Intermittent pneumatic compression for the treatment of lower extremity arterial disease: a systematic review

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Abstract: This study aimed to identify the role of intermittent pneumatic compression in treating peripheral arterial disease and to investigate the types of treatment programs that are most effective. Data was sourced from English-language articles which were identified by a computer search using MEDLINE from 1966 to 2001, followed by extensive bibliography review. Studies were included if they contained pertinent material involving a compression device and arterial flow dynamics in lower limbs. A total of 26 English-language studies were identified that met the inclusion criteria. The diverse patient criteria and methods used in the studies provided an opportunity to examine the effectiveness of each, but made it difficult to compare one study with another. To assist in focusing on overall trends in improvement, patient type and treatment type disparities must be identified. In conclusion, it is evident that an intermittent pneumatic compression program appears promising and may be used in patients with severe peripheral arterial disease who are not candidates for revascularization using surgery or percutaneous angioplasty. It is now the goal to establish randomized, prospective, controlled trials to clarify the most beneficial regimen for treating such disease.

Key words: acute effects; clinical outcomes; intermittent pneumatic compression; peripheral arterial disease

Introduction

The biennial incidence rates of intermittent claudication is currently 26.6 per 1000 men and 13.3 per 1000 women, both of which are expected to increase in the coming decade.[1] Peripheral arterial disease (PAD) is currently the leading cause of morbidity in elderly people.[2]

Previous studies have shown that alternating high and low pressure around the lower extremity, a process called intermittent pneumatic compression (IPC), is effective in increasing arterial flow to distal limbs, and may be a relevant treatment for patients with PAD. Although both interventional and conservative treatments are currently implemented in treating these patients the practicality and low cost of IPC make it a favorable alternative.

Percutaneous transluminal angioplasty is frequently inapplicable, yielding poor long-term patency rates; surgical intervention is only undertaken in cases of severely debilitating claudication and may result in further complications.[3] Historically, the classes of drugs used to treat claudication include rheologic agents, vasodilators, antiplatelet agents, and anticoagulants. Recently, designer drugs, such as pentoxifylline and cilostazol have shown minimal success in only a small subset of select patients.[2] Conservative management of diabetes, hypertension and hyperlipidemia may slow atherosclerotic progression, but unfortunately do not change existing symptoms or cause regression. Exercise therapy is useful in improving claudication distance and while walking is not physically possible in more severe cases of PAD, upper body exercise may provide similar benefits.[4]

Conservative means to increase blood flow are needed in cases of multiple revascularization procedures, limbs with graft infections, and when distal arterial beds offer no suitable site for anastomosis.[5] In ischemic limbs, IPC can increase blood flow, relieve rest pain, and limit tissue damage. IPC placed on foot and calf, referred to as arterial assist device (AAD), has shown to generate a three- to four-fold augmentation in popliteal artery blood flow.[6] AAD may also maintain uncertain graft flow, reduce swelling and compartmental pressure after injury, and act as a prophylaxis of venous thrombosis. The mechanisms for this action include a decreased local vascular resistance because of the release of vasodilatory substances such as nitric oxide and prostacyclins, and the transient suspension of the arteriovenous reflex as well as an increased arterial-venous pressure gradient in dependent patients.

It is now necessary to establish a clinical protocol under which there might be shown substantial proof of IPC's effectiveness on patients with leg ischemia. The goal of this meta-analytic study was to evaluate from the literature the most effective program of IPC on patients with lower limb arterial disease and to assess whether a prospective randomized trial is warranted.

Methods

Literature search

Literature was included from 1966 through 2001 using MEDLINE and an extensive manual search was carried out using bibliographies of reviews and full articles. The princi-

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Table 1 Acute studies.

Studies	Treatment type	Treatment parameters	No. of subjects	Subject profile	Measurement used	Effect
Landis and Gibbon, 1934[7]	Whole foot and calf compression boot	–80 mmHg to 80 mmHg for 25 s and 5 s respectively	$n = 16$	Advanced peripheral disease, no vasodilation ($n = 12$)	Lewis scale Pain level Skin temperature	Mild cyanosis → normal color Severe claudication → relief of rest pain 6°C rise
Gaskell and Parrott, 1978[8]	Vinyl boot	75 mmHg for 2 s every 15 s pump/pump + erect posture	$n = 22$	Ankle pressure <60 mmHg ($n = 14$) >60 mmHg ($n = 8$)	Xe clearance dorsum of foot	 186% increase 42% increase
Salzman and McManama, 1987[9]	Circulator boot – groin to toes, end-diastolic compression 56 mmHg for 40 ms	$n = 45$ graded sequential compression	$n = 136$	Neurosurgical patients	MFI	92% increase
		$n = 50$ uniform pressure gradient		Neurosurgical patients	MFI	60% increase
		$n = 41$ single bladder compression		Neurosurgical patients	MFI	56% increase
Morgan et al, 1991[10]	Gaymar Industries Pumps, Orchard, NY, USA	4 compartments: graded sequential, uniform pressure	$n = 10$	ABI 0.60, arteriopaths, 56 years old	Popliteal artery blood flow	84% increase after 5 min
			$n = 12$	ABI >1.0, normal, 32 years old	Same	93% increase after 5 min
Abu-Own et al, 1996[11]	Supine to dependent position	n/r	$n = 15$	ABI 0.52, 65 years old with PAD, severe claudication	Laser Dopper flow $tcpO_2$	67% decrease (100 AU) 8% increase (6 mmHg)
				ABI >1.0, 62 years old with no venous or arterial disease	Laser Dopper flow $tcpO_2$	75% decrease (205 AU) no change
	Felt boots, plastic casting compression	Pressure 30% below atm. 2 months, 25 treatments	$n = 15$	ABI 0.52, 65 years old with PAD, severe claudication	Laser Dopper flow $tcpO_2$	57% increase (82 AU) 8% increase (6 mmHg)
				ABI >1.0, 62 years old with no venous or arterial disease	Laser Dopper flow $tcpO_2$	66% increase (124 AU) 10% increase (6.5 mmHg)
Van Bemmelen et al, 1994[5]	AV Impulse System (Novamedix)	100 mmHg max for 3 s, 3 cycles/min	41 legs, $n = 38$	ABI <0.85, 69 years old claudication (29), rest pain (7)	Relative flow rate	3.2 ± 1.6 increase
			11 legs, $n = 6$	ABI 1.20, 36 years old, normal	Relative flow rate	4.4 ± 2.0 increase
						IPC_{calf} IPC_{foot} $IPC_{foot+calf}$
Eze et al, 1996[12]	ArtAssist AA 1000 (ACI Medical)	120 mmHg calf, foot, calf and foot. Max for 10 s, 2 cycles/min	10 legs, $n = 7$	ABI <0.8, 44–64 years old, SFA occlusion	Popliteal artery flow Foot skin perfusion	76% 13% 50% increases 116% 246% 188% increases
			22 legs, $n = 14$	ABI >0.96, 20–35 years old, normal	Popliteal artery flow Foot skin perfusion	124% 54% 173% increases 260% 500% 328% increases
Labropoulos et al, 1998[13]	ArtAssist AA 1000 (ACI Medical)	120 mmHg max for 3 s, 4 cycles/min	40 legs, $n = 30$	33 ± 6 years old, normal	Popliteal artery blood flow PSV EDV RFV EDV duration	240% increase 24 ± 21% increase 63 ± 46% increase 72 ± 53% decrease 230% increase
Van Bemmelen et al, 2000[14]	ArtAssist AA 1000 (ACI Medical)	120 mmHg calf + foot 1 s delay max for 3 s, 3 cycles/min	16 legs, $n = 8$	ABI 0.51, 71 years old, diabetic (11)	Laser Dopper flow	3.86 AU increase
			26 legs, $n = 13$	ABI >0.92, 69 years old, normal	Laser Dopper flow	3.74 AU increase
Delis et al, 2000[2]	ArtAssist AA 1000 (ACI Medical)	Foot compression (140 mmHg)	6 legs, $n = 6$	ABI > 1.0, 36 years old, normal	VP min/VP max	30 mmHg drop
		Calf compression (100 mmHg)			VP min/VP max	30 mmHg drop
		Foot + calf compression (140 mmHg)			VP min/VP max	44 mmHg drop

continued

Table 1 continued.

Studies	Treatment type	Treatment parameters	No. of subjects	Subject profile	Measurement used		Effect		
Delis et al, 2000[6]	ArtAssist AA 1000 (ACI Medical) for $IPC_{foot+calf}$ and IPC_{calf}, AV Impulse System (Novamedix) for IPC_{foot}	120 mmHg max for 3 s, 3 cycles/min 0.5 s delay	25 legs	ABI = 0.57, 63 years old, intermittent claudicants, PVD	Peak venous velocity		20× > resting velocity		
					Mean venous flow velocity		9× > resting velocity		
					$IPC_{foot\ 180\ mm}/IPC_{foot\ 120 mm}$		No significant change		
					Ratio of expelled vein volume				
					for $IPC_{calf\ 120\ mm}/IPC_{foot\ 180\ mm}$		1.9–2.6		
					for $IPC_{calf\ +\ foot\ 120\ mm}/IPC_{foot\ 180\ mm}$		3.2		
Delis et al, 2000[15]	AV Impulse System (Novamedix)	120 mmHg max for 3 s, 3 cycles/min	40 legs, n = 32	ABI = 0.41–0.72, claudicants	vFI		51% increase		
					mV		49% increase		
	Foot pump		25 legs, n = 20	ABI >1.0, normal	vFI		111% increase		
					mV		115% increase		
							IPC_{foot}	IPC_{calf}	$IPC_{foot+calf}$
Delis et al, 2000[16]	ArtAssist AA 1000 (ACI Medical) for $IPC_{foot+calf}$ IPC_{foot} and IPC_{calf}	120 mmHg max for 4 s, 3 cycles/min	n = 31	ABI 0.55, claudicants	Popliteal artery	Initial	58%	132%	174% increase
					vFI				
					mV	~10.2 ± 4.7	15.9 ± 5.6	23.6 ± 8.6	27.5 ± 10 cm/s
					PSV, EDV		Similar to vFI and mV		
					PI	~2.1 ± 1.0	1.58 ± 0.5	1.3 ± 0.4	1.15 ± 0.4
			n = 25	ABI >1.05, normal	vFI		98.8%	188%	274% increase
					mV	~4.7 ± 2.7	9.3 ± 4.1	14 ± 5.3	17.4 ± 6.8 cm/s
					PSV, EDV		Similar to vFI and mV		
					PI	~8.5 ± 3.5	4.9 ± 1.8	3.5 ± 1.1	3.2 ± 1.4
Delis et al, 2001[17]	ArtAssist AA 1000 (ACI Medical) for $IPC_{foot+calf}$ IPC_{foot} and IPC_{calf}	120 mmHg max for 4 s, 3 cycles/min	16 legs	ABI >1.0			IPC_{thigh}	IPC_{calf}	$IPC_{calf+thigh}$
					mV		95%	313%	365% increases
					Diameter		no effect	no effect	0.2 mm increase
					PSV		increased in all with $IPC_{calf} \cong IPC_{calf+thigh}$		
					EDV		increased in all with $IPC_{calf} \cong IPC_{calf+thigh}$		
					PI		decreased in all with $IPC_{calf} \cong IPC_{calf+thigh}$		
			17 legs	ABI <0.8	mV		51%	137%	182% increases
					Diameter		no effect	no effect	0.2 mm increase
					PSV		increased in all with $IPC_{calf} \cong IPC_{calf+thigh}$		
					EDV		increased in all with $IPC_{calf} < IPC_{calf+thigh}$		
					PI		decreased in all with $IPC_{calf} \cong IPC_{calf+thigh}$		
			16 legs	Infrainguinal autologous bypass grafting	mV		98%	290%	385% increases
					Diameter		n/r	n/r	n/r
					PSV		increased in all with $IPC_{calf} \cong IPC_{calf+thigh}$		
					EDV		increased in all with $IPC_{calf} \cong IPC_{calf+thigh}$		
					PI		decreased in all with $IPC_{calf} \cong IPC_{calf+thigh}$		
							Before treatment	*During treatment*	*After treatment*
Ubbink et al, 2001[18]	ArtAssist AA 1000	3 s max compression, 3 cycles/min One treatment for 1 h	n = 9	ABI = 0.46 claudicants and/or ABI = 0.32 with rest pain and claudication	$tcpO_2$		50.5	38.5*	31*mmHg
					Laser Dopper flow (big toe)		0.15	0.35	0.20 V
					Skin temperature of foot		25.4	27.3	27.8°C
			n = 11		CRV (big toe nail fold)		20	n/r	128 m/s
							*Note: decrease in $tcpO_2$ may be due to experimental design		

MFI, mean fibrinolytic index; n/r, not reported/relevant; AU, arbitrary units; SFA, superficial femoral artery; PSV, peak systolic velocity; EDV, end diastolic velocity; RFV, reverse flow velocity; VP, venous pressure; vFI, popliteal artery volume flow; mV, mean velocity; PI, pulse index; CRV, capillary red blood cell velocity.
Other abbreviations given in main text.
Foot skin perfusion measured by laser Doppler.

Table 2 Variable length studies.

Studies	Treatment type	Treatment parameters	No. of subjects	Subject profile	Measurment used	Effect
Herrmann and Reid, 1934[19]	Pavaex: passive vascular exercises with foot elevated above heart	–70 mmHg to 70 mmHg, 30 s cycle, 5 s pos. pressure, 10 s neg. pressure 4–8 h/day – 3–7 h/week	$n = 10$	Arteriosclerosis obliterans in major pathway	Relief of pain	100% relief within 12 h
			$n = 46$	Secondary arteriole obstruction	Relief of pain	44% complete relief, 48% partial
			$n = 19$	Atherosclerosis involving foot	Relief of pain	16% complete relief, 42% partial
Dillon, 1980[20]	Circulator Boot CLC	40 min single treatments, variable overall length of treatments	$n = 8$	Ambulatory patients with mild PAD	Claudication severity Pulse volume (OI)	5 significant, 3 modest improvement $9.9 \pm 2.5 \rightarrow 11.7 \pm 2.9$
			25 legs, $n = 21$	Severe PAD	Claudication severity Ulcer severity Pulse volume (OI)	4/6 relieved of rest pain 5/9 healed, 2/9 improved $3.2 \pm 2.3 \rightarrow 6.1 \pm 4.2$
			$n = 6$	Normal	n/r	n/r
Dillon, 1986[21]	Circulator Boot – groin to toes with multi-electrolyte antibiotic solution and CLC	n/r	$n = 17$	Refractory stasis dermatitis/ulcers Outpatients $n = 8$ Combined venous and arterial disease $n = 7$	Ulceration Thrombi Anterior tibial flow Posterior tibial flow Peroneal flow	Healing of partial to full ulceration Decreased palpable thrombi 31.6 ± 17% increase 24.6 ± 15% increase 5.4 ± 10% increase
Dillon, 1986[22]	Circulator Miniboot with antibiotic solution and CLC	76 mmHg for 32 ms, 40–60 ms after every other QRS	34 legs, $n = 28$	Ischemia, necrosis Failure of conservative treatment, $n = 22$	Amputation rate Osteomyelitis Walking distance Mortality Relapse rate	94% saved 90% cured Improved 7 died after median of 23 months 11 (~32%) went 22 months without relapse
Steinberg, 1992[23]	CLC Syncarbon by Contilabo Vascular pump by Rheomedix	100 mmHg max for 3 s, 3 cycles/min Dependent position Treated up to 4 months	$n = 17$	ABI <0.7, 51–83 years old 12 with non-healing ulcers	Rest pain Claudication distance Ulcer improvement Skin temperature	6 patients relieved 2 patients increased 9 ulcers healed 6°C rise
			$n = 10$	ABI <0.7, ischemic limbs, unsuitable for bypass	ABI PPG waveform	53% increase 482% increase
Mehlsen et al, 1993[24]	Alternating suction/pressure	80–140 mmHg for 0.25 s then deflates for 0.7 s	$n = 34$	ABI 0.34–0.83, 67 years old, PAD for ≥4.5 years $n = 12$ for active treatment	ICD ACD ABI	45 m (83%) improvement 80 m (87%) improvement 0.12 (26%) increase
Dillon, 1997[25]	Circulator Boot with antibiotic solution and CLC	76 mmHg for 32 ms, 40–60 ms after every other QRS	1514 legs, $n = 1035$	Presence of arteriosclerosis obliterans, neuropathy or stasis Diabetic legs = 907	Relapse rate Deterioration rate of control Wagner 0 class improvement Wagner 2 class improvement	21.6% 38.7% of control legs progressed to disease 84% cured or improved 88% diabetics improved 65% non-diabetics improved

continued

Table 2 continued.

Studies	Treatment type	Treatment parameters	No. of subjects	Subject profile	Measurment used	Effect			
						Initial	3 months	4.5 months	% increase
Delis et al, 2000[26]	AV Impulse System (Novamedix) Foot Pump	180 mmHg max for 3 s, 3 cycles/min	$n = 25$	SFA occlusion, claudicants ≥2 years	r-ABI p-eABI	0.57 0.21	0.63 0.43	0.67 0.44	18% 110%
		IPC_{foot} 4 h/day + 75 mg aspirin			ICD	78	183	191 meters	146%
					ACD Resting volume flow	124 100	245	255 136 ml/min	106% 36%
		Control: no treatment	$n = 12$	SFA occlusion, claudicants ≥2 years	Same as above	No significant changes			
Delis et al, 2001[27]	n/r	120 mmHg max for 4 s, 3 cycles/min $IPC_{foot+calf}$ 2.5 h/day for 5 months + 75 mg aspirin daily	$n = 21$	Stable claudicants	ICD ACD r-ABI p-eABI Quality of life	197% increase 212% increase 17% increase 64% increase Significant improvement			
		Control: 75 mg aspirin daily	$n = 20$	Stable claudicants	Same as above	No significant change			
Vella et al, 2000[28]	Circulation boot and impulse-type intermittent pneumatic pump (AIRCAST®, Arterio Flow™, PlexiPulse®, NuTech™)	Circulation boot – 55–80 mmHg during diastole Impulse type – 100 mmHg max for 2–3 s, 3 cycles/min	$n = 98$	Ischemic ulceration that was not immediately amenable to surgical or endovascular intervention	Favorable Unfavorable	77 favorable (25 completely healed) 19 unfavorable (15 amputations)			
Van Bemmelen et al, 2001[29]	ArtAssist AA 1000 (ACI Medical) for $IPC_{foot+calf}$	120 mmHg calf + foot 1 s delay max for 3 s, 3 cycles/min	$n = 13$ (14 legs)	Critically ischemic legs (rest pain = 14, tissue loss = 13)	Pulse-volume amplitude Limb salvage	9/14 increased pulse amplitude 9/14 limbs were salvaged			

OI, oscillometry index; PPG, pulse-pressure gradient.
Other abbreviations given in Table 1 and main text.
Pulse volume measured using a Collens oscillometer.

pal terms for inclusion were: IPC or other form of lower limb pressure device and arterial hemodynamics. Other minor search terms were: claudication and PAD. Papers were chosen by their cohesion and relevance of data. Studies were excluded from the database if they did not contain relevant terms. A total of 26 studies were included in the database.

Data analysis and abstraction

Studies were ordered chronologically and divided between acute (Table 1) and variable length (Table 2). Three components were recorded from each study that formed the database of the meta-analysis: (1) subject profile, (2) treatment type, and (3) measurements of vascular change. Not every study contained complete components of measurement nor correlated with other study dimensions. *Subject profiles* considered were mean age, duration of symptoms, number of legs affected, ankle pressure, resting ankle–brachial index (r-ABI), clinical presentation of symptoms and outstanding inclusion or exclusion requirements. *Treatment types* considered were type of pump, duration of treatment, pattern of pump pressure cycles and concomitant use of aspirin. Since patients varied on how long their symptoms persisted, the overall treatment periods varied drastically even within a single study and thus were not reported. Some measurements of *vascular changes* included initial claudication distance (ICD), absolute claudication distance (ACD), r-ABI, post-exercise ankle–brachial index (p-eABI), popliteal artery volume flow, peak venous velocity, skin blood flow, laser Doppler flow (LDF), transcutaneous oxygen pressure ($tcpO_2$), venous pressure via cannulation, and skin temperature.

Weaknesses

The primary weakness is the paucity of comparisons among studies on the effects of compression on lower limb arterial blood flow. This is due to differently engineered devices (foot versus calf versus foot and calf), differences in cycle length and duration of treatment, criteria for patient treatment (stage of disease), means of flow measurement and endpoint analysis. Therefore, it was crucial to form a table that emphasized generalized trends, allowing differences to be documented without losing the uniqueness of each study.

Of all studies directly pertaining to compression treatment of PAD, three[24,26,27] were prospective-randomized. Sample sizes for the three controlled studies as well as most other studies were relatively low. Two tables were used to make generalized comparisons and extrapolate trends that exhibit the effects of IPC on PAD.

Results

Various methods, measurements and subjects were used in the studies reviewed and the combinations of them varied in every study, making direct comparison difficult. Despite this, however, trends were observed from papers that utilized similar outcomes, comparing, when possible, subjects and methods used.

Lower extremity arterial flow increased from between 13% and 240% as measured in the popliteal,[10,12,13,15,16] anterior, posterior and peroneal arteries.[21] The greatest increases were seen in studies that used concomitant foot and calf compression.[12,13,16] The lowest increases were in studies using only foot compression.[12,15,16,26]

Intermittent compression increased the flow of arterial blood measured by laser Doppler from 57% to 246% in non-normals.[11,12,14,18] The lowest increase was with the use of felt boots and plastic casting compression[11] and the greatest increase measured foot skin perfusion and used an AAD covering the foot.[12] AAD covering the foot and calf also demonstrated consistent significant increases in flow.[11,12,14]

Velocity of arterial flow increased from between 15% and 320% in non-control patients.[4,15–17] In studies that compared the effect of AAD compression in two areas of the lower limb to that of one, the compression of two areas provided the greatest increase in arterial velocity,[16,17]

Peak systolic velocity, end diastolic velocity and pulse volume all increased in their respective compression studies.[13,16,17,20,29] Unfortunately, the results were reported using different parameters so individual results were not compared.

Rest pain and claudication distance were also improved across the spectrum of trials performed. Resting pain was relieved in varying percentages from 100% of patients with arteriosclerosis obliterans to 16% complete and 42% partial relief of patients with atherosclerosis involving the foot.[19] Other studies reported results qualitatively as modest or significant improvement,[20] or just relieved.[7,23] ICD and ACD increased from 146% to 197% and from 106% to 212% respectively in patients suffering from mild PAD to those with non-healing necrosis.[22–24,26,27]

Two studies measured the healing of ulcers. One reported the healing of nine of 12 ulcers in patients with otherwise non-healing ulcers.[23] The other study reported the healing of partial to full ulceration in refractory stasis ulcer or combined venous and arterial disease patients.[21]

Limb salvage was reported in 94% of 38 legs with ischemia, necrosis and failure of conservative treatment.[22] In another study, nine of 14 limbs were salvaged in patients with critically ischemic legs.[29]

Resting ABI increased between 17% and 26% in stable claudicants.[24,26,27]

Discussion

Although the pneumatic devices, treatment parameters and resulting measurements differ between most, if not all of the studies, they all present favorable effects of increasing limb hemodynamics. It was a matter of separating patients into diseased and healthy, unifying treatment types into compression treated versus untreated, and relegating short- and long-term results into improved flow versus unchanged or worsening flow. By examining the studies in a chronological fashion it may be easier to see where the future of compression devices for leg ischemia lies.

The first studies that addressed the issue of ischemic rest pain observed that taking a more erect posture or walking around could relieve patients. This led to early studies[10,12] that used rudimentary pressure devices. The problem was that they took a long time to reach sub-optimal pressures, only maintained lower pressures for short periods, and were impractical for an outpatient setting because of size and difficulty of use. The focus of benefit was the limiting of ulceration, which was attributed to the formation of collateral vessels.

After the cursory benefits of pavaex (passive vascular exercises), which placed the foot above the heart for treatment, were shown,[19] a more advanced pump that changed pressures rapidly with the patient placed in a dependent position resulted in better outcomes.[7] The quantitative physiological effect of compression to increase blood flow in an additive manner with an erect posture was then shown.[8]

Long-lasting (6 months and 2 years) improvements in vascular tests were shown with the use of a compression system that initiated pulses coordinated with the diastole of the heart.[20] Improvements in re-channeling of blood through previously obstructed arterioles or else some fibrinolytic activity was thought to be the mechanism of improvement.[21] It was at this point that cardiosynchronous limb compression (CLC) was thought to be used as a possible adjunct to surgery, and possibly as a more cost-effective alternative[22] for some patients.

The cause of hyperemia after compression was identified as the lowering of peripheral vascular resistance following the liberation of endothelial-derived relaxing factors.[10,11]

Looking at how different areas of compression affect hemodynamic changes, it was found that the coordinated effect of foot and calf pumps, known as AAD, may have the greatest overall benefit.[12] Further studies using AAD indicated a drop in the peripheral resistance and augmentation of the limb blood flow,[13] and that blood was getting into microcirculation to feed ischemic tissue.[14]

In a series of confirmation studies using AAD, it was suggested that the vasoactive response of the vessel walls to increasing pressure is slightly debilitated in arteriopaths.[30,31] It was also found that the greatest improvement in several vascular and walking tests occurred in the first 3 months of treatment.[26] Blood flow remained elevated above baseline following treatment,[15,27] but a single treatment was shown to be insufficient to produce this effect.[18] Optimum treatment variables were found to be compression of foot and calf at 120 mmHg for 3–4 s, three times a minute with the calf compressed 0.5–1 s after the foot.[2,6]

A recent review article studying the physiological mechanisms of IPC devices concluded that their effects are not purely mechanical and that the release of biochemical mediators may play an important role.[32]

Another recent study achieved complete healing in 25 patients who could not undergo any other treatment than amputation.[28] In fact, four of those patients had a $tcpO_2$ of less than 20 mmHg and another seven had a $tcpO_2$ between 20 and 40 mmHg. This is in contrast with an earlier study from the same center which showed such values were unlikely to heal their amputations.[33] Beneficial use of CLC in inoperable patients was augmented by a study over 3 months of at-home use for 2.38 hours a day, which salvaged legs that would otherwise be amputated.[33]

Three of the studies were prospective-randomized and thus likely report the most reliable data. The earliest was conducted by Mehlsen and colleagues,[24] and the later two by Delis and colleagues.[26,27] The first,[24] a double-blind study, used intermittent suction and pressure to relieve stable intermittent claudication in 25 patients compared to placebo in another 25. The study was conducted for 2 months. The significant improvement in the treated group with no improvement in the placebo group showed that further studies should be conducted. The small scale and brevity of the study, however, prevented conclusions from being made about absolute and long-term benefits of therapy.

The first Delis prospective study[26] was slightly better designed. Similar to Mehlsen's study, it also used a population of stable claudicants but matched them for age, sex, risk factors and claudication distances as well as lasting for a longer 4.5 months.[26] The Delis study used a foot pump for compression that provided only positive pressure. The results of this study, while encouraging, were not as spectacular as those from Mehlsen. Two possible explanations are the difference in compression device used or the difference in study design.

Testing the long-term effects of foot and calf compression on stable claudicants, Delis designed his second prospective randomized study similarly to his first, comparing stratified treatment groups with controls for the duration of 5 months.[27] This is likely the strongest study reviewed in this paper because of its design. The results, which are similar to those of other studies reviewed in this paper, show improvement in both lower extremity arterial flow and symptoms. This is encouraging for the use of IPC as a treatment for those with lower extremity arterial disease. What is lacking, however, are large-scale, prospective, randomized studies with longer follow-up to show with greater authority the efficacy of such treatment.

Conclusion

This systematic review demonstrates that an IPC program appears promising and may be used in patients with severe PAD who are not candidates for revascularization using surgery or percutaneous angioplasty. Although the history of limb compression is varied and small in size, the studies considered demonstrate conclusive physiological benefits. Evident, yet indirect benefits include low cost of treatment, ease of outpatient care in the clinic by CLC or at home with AAD, and avoidance of costly and dangerous surgery. Large-scale, randomized, double-blind trials will be necessary to clarify the most beneficial regimen for increasing lower limb blood flow and improving the quality of life of patients with PAD.

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