ORIGINAL ARTICLE

Limb Salvage Using High-Pressure Intermittent Compression Arterial Assist Device in Cases Unsuitable for Surgical Revascularization

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Hypothesis: Intermittent compression therapy for patients with inoperable chronic critical ischemia with rest pain or tissue loss may have beneficial clinical and hemodynamic effects.

Study Design: Case series of 14 consecutive ischemic legs that underwent application of a 3-month treatment protocol during a 2½-year study.

Setting: Veterans Administration Hospital.

Patients: Thirteen patients with 14 critically ischemic legs (rest pain, n=14; tissue loss, n=13) who were not candidates for surgical reconstruction were treated with rapid high-pressure intermittent compression. The patients had a mean age of 76.2 years, 8 were diabetic, and they represented 10% of referrals for chronic critical ischemia. They were not amenable to revascularization owing to lack of outflow arteries (n=7), lack of autogenous vein (n=5), or poor general medical condition (n=3).

Intervention: All patients were instructed to use the arterial assist device for 4 hours a day at home for a 3-month period.

Main Outcome Measures: Limb salvage and calibrated pulse volume amplitude.

Results: After 3 months, 9 legs had a significant increase in pulse-volume amplitude ($P<.05$). These legs were salvaged, whereas the 4 amputated legs demonstrated no hemodynamic improvement. We noted a direct correlation between patient compliance and clinical outcome. Patients in whom limb salvage was achieved used their compression device for longer periods of time (mean time, 2.38 hours a day) compared with those who underwent amputation (mean time, 1.14 hours a day) ($P<.05$). These mean hours of use were derived from an hour counter built into the compression units.

Conclusions: Intermittent high-pressure compression may allow limb salvage in patients with limb-threatening ischemia who are not candidates for revascularization. Further studies are warranted to assess intermittent compression as an alternative to amputation in an increasingly older patient population.

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SURGICAL CORRECTION of distal arterial obstruction in the leg has made enormous progress in the last 3 decades. Distal to the crural level, the dorsalis pedis bypass has been shown to be often feasible in diabetic patients[1] with moderate[2] to good[3] long-term results. Patient selection remains crucial for achieving a good outcome. In a large series of these bypass procedures, the dorsalis pedis artery was visible on preoperative angiogram in 95% of cases.[1] For other pedal arteries, including common plantar, lateral plantar, medial plantar, tarsal, metatarsal, and unnamed branch arteries, successful bypasses have been described as well.[4-6] Since no large series involving these bypasses have been reported to our knowledge, they are often lumped together with dorsalis pedis bypasses under the group name "inframalleolar bypass." Unfavorable results, though they might occur, may not be frequently submitted for publication.

See Invited Critique at end of article

Less favorable results are experienced when foot arteries are not visualized on preoperative arteriography or when limited autogenous vein is available. The long-term patency of prosthetic conduits for distal (below-knee) bypasses is limited.[7] Adjunct techniques, such as vein cuffs and distal arteriovenous fistulas, have been advocated. The limb salvage rate after previous bypass is reduced when compared with legs without prior bypass.[8] Even with the most aggressive approach to distal revascularization, intimal hyperplasia

PATIENTS AND METHODS

INCLUSION CRITERIA

Patients with either progressive tissue loss or persistent rest pain (documented at ≥2 visits) and who met the hemodynamic criteria of chronic critical ischemia were selected by a team of 2 vascular surgeons and a foot surgeon to undergo 3 months of intermittent compression on the basis of 1 or more of the following criteria (**Table**):

- No visible run-off arteries visualized in the foot on selective digital subtraction angiography (n=7)
- Inability to find suitable autogenous vein by duplex ultrasound mapping of greater and lesser saphenous and cephalic veins (n=5)
- A history of multiple failed ipsilateral bypasses (n=9) (mean number of prior bypasses, 2.0)
- General condition too poor for surgery (n=3) (severely disabling stroke in 2 cases, aged 90 years, and multiple medical contraindications in the third patient.)

For the purpose of eligibility for compression therapy, tissue loss was defined as one or more spontaneously occurring ischemic skin lesions on the forefoot.

HEMODYNAMIC CRITERIA

In all patients, noninvasive studies confirmed the presence of hemodynamically critical ipsilateral disease on the basis of an absolute toe pressure equal to or less than 35 mm Hg. The PVR (pulse volume recording) waveforms were blunted at the metatarsal level. Absolute ankle pressure was reduced in all patients with compressible arteries. Based on previous studies,[16] the ankle-brachial index was not considered useful in patients with diabetes, who composed 62% of the study population.

EXCLUSION CRITERIA

The following conditions are not contraindications for compression treatment, but to achieve a homogeneous study group, these conditions were excluded: ulcers at the ankle; isolated ulcers of the heel (these usually have a decubitus and/or pressure component); pretibial ulcers (often having a traumatic origin and/or component); neuropathic-diabetic ulcers on the plantar aspect of the foot or toes, which occur at localized pressure sites and are related to skeletal deformities such as metatarsal prominence and hammer toes; and patients with indication for primary amputations, as described in the "Patient Acceptance" section.

After patients gave informed consent, they were instructed to apply a compression protocol, which consisted of 4 applications of 1 hour at a time, spread out over the day. This was performed prospectively on 14 consecutive legs, which presented with rest pain and/or progressive tissue loss at the forefoot. The severity of rest pain and progression of tissue loss required intervention, but these patients were deemed to be unsuitable for bypass and were hence facing the immediate prospect of major amputation.

All but 1 patient underwent arteriography, which confirmed extensive disease, distal to the knee, in each case. Photographic documentation of foot lesions was performed with a macrocamera (Yashica dental eye III; Kyocera Co, Tokyo, Japan) at monthly intervals.

In legs with tissue loss, the extent of the necrosis at the start of treatment ranged from 1 to 3 necrotic toes (mean, 1.4 toes), with 0 to 1 involved metatarsal heads (mean, 0.25). Fourteen legs of 13 patients treated with intermittent compression form the basis of this study; all patients were male. The mean age was 76.2 years. Only 1 patient had rest pain without tissue loss. Eight (62%) of 13 patients had diabetes.

Treatments were performed at the patient's home with patients sitting upright in a comfortable chair. Patient compliance was monitored monthly with an hour counter hidden inside the device. The compression device (ArtAssist; ACI Medical Inc, San Marcos, Calif) is a commercially available unit that applies pressure to the foot and leg of 100 to 120 mm Hg for a short period (3 seconds). This period alternates with a longer period (17 seconds) of zero-compression pressure, while the pressure rise and fall times are extremely short (<0.3 second). This time-pressure cycle was based on our earlier work.[12] There is a 1-second delay between the start of foot compression and the start of calf compression.

Calibrated PVR machine (Healthwatch, Life Sciences Cambridge, Vista, Calif) recordings were performed at the ankle and metatarsal levels, prior to and on completion of the compression treatment. If the 3-month treatment was not completed, a repeated PVR was performed prior to amputation.

A source of problems in all diabetic limbs with critical ischemia, regardless of treatment, is the unpredictable onset of invasive infection. Gram-negative organisms, in particular *Pseudomonas*, have been linked to a high incidence of amputation.[17] Antibiotic treatments were given based on wound culture results whenever clinically indicated. Deep vein thrombosis was ruled out in swollen legs by duplex ultrasound prior to the start of compression treatment to avoid the possible risk of pulmonary embolization. No patients had symptoms or signs of pulmonary embolization during the study period.

STATISTICAL METHODS AND ANALYSIS

Differences in patient compliance and body weight were assessed using unpaired *t* tests. Categoric variables between groups (limb salvage vs amputees) were compared using χ^2 analysis.

and progression of the disease will ultimately cause many grafts to fail within 24 months.

Despite the continued improvements in our treatment armamentarium, a nationwide study[9] found no evidence that major amputation (below-knee amputation [BKA] and above-knee amputation [AKA]) rates have decreased over the past decade, with an estimated number of 73 717 major amputations being performed in 1996. These considerations have stimulated interest in alternative treatment modalities, such as angiogenic gene therapy, intermittent pneumatic limb compression,[10-13] and vacuum suction devices.[14,15] Despite increasing numbers of publications on these physical treatments, there have been limited reports on intermittent compression for the purpose of limb salvage. This may be an important void as vascular surgeons have a unique position to

Inclusion Criteria

Case No.	No Target Outflow Artery	No Autogenous Vein Material	General Condition Too Poor for Surgery	No. of Previous Ipsilateral Failed Bypasses
1	N	N	Y	0
2	N	Y	N	1
3	Y	N	N	0
4	N	Y	N	3
5	Y	N	N	1
6	Y	N	N	0
7	N	N	Y	0
8	Y	Y	N	3
9	N	Y	N	2
10	N	Y	N	4
11	Y	N	N	1
12	Y	N	N	1
13	Y	N	N	2
14	N	N	Y	0
Total*	**7**	**5**	**3**	**18**

*Total indicates total No. of cases with "Y" criteria or total No. of instances.

select patients for compression therapy, based on clinical, hemodynamic, and angiographic findings, and can institute treatment before irreversible damage to the foot has occurred. We report our findings on the use of this treatment modality for limb salvage in patients unable to undergo surgical revascularization.

The purposes of this study were to (1) evaluate whether a 3-month course of intermittent compression had lasting beneficial clinical or hemodynamic effects for nonsurgical patients with rest pain and/or progressive tissue loss, and (2) assess the applicability of this treatment in terms of patient acceptance and prevalence of suitable cases.

RESULTS

CLINICAL RESULTS

No patients were lost to follow-up during the 30 months of the study. Owing to the limited life expectancy and serious limb loss, the mean follow-up was 8.7±6.9 months (range, 0.5-23 months).

Limb Salvage

As illustrated in **Figure 1**, 4 amputations were performed on compression patients during the study period (3 BKA, 1 AKA). Despite rehabilitation efforts, no patients undergoing amputation were ambulatory with a prosthesis at the time of this study.

Patient Survival

Two patients died during the study period; neither had undergone amputation prior to death. The first patient died of a myocardial infarction 2 weeks after the initiation of treatment. Compression treatment was stopped while patient was intubated and bedridden; he subsequently died from cardiac arrhythmia. The second patient died (with a healed foot and no rest pain) 1½ years after the start of compression treatment; he did not require additional treatment after completion of the 3-month protocol.

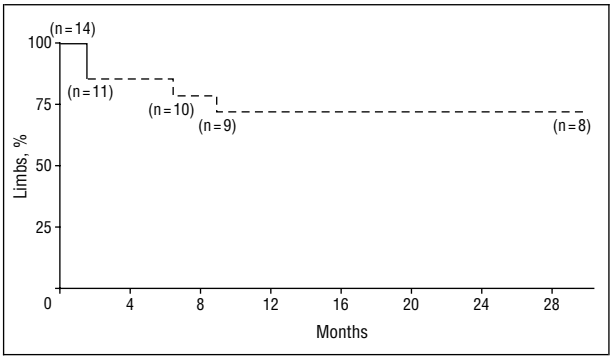

Figure 1. Kaplan-Meier curve for cumulative limb salvage in 14 legs treated with intermittent compression.

Patient Acceptance

In all but 1 patient, the rest pain improved at least temporarily during the compression sessions. This allowed us to continue to treat these feet conservatively. If the foot was tender, the compression was temporarily limited to the calf.

The applicability of compression treatment was studied by comparison to the total number of patients treated during the study period for critical ischemic legs. From April 1998 to October 2000, 137 legs underwent operations for chronic critical ischemia at the VA Medical Center in Northport, NY. Of these, 107 underwent lower extremity revascularization. During this time, 30 legs underwent major amputation (BKA or AKA). Fifteen amputations were performed after a mean of 2.7 bypass procedures (range, 1-6 procedures). The remaining 15 had primary amputations (ie, without any reconstructive attempts prior to amputation). The indications for primary amputations included (1) extensive gangrene and (2) bedridden patients living in a nursing home with severe contractures of the hip and knee joints, with either poorly controlled rest pain or tissue loss. These patients did not undergo compression therapy.

HEMODYNAMIC RESULTS

The PVR waveform amplitudes prior to treatment were decreased; the mean amplitude at metatarsal level was 2.9 mm. **Figure 2** shows the PVR at ankle and metatarsal levels, before and after completion of the compression protocol in one of the patients. Improvement did not always occur in those legs that were extremely ischemic at the start of treatment, as seen by a completely flat waveform at the ankle. **Figure 3**A and 3B show the ankle and metatarsal PVR amplitudes in 14 legs before and after completion of the 3-month protocol. The increases in amplitudes at ankle and metatarsal levels were significant ($P<.05$) (paired t test) on the 9 salvaged limbs; the early death was excluded from this subanalysis. **Figure 4** shows mean PVR amplitudes for amputated vs salvaged legs. While lack of hemodynamic improvement was noted with ultimate amputation, this did not

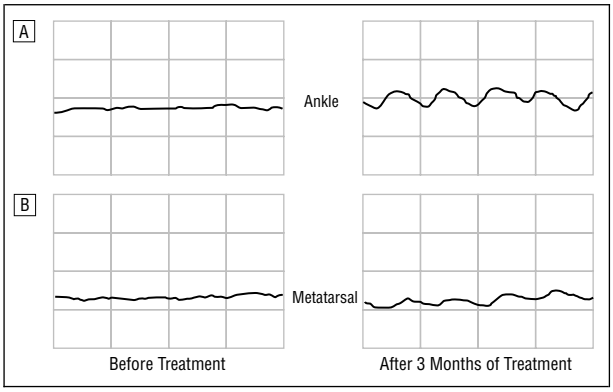

Figure 2. Pulse volume recording (PVR; Healthwatch, Life Sciences Cambridge, Vista, Calif) of one of the legs at the ankle (A) and metatarsal (B) levels, before and after 3 months of treatment. Increase in amplitudes is evident.

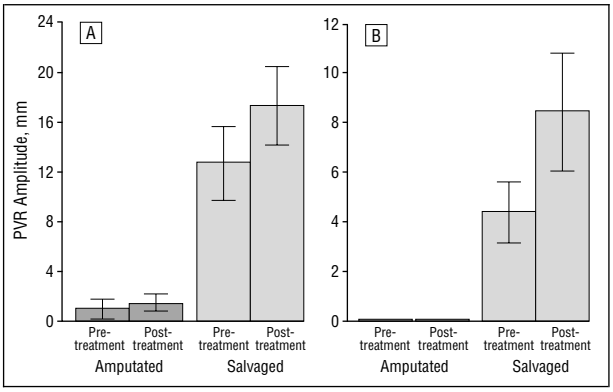

Figure 4. Mean±SE ankle (A) and metatarsal (B) pulse volume recording (PVR; Healthwatch, Life Sciences Cambridge, Vista, Calif) amplitude before and after treatment in amputated vs salvaged legs.

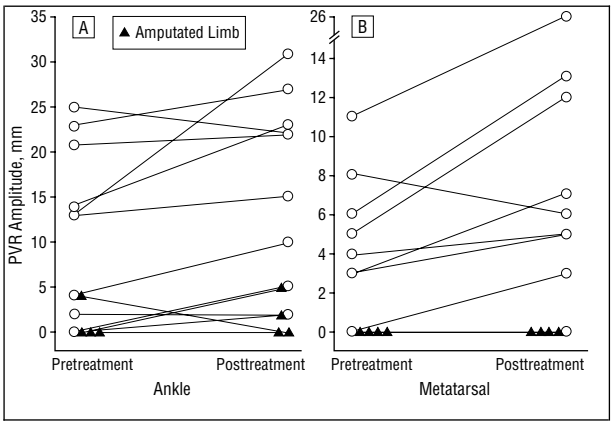

Figure 3. Pulse volume recording (PVR; Healthwatch, Life Sciences Cambridge, Vista, Calif) amplitudes at ankle level (A) and metatarsal level (B) in 14 legs, before and after treatment.

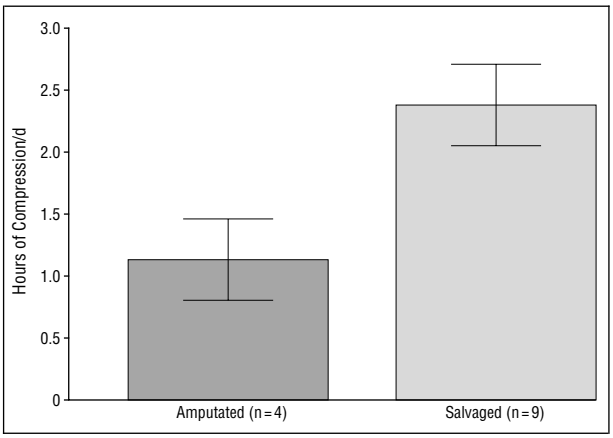

Figure 5. Mean (±SE) number of actual hours of compression applied per day in amputated vs salvaged legs, based on hour-counter readings.

reach statistical significance ($P<.20$) (χ^2 analysis). Analysis of the amputated cases revealed several factors and trends that may have contributed to limb loss.

Lack of Patient Compliance

A low mean number of hours used per day, based on the counter readings, resulted in a greater risk of failure. When averaged over the active treatment period, patients undergoing amputation used the compression on average only for 1.14 hours a day (instead of the prescribed 4 hours a day), while patients not undergoing amputation used their device for 2.38 hours a day ($P<.05$) (**Figure 5**). It is possible that the patients who were less compliant were more infirm.

Extremely Low Body Weight

Prior to amputation, the body weight of 2 of the patients undergoing amputation (who were of average height) was 54.3 kg and 58.9 kg vs a mean weight of 79.3 kg in patients not undergoing amputation ($P<.05$). This finding probably reflects a very poor (emaciated) patient condition.

Flat-Line PVR at the Ankle Level

Prior to treatment, 3 of 4 amputated limbs had a flat-line PVR at the ankle in contrast to 1 of 9 patients for whom limb salvage was achieved ($P<.05$). (The one early death was excluded from this subanalysis.) *Pseudomonas* infection was seen in 1 of 4 amputated limbs but also seen in 1 of 9 limbs that did not require amputation (findings from χ^2 analysis were not significant). One of 4 amputated limbs had a recently occluded distal bypass, while none of the successfully treated limbs had a recent bypass failure. This did not reach statistical significance.

COMMENT

Although substantial world literature exists regarding the immediate effects of intermittent compression on arterial blood flow,[10-13,18-21] there are few[22-24] reports demonstrating a clinical benefit with long-term use. Until recently, these were single-author articles originating from "the angiologic wilderness."[25] Dillon[22] used a thigh-high boot with end-diastolic compression. In that report, 22 of 25 patients with severely diseased legs were reported to have improved from the treatment. Steinberg[23] used cardiosynchronous limb compression trig-

gered by the electrocardiogram. Only 2 of his patients had rest pain, which improved after 4 to 7 weeks of treatment. Twelve patients had nonhealing pedal ulcers in combination with abnormal findings on noninvasive studies (ankle-arm index and photoplethysmograph waveform amplitude). Inclusion of patients with pedal ulceration is problematic because of the multifactorial origin, namely neuropathy, skeletal deformity with pressure, and angiopathy.

In 1993, Mehlsen et al[15] demonstrated a beneficial effect of 2 months of intermittent suction compression treatment in a double-blinded, randomized study of 22 patients with stable intermittent claudication. Delis et al[24] published a study on the effects of intermittent compression of the foot on patients with intermittent claudication. In the latter 2 studies, an increase was found in pain-free and maximal walking distances, as well as a significant increase in the ankle-brachial blood pressure index.

The compression used in each of these studies[22-24] was different from the compression used in the current study. Compression of the calf results in a much larger increase in popliteal blood flow than compression of the foot alone.[12] An upright patient position during the compression maximizes the effect on arteriovenous pressure differences[26] and is important to obtain arterial flow augmentation. Devices that include the thigh require an extended knee position with the patient in a horizontal position, which minimizes the increase in arteriovenous pressure differences. One problem with many early devices was the long amount of time it took for the slow air pumps to inflate the large garment bladders. Typically, up to a minute was required to inflate the bladder and to reach the desired pressure level, during which time there is an actual reduction in skin perfusion as soon as the bladder pressure reaches 10 to 20 mm Hg.[27] As soon as the cuff pressure reached the preset point (typically 60-70 mm Hg), the air pump would stop and the air would slowly vent through relatively small tubing. The skin perfusion would remain decreased until the compression pressure fell below 10 mm Hg. A short time to reach a high pressure (>100-120 mm Hg) can be obtained with the use of a small bladder compressing only the foot, but this does not result in the larger flow augmentation that can be obtained by compression of the calf. Pressures greater than 120 mm Hg are generally uncomfortable on the calf. The use of relatively small bladders on the calf and foot, in conjunction with a storage tank for compressed air, results in optimum conditions for arterial flow increase with the device used in the current study.

In addition to the simple mechanical effect, it was previously[12] calculated that a reduction of vascular resistance was an additional short-term effect of compression. This is contrary to the widely held belief that vascular resistance distal to an area of obstruction cannot be further reduced[28,29] and that distal vasodilation is already maximal in areas of ischemia. The immediate effect of intravascular prostacyclin analogues on distal resistance supports the idea that distal resistance is not minimal in ischemic legs.[30-32]

Conditions that temporarily increase flow velocity and shear stress such as exercise,[33] mechanical deformation of the vessel wall,[34] arteriovenous fistula,[35] and post-compression flow enhancement result in increased nitric oxide activity and vasodilation. Recent in vitro studies[36] of endothelial cells have confirmed that an up-regulation of endothelial nitric oxide synthase occurs after 6 hours of compression and increased shear.

Application of compression treatment to the more advanced stages of rest pain and tissue loss has important implications for daily practice but presents unique problems. Rest pain is not readily quantifiable; although a subjective pain scale can be applied, the pain that a patient experiences is the end result of ischemic and inflammatory pain surrounding the foot lesions and the loss of pain perception owing to diabetic neuropathy. Likewise, healing of foot lesions is a multifactorial process, which, in addition to the severity of ischemia, is affected by the absence of recurrent trauma, the presence and virulence of bacterial infection, diabetes, nutritional status, etc. It is apparent that our patients had profound ischemia; the mean pretreatment PVR at the metatarsal level (2.9 mm) in our compression treatment group is comparable to the mean preoperative PVR amplitude (4 mm) in a large series of dorsalis pedis bypasses.[1]

The spontaneous appearance of multiple skin lesions on non–weight bearing areas of the forefoot is probably the most specific sign of hypoperfusion of the forefoot; therefore, the current study was limited to necrosis of the forefoot. Major amputation and death are the main clinical endpoints in this study.

The transformation of the documented immediate effect on blood flow into a sustained benefit after several months of compression therapy is likely to involve the development of collaterals. The stimulus for collateral vessels to increase in size has been shown[37] to be the shear stress at the endothelial surface, which results in nitric oxide release and relaxation of the underlying muscle. With compression treatment, this would occur periodically, both owing to the mechanical effects of intermittent compression and because of the reduction in peripheral resistance.

If compression therapy were to effectively reduce the number of major amputations, this would potentially affect short-term survival by eliminating the surgical mortality of major amputation, which was as high as 82% (9 of 11) in the subgroup aged 80 years in one series.[38] Another relevant point is that rehabilitation outcome after amputation for nonreconstructable arterial disease is much worse than generally assumed. In one report,[39] only 26% of patients with a mean age of 72 years were able to ambulate with a prosthesis outdoors, 2 years after amputation.

CONCLUSION

A 3-month period of intermittent compression treatment was associated with limb salvage in 9 legs (70%) at maximum follow-up of 2.5 years in 14 treated legs. The study group consisted of 10% of the patients referred for chronic critical ischemia. These patients were deemed to face amputation if left untreated but were not considered candidates for surgical revascularization. Treatment was well tolerated by nearly all patients and did not result in serious adverse effects, allowing for prolonged conservative treatment of these legs. The hemodynamic

effect consisted of significant increases in ankle and foot PVR amplitudes in most limbs.

We have demonstrated that rapid intermittent high-pressure compression treatment may be a useful addition to our treatment options in patients with limb-threatening ischemia who are unable to undergo reconstruction. While the numbers in our study are small owing to selection of a homogeneous patient group, the potential to offer considerable improvements in quality of life warrants further controlled multicenter studies to evaluate the role of compression therapy for limb salvage.

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