were excluded from the study if they had noncompressable vessels (ABI > 1.3), gangrene, active infection, had a myocardial infarction within 6 months, were unable to walk, were taking systemic corticosteroids, were receiving treatment with hyperbaric oxygen therapy, or had an inflammatory condition that affected healing.

All subjects were followed up weekly for a period of 16 weeks and then once monthly depending on symptom relief. The evaluations at each visit were PWT, wound surface area, resting ABI, pain, QOL, and adverse events. All patients including controls were allowed to continue their pharmacological treatments. Treadmill testing was at a constant load with 10% gradient at 3.5 km/h. Peak walking time = maximum time (distance of absolute claudication [ACD]) terminated by pain (PWT = ACD). Treadmill testing was supervised by an exercise physiologist at The Bronx YMCA, Bronx, NY, but the exercise routine was unsupervised. Wound surface area was measured using photodigital planimetry software (PictZar Digital Planimetry Software, BioVisual Technologies, LLC, Elmwood Park, NJ). Ankle brachial indices were measured using a directional continuous wave hand-held doppler (Dopplex D900, ArjoHuntleigh, Inc, Addison, IL), and testing was at dorsalis pedis and posterior tibial arteries. The ABI was determined by taking the highest of the 3 ankle Doppler readings and dividing it by the average of 3 brachial systolic readings. Pain relief was measured using the Wong-Baker Faces Pain Rating Scale. The Short Form-36 Health Survey Questionnaire was used to determine physical and mental QOL parameters.[12] The questionnaire was administered at baseline (prior to treatment), at week 8 and again at week 16.

To demonstrate increased blood flow associated with HPIPC therapy, volume and velocity was measured in the popliteal artery using an 18-5 MHz, 38-mm wide linear array transducer and Noblus Ultrasound Scanner (Hitachi Aloka Medical America Inc, Wallingford, CT). The internal arterial diameter was measured by imaging the vessel longitudinally with real-time B-mode. Velocity measurements were performed at an angle of 60°, with the gate of the sample volume matching the internal diameter of the artery. Mean volume flow was calculated from the average mean velocity of 5-10 consecutive cycles. Measurements were performed on 1 diseased and 1 normal lower extremity.

Percent change from baseline PWTs were compared using Wilcoxon rank sum test. Chi-Square test was used for categorical values and Student's *t* test used for continuous variables. The analysis was by intention to treat. and SPSS statistics software Windows version 11.5 (SPSS Inc, Chicago, IL) was used for all statistical calculations.

Results

The evaluation of volume blood flow was conducted

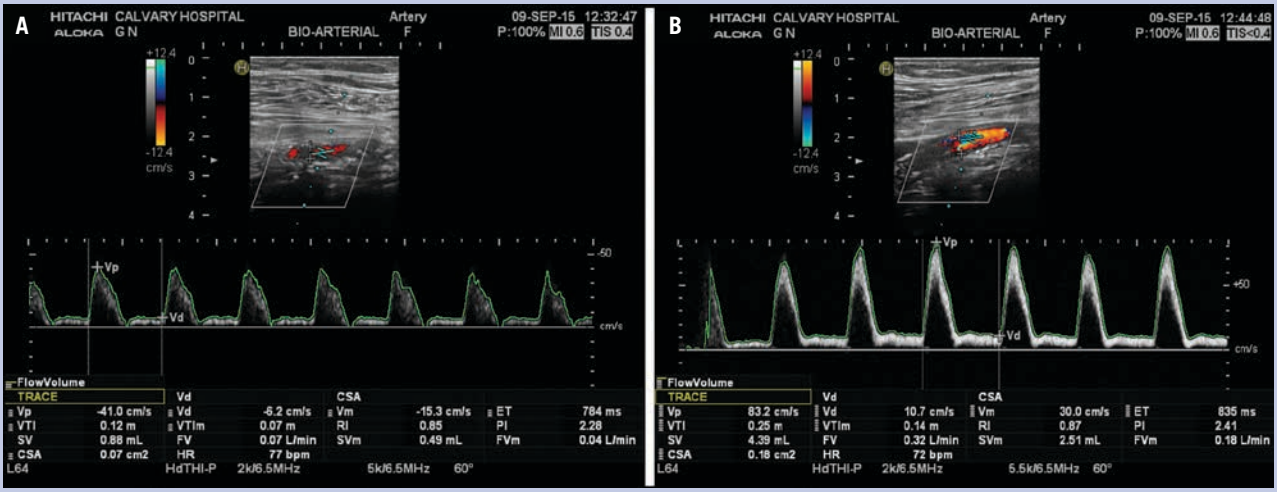

Figure 3. Color flow duplex image and evaluation of volume blood flow in the popliteal artery at (A) rest and (B) during high-pressure, intermittent pneumatic compression therapy.

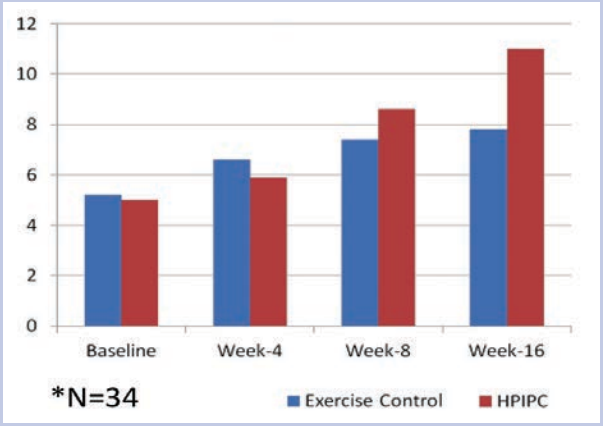

Figure 4. Mean peak walking time for both treatment groups.* PWT: peak walking time; HPIPC: high-pressure, intermittent pneumatic compression

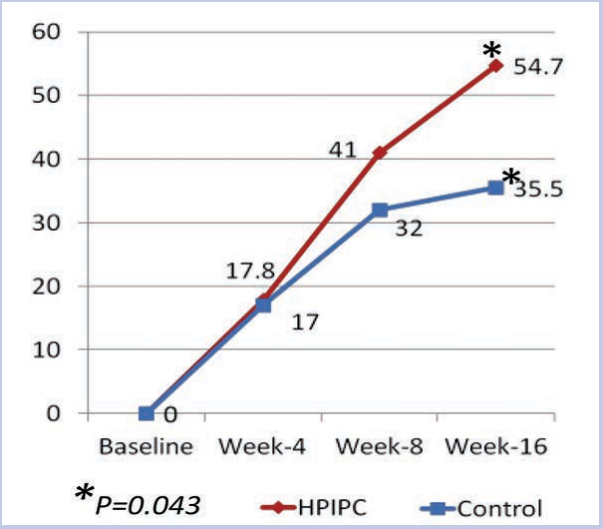

Figure 5. Mean change from baseline in peak walking time at 4, 8, and 16 weeks for high-pressure, intermittent pneumatic compression (HPIPC) and exercise (control) groups (N = 34).

after completion of the study and limited to 1 study participant who was randomized to the HPIPC treatment arm.The color flow duplex imaging in the popliteal artery at rest and during HPIPC therapy is presented in Figure 3. During HPIPC therapy, the volume flow in the popliteal artery (0.18 L/min) increased fourfold compared to baseline value (0.04 L/min).After cessation of HPIPC therapy, the flow returned to baseline. This was associated with the increase of average velocity as the diameter of the artery stayed the same.

Baseline ABIs, PWTs (1-6 minutes), wound surface area, and risk factors were similar in both treatment groups.At 4 weeks, the percent change from baseline in PWT did not vary significantly between treatment groups (17.8% for HPIPC and 17% for standard care).After 8 weeks, the percent change in PWT for the HPIPC group was 41% compared to 32% for the group receiving standard care ($P = 0.062$).At the 16-week time point, the percent change from baseline in PWT was significantly different between treatment arms (35.5% for the standard care group and 54.7% for the group receiving HPIPC [$P = 0.043$]). The mean PWTs for both treatment groups are presented in Figure 4, and the mean change from baseline PWTs for HPIPC and exercise controls are shown in Figure 5.

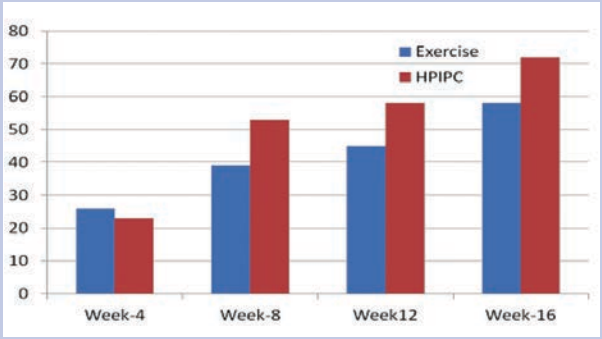

Figure 6. Mean percent reduction in wound surface area. HPIPC: high-pressure, intermittent pneumatic compression

The mean percent reduction in wound surface area was 57% and 71% at 12 weeks and 16 weeks, respectively, for the HPIPC group compared to 45% and 56% for the control group (Figure 6). The HPIPC group reported less pain and significantly greater pain relief at the 12-week (P = 0.044) and 16-week (P = 0.038) time points (Figure 7).

The mean ABIs at baseline and at 4 weeks, 8 weeks, and 16 weeks are presented in Table 1. There was a slight improvement—but not statistically significant—in the ABIs of both treatment groups through time. However, the ABIs between the 2 treatment arms were similar throughout the 16-week study period.

The prolonged effect of HPIPC on skin temperature is presented in Table 2. The foot-to-chest skin temperature index (FCSTI) increased in the HPIPC group from 0.73 at baseline to 0.81 after 8 weeks and 0.88 after 16 weeks. Temperatures at the dorsum of the foot did not significantly change in the exercise control group. The FCSTI was 0.71 at baseline and 0.75 after 16 weeks. These differences were statistically significant at both the 8-week and 16-week time points ($P < 0.05$).

Perceived improvement in QOL from the HPIPC and exercise control group is presented in Figure 7. Compared to the control group, the HPIPC group reported improvement in both physical function and bodily pain. These differences were statistically significant at the 4-month evaluation period.

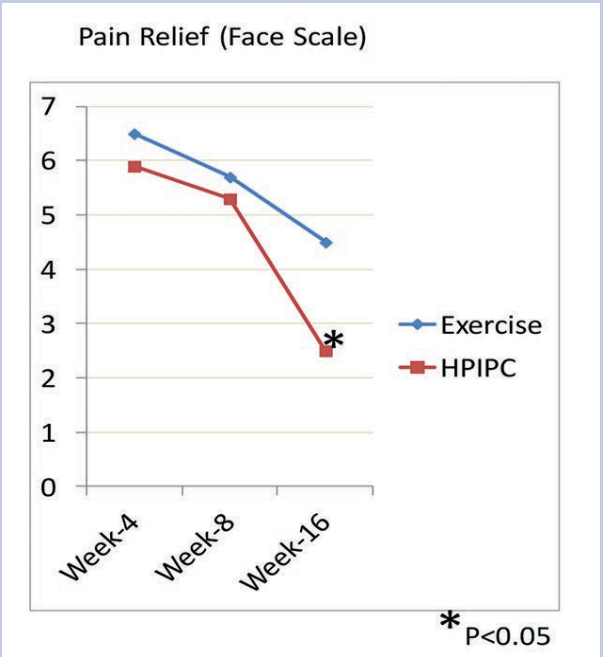

Figure 7. Leg pain at baseline and after treatment. HPIPC: high-pressure, intermittent pneumatic compression

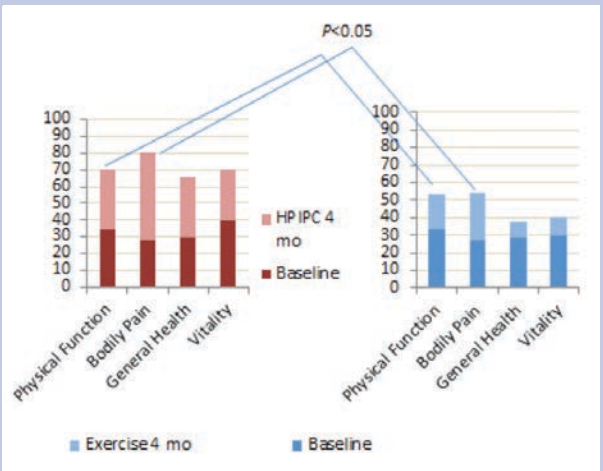

Figure 8. Perceived improvement in quality of life from high-pressure, intermittent pneumatic compression (HPIPC) and exercise: Short Form-36 Health Survey Questionnaire.

Discussion

In 1917 Sinkowich and Gottlieb[13] were the first to report the benefits of intermittent compression for the treatment of thromboangiitis obliterans (Burger's Disease). In 1934, Herman and Reid[14] demonstrated pneumatic compression improved tissue perfusion in patients with PAD. Since then, several trials on the effects of HPIPC for the treatment of arterial claudication and CLI have been reported. The first prospective, randomized, controlled evidence for an increase in arterial blood flow with HPIPC in patients with intermittent claudication was reported in 1993.[15] The study device

Table 1. Mean r-ABIs at baseline and at 4 weeks, 8 weeks, and 16 weeks.*

Time	HPIPC	Exercise Control
Baseline	0.58	0.61
Week 8	0.64	0.69
Week 16	0.63	0.64

*Resting ABI (N=30)
ABI: ankle brachial indices; HPIPC: high-pressure, intermittent pneumatic compression

Table 2. Mean foot-to-chest skin temperature index at baseline, 8 weeks, and 16 Weeks

Time	HPIPC	Exercise Control
Baseline	0.73	0.71
Week 8	0.81*	0.74
Week 16	0.88*	0.75

*$P < 0.05$
HPIPC: high-pressure, intermittent pneumatic compression

provided intermittent suction and compression. The study included 34 patients with moderate, stable intermittent claudication. Twenty-two of the study subjects participated in a double-blinded, randomized trial comparing the effects of 25 treatments to 25 placebo applications given over a period of 2 months. Twelve study subjects participated in an open trial investigating the possible effects of the treatment on platelet aggregation and fibrinolysis. Pain-free and maximal walking distances were measured on a treadmill, and systolic blood pressure was measured on the upper limb, the ankle, and the first toe bilaterally. The threshold for adenosine diphosphate (ADP)-induced platelet aggregation was tested. Active treatment resulted in significant improvements in pain-free and maximal walking distances, whereas no changes could be found during placebo administration. The treatment caused significant increments in the ADP thresholds for platelet aggregation. It was concluded that intermittent suction and pressure treatment offered a novel approach for conservative treatment of intermittent claudication.

From 2000 to 2005 there were 3 prospective, randomized, controlled trials reported that evaluated the effectiveness of HPIPC on patients with symptomatic PAD.[16] In all of these studies, the investigators reported significant beneficial effects on pain-free walking distance, symptoms, and systolic blood pressure measurements on both upper and lower limbs with therapy. Many published reports on the effects of HPIPC on CLI have been limited to clinical outcomes[17-21] and case series that, for the most part, have been retrospective.[20,22] Kavros et al[17, 23] reported results of a retrospective survey of 24 consecutive patients with CLI who were treated with HPIPC. These findings were compared to a control group consisting of 24 patients who received standard pharmacological therapy and wound care but were not treated with HPIPC. Wound healing and limb salvage were significantly better ($P < 0.01$) in the HPIPC group. In addition, when compared to the HPIPC group, the odds ratio of limb loss in the control group was 7.0. At the end of the 18-month follow-up period, tissue perfusion measured by resting transcutaneous oxygen (TcPO2) levels was significantly higher in the HPIPC group ($P = 0.0038$). Also in 2008, Sultan, Esan, and Fahy[24] reported results of a parallel group longitudinal observational study on 35 patients with 39 critically ischemic limbs treated with HPIPC therapy. Their data showed HPIPC reduced amputations, significantly increased toe pressures, and improved popliteal artery blood flow. More recently, Sultan et al[25] reported their assessment of 171 CLI patients who were unsuitable for surgery and received HPIPC therapy as a last resort to amputation. The study consisted of HPIPC therapy for 3 months with a 13-month follow up. Treatment with HPIPC resulted in significant increases in mean toe pressure and popliteal flow. The median amputation-free survival was 18 months and limb salvage at 3.5 years was 94%. Sultan and colleagues[25] concluded that HPIPC therapy was a cost-effective and a clinically efficacious solution for patients with PAD or CLI who had no option of revascularization. Furthermore, it provided adequate limb salvage and improved amputation-free survival while providing relief of rest pain without the use of pain medications.

To the authors' knowledge, this is the first prospective, randomized, exercise-controlled, clinical study to evaluate the safety and efficacy of HPIPC. The results reported here are generally consistent with the findings of van Bemmelen et al[20] and others[21-27] who have reported on a variety of other case series, and observational and controlled studies.

In this study, the therapeutic HPIPC regimen was for 1 hour twice daily for a 16-week period. The HPIPC device has 2 pressure cuff bladders, with 1 applied to the foot and ankle and the other to the calf. It delivers pressure of 120 mm Hg with a time to inflation of 0.6 seconds. Cycle times provide sequential compression (first to the foot) for 4 seconds (+/-0.5 seconds), followed by

a 17-second rest period (+/-3.0 seconds), resulting in a 20-second cycle or 3 cycles per minute.

In the Montori et al[19] and Kavros et al[23] studies, the requested HPIPC treatment regimen consisted of three 2-hour sessions per day using the ArterialFlow System (DJO Global, Vista, CA). This compression device consists of a single pressure cuff bladder applied to the calf. The inflation pressure was 85-95 mm Hg, delivered for 2 seconds with a time to inflation of 0.2 seconds, followed by an 18-second rest period at 0 pressure, resulting in a 20-second cycle 3 times per minute.

In the Labropoulus et al,[10] van Bemmelen et al,[20,22,32] Sultan, Esan, and Fahy,[24] and Sultan et al[25] studies, the requested HPIPC regimen consisted of two 3-4 hour sessions per day using an arterial assist device (ArtAssist, ACI Medical Inc, San Marcos, CA). This compression device consists of 2 cuff bladders, 1 for the foot/ankle and the other for the calf. It delivers pressure of 120 mm Hg with a time to inflation 0.3 seconds and an inflation time of 4 seconds, followed by a 16-second rest period at 0 pressure, resulting in a 20-second cycle 3 times per minute.

Interestingly, although the specifications of the pneumatic devices used in these studies vary to some extent (eg, maximum pressure, foot and calf compression vs calf alone, and time to inflation), the measured parameters and clinical effects reported in all studies were similar. The commonality all HPIPC devices possess is that they deliver a short burst of high pressure (85-120 mm Hg) to the calf with a similar rest period and cycle times.

For this study, the protocol of HPIPC of 120 days with 1 hour in the morning and 1 hour in the evening materialized from a feasibility pilot study performed earlier on 12 subjects.[26] The 1 hour, twice daily regimen produced the most compliance and was generally adhered to by most patients. Also, twice daily therapy correlated with the exercise program performed by the control group. This protocol varies from the treatment regimen used previously in the van Bemmelen et al study,[22] which employed 6-8 hours of treatment daily, and the treatment regimen of other studies,[24, 25] where HPIPC therapy varied between 3 and 6 hours daily. During the pilot feasibility study, the authors of the current study found that a treatment regimen of more than 4 hours a day was unrealistic for the included patient population.

The findings of the present study are also consistent with those of Labropoulus et al,[10] Louridas et al,[18] and Delis et al,[30] who noted HPIPC increases popliteal artery blood flow, relieves resting pain, and limits tissue damage. The response of increased blood flow during HPIPC appears analogous to exercise–induced blood flow in the popliteal artery after muscle contraction during plantar flexion.[31] Also like dynamic exercise, characterized by relaxation periods between contractions, HPIPC has a relaxation period within its compression cycle. In the authors' experience, therapy with HPIPC can cause reactive hyperemia. This finding was first reported by Abu-Own et al,[32] who noted that HPIPC lowers vascular resistance with the release of endothelial-derived relaxing factors.

Compared with the control group, subjects treated with HPIPC demonstrated an increase in skin temperature on the foot of the affected limb. The authors attribute this increase to greater skin blood flow. In many laboratory and clinical studies, skin blood flow has been estimated by skin temperature measurements, and a robust correlation (r = 0.87) exists between skin blood flow measured by laser Doppler flowmetry and skin temperature.[33,34]

High-pressure, intermittent pneumatic compression therapy was well tolerated. Only 5 patients (28%) in the HPIPC treatment group reported mild to moderate pain (VAS 2-5) while receiving HPIPC therapy, and no one had to discontinue use. The pain was attributed to localized wound pain and improved or resolved with an application of topical lidocaine 2.5% cream under the dressing prior to the initiation of therapy. In the Montori et al study,[19] only 7 of the 107 patients (6.5%) had to discontinue the device because of pain, and in the Labropoulus CLI study,[10] only 1 of the 20 patients (5%) reported severe pain.

The present study showed no significant differences in ABIs between the HPIPC group and the exercise control group at baseline or at any of the evaluation periods (4 weeks, 8 weeks, or 16 weeks). This finding is in agreement with Kavros et al[23] who also noted no significant differences in ABIs at baseline or upon completion of their study. All but 1(97%) of the patient population in the present study had diabetes, and ABI measurements in patients with diabetes can be unreliable. It was for this reason the authors chose to exclude patients from the study if they had noncompressible vessels.

It is also important to consider that patient compliance could factor into the results. Based on patient treatment diaries, compliance to the recommended treatment regimen was 86% in the HPIPC group and 58% in the exercise control group. This was likely due to the convenience of HPIPC as it could be performed by the patient at home. In the present study, the exercise regimen was unsupervised. It is likely that a supervised exercise program may have improved patient compliance.

The proposed mechanism of action of HPIPC is that it enhances the development of collateral vessels. This seems to occur as a result of the increase in the arteriovenous pressure gradient, suspension of peripheral sympathetic autoregulation, and enhanced release of nitric oxide secondary to augmented flow and greater shear stress on both venous and arterial endothelial cells.[28,35-37]

Conclusion

High-pressure, intermittent pneumatic compression therapy consisting of 2 hours daily for a period of 16 weeks significantly improved PWT, reduced resting pain, and improved healing rates, physical function, and bodily pain. There were no device-related complications, allowing for long-term use. This study further supports that HPIPC is safe and effective and should be considered for patients who are not candidates for endovascular or surgical procedures. Furthermore, HPIPC offers an excellent alternative for the palliative care of patients who suffer from the symptoms of PAD and CLI.

Acknowledgements

The authors thank Laurie Nicusanti, Applications Specialist with Hitachi Aloka Medical America Inc, Wallingford, CT, who generously donated her time and assistance in conducting the flow studies, and The Bronx YMCA (Bronx, NY) which provided temporary memberships at no cost to the patients participating in this study.

References

1. Hackman DG. Medical management of peripheral arterial disease. *JAMA*. 2006;296(1):41-42.
2. Schanzer A, Conte MS. Critical limb ischemia. *Curr Treatment Options Cardiovasc Med*. 2010;12(3):214-229.
3. Hankey GJ, Norman PE, Eikelboom JW. Medical treatment of peripheral arterial disease. *JAMA*. 2006;295(5):547-553.
4. Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FGR; TransAtlantic Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II) Working Group. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). Eur *J Vasc Endovasc Surg*. 2007;33(suppl 1): S1-S75.
5. Sontheimer DL. Peripheral vascular disease: diagnosis and treatment. *Am Fam Physician.* 2006;73(11):1971-1976.
6. Hirsch AT, Haskal CJ, Hertzer NR, et al; American Association for Vascular Surgery/Society for Vascular Surgery; Society for Cardiovascular Angiography and Interventions; Society for Vascular Medicine and Biology; Society of Interventional Radiology; ACC/AHA Task Force on Practice Guidelines. ACC/AHA Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Associations for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (writing committee to develop guidelines for the management of patients with peripheral arterial disease)–summary of recommendations. *J Vasc Interv Radiol*. 2006;17(9):1383-1397.
7. Provost P, Lam JY, Lacoste L, Merhi Y, Waters D. Endothelium-derived nitric oxide attenuates neutrophil adhesion to endothelium under arterial flow conditions. *Arterioscler Thromb*. 1994;14(3):331-335.
8. Delis KT, Nicolaides AN. Effect of intermittent pneumatic compression of foot and calf on walking distance, hemodynamics, and quality of life in patients with arterial claudication: a prospective randomized controlled study with 1-year follow-up. *Ann Surg*. 2005;241(3):431-441.
9. Ramaswami G, D'Ayala M, Hollier LH, Deutsch R, McElhinney AJ. Rapid foot and calf compression increases walking distance in patients with intermittent claudication: results of a randomized study. *J Vasc Surg.* 2005;41(5):794-801.
10. Labropoulos N, Leon RL Jr, Bhatti A, et al. Hemodynamic effects of intermittent pneumatic compression in patients with critical limb ischemia. *J Vasc Surg*. 2005;42(4):710-716.
11. Future Local Coverage Determination (LCD): Pneumatic Compression Devices (L33829). med.noridianmedicare.com/documents/2230715/2240929/Pneumatic+Compression+Devices+L33829.pdf. Published March 31, 2015.
12. Brazier, JE, Harper R, Jones NM, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ*. 1992;305(6846):160-164.
13. Sinkowitz SJ, Gottlieb I. Thromboangiitis obliterans—the conservative treatment by Bier's hyperemia suction apparatus. *JAMA.* 1917;68(12): 961-963.
14. Herrmann LG, Reid MR. The conservative treatment of arteriosclerotic peripheral vascular diseases: passive vascular exercises (pavex therapy). *Ann Surg.* 1934;100(4):750-760.
15. Mehlsen J, Himmelstrup H, Himmelstrup B, Winther K, Trap-Jensen J. Beneficial effects of intermittent suction and pressure treatment in intermittent claudication. *Angiology*. 1993; 44(1):16-20.
16. Delis KT, Nicolaides AN, Wolfe JH, Stansby G. Improved 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*. 2000; 31(4):650-661.

17. Kavros SK, Geroulakos G, Nicolaides A. Improvement in the walking ability in intermittent claudication with supervised exercise and pneumatic foot and calf compression: Results at 6 months of a randomized controlled trial. Paper presented at:The XVII European Society of Vascular Surgery Annual Meeting; Sep. 17-19, 2004; Innsbruck, Austria.
18. Louridas G, Saadia R, Spelay R, et al. The ArtAssist device in chronic limb ischemia. A pilot study. *Int Angiol.* 2002;21(1):28-35.
19. Montori VM, Kavros SJ, Walsh EE, Rooke TW. Intermittent compression pump for nonhealing wounds in patients with limb ischemia. The Mayo Clinic experience (1998-2000). *Int Angiol.* 2002;21(4):360-366.
20. van Bemmelen PS, Gitlitz DB, Faruqi RM, et al. Limb salvage using high-pressure intermittent compression arterial assist device in cases unsuitable for surgical revascularization. *Arch Surg*. 2001;136(11):1280-1285.
21. Vella A, Carlson LA, Blier B, Felty C, Kuiper J, Rooke TW. Circulator boot therapy alters the natural history of ischemic limb ulceration. *Vasc Med*. 2000;5(1):21-25.
22. van Bemmelen P, Char D, Giron F, Ricotta JJ. Angiographic improvement after rapid intermittent compression treatment [ArtAssist] for small vessel obstruction. *Ann Vasc Surg.* 2003;17(2):224-228.
23. Kavros SK, Geroulakos G, Nicolaides AN. Improvement of the walking ability in intermittent claudication due to superficial femoral artery occlusion with supervised exercise and pneumatic foot and calf compression: a randomised controlled trial. *Eur J Vasc Endovasc Surg.* 2005;30(2):164-175.
24. Sultan S, Esan O, Fahy A. Nonoperative active management of critical limb ischemia: initial experience using a sequential compression biomechanical device for limb salvage. *Vascular*. 2008;16(3):130-139.
25. Sultan S, Hamada N, Soylu E, Fahy A, Hynes N, Tawfick W. Sequential compression biomechanical device in patients with critical limb ischemia and nonreconstructible peripheral vascular disease. *J Vasc Surg.* 2011;54(2):440-446..
26. Alvarez OM, Wendelken M, Markowitz L, Comfort C. A Randomized, Controlled, Feasibility Trial to Evaluate the Effectiveness of High-Pressure, Rapid Sequence, Intermittent Pneumatic Calf and Foot Compression (HPIPC) for the Treatment of Intermittent Claudication, Pain and Ulcer Healing in Subjects with Mild to Moderate Peripheral Arterial Disease (PAD).Abstract presented at: 22nd Annual Symposium on Advance Wound Care; April 29-30, 2009; Dallas, TX.
27. Dillon RS. Fifteen years of experience in treating 2177 episodes of foot and leg lesions with the circulator boot. *Angiology.* 1997;48(5 Pt 2):S17-S34.
28. Chen AH, Frangos SG, Kilaru S, Sumpio BE. Intermittent pneumatic compression devices–physiological mechanisms of action. *Eur J Vasc Endovasc Surg*. 2001;21(5):383-392.
29. Delis KT, Husmann MJ, Chesire NJ, Nicolaides AN. Effects of intermittent pneumatic compression of the calf and thigh on arterial calf inflow: a study of normals, claudicants, and grafted arteriopaths. *Surgery*. 2001;129(2):188-195.
30. Delis KT, Labropoulos N, Nicolaides AN, Glenville B, Stansby G. Effect of intermittent pneumatic compression on popliteal artery haemodynamics. *Eur J Endovasc Surg.* 2000; 19(3):270-277.
31. Ohmori F, Shimizu S, Kagaya A. Exercise-induced blood flow in relation to muscle relaxation period. *Dyn Med.* 2007;6:5. doi:10.1186/1476-5918-6-5.
32. Abu-Own A, Cheatle T, Scurr JH, Coleridge Smith PD.. Effects of intermittent pneumatic compression of the foot on the microcirculatory function in arterial disease. *Eur J Vasc Surg*. 1993;7(5):488-492.
33. Koman LA, Numley JA, Goldmer JL, Seaber AV, Urbaniak JR. Isolated cold stress testing in the assessment of symptoms in the upper extremity: preliminary communication. *J Hand Surg Am*. 1984;9(3):305-313.
34. Nilsson AL. Blood flow, temperature, and heat loss of skin exposed to local radiative and convective cooling. *J Invest Dermato*l. 1987;88(5):586-593.
35. van Bemmelen PS, Mattos MA, Faught WE, et al. Augmentation of blood flow in limbs with occlusive arterial disease by intermittent calf compression. *J Vasc Surg.* 1994;19:1052-1058.
36. Delis KT, Nicolaides AN, Labropoulos N, Stansby G. The acute effects of intermittent pneumatic foot versus calf versus simultaneous foot and calf compression on popliteal artery hemodynamics: a comparative study. *J Vasc Surg*. 2000;32(2):284-292.
37. Unthank JL, Nixon JG, Dalsing MC. Inhibition of NO synthase prevents acute collateral artery dilatation in the rat hindlimb. *J Surg Res*. 1996;61(2):463-468.