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Non-Invasive Management of Peripheral Arterial Disease

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Abstract

Background

Peripheral arterial disease (PAD) is common and symptoms can be debilitating and lethal. Risk management, exercise, radiological and surgical intervention are all valuable therapies, but morbidity and mortality rates from this disease are increasing. Circulatory enhancement can be achieved using simple medical electronic devices, with claims of minimal adverse side effects. The evidence for these is variable, prompting a review of the available literature.

Methods

Embase and Medline were interrogated for full text articles in humans and written in English. Any external medical devices used in the management of peripheral arterial disease were included if they had objective outcome data.

Results

Thirty-one papers met inclusion criteria, but protocols were heterogenous. The medical devices reported were intermittent pneumatic compression (IPC), electronic nerve (NMES) or muscle stimulators (EMS), and galvanic electrical dressings.

In patients with intermittent claudication, IPC devices increase popliteal artery velocity (49–70 %) and flow (49–84 %). Gastrocnemius EMS increased superficial femoral artery flow by 140 %. Over 4.5–6 months IPC increased intermittent claudication distance (ICD) (97–150 %) and

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absolute walking distance (AWD) (84–112 %), with an associated increase in quality of life. NMES of the calf increased ICD and AWD by 82 % and 61–150 % at 4 weeks, and 26 % and 34 % at 8 weeks.

In patients with critical limb ischaemia IPC reduced rest pain in 40–100 % and was associated with ulcer healing rates of 26 %. IPC had an early limb salvage rate of 58–83 % at 1–3 months, and 58–94 % at 1.5–3.5 years. No studies have reported the use of EMS or NMES in the management of CLI.

Conclusion

There is evidence to support the use of IPC in the management of claudication and CLI. There is a building body of literature to support the use of electrical stimulators in PAD, but this is low level to date. Devices may be of special benefit to those with limited exercise capacity, and in non-reconstructable critical limb ischaemia. Galvanic stimulation is not recommended.

Keywords

Chronic venous disease • Thrombosis • DVT • Pulmonary embolism • Electrical stimulation • NMES

1 Background

Peripheral arterial disease (PAD) is common, and often co-exists with cardio-respiratory disease, stroke, and diabetes [1]. Its incidence is estimated at 7–14 % in the general population [1, 2], increasing with age to approximately 20 % in the over-seventies [3]. It is associated with progressive and profound effects on mobility, skin integrity and quality of life [4]. Significant clinical manifestations include intermittent claudication, rest pain, gangrene, and limb loss. Risk management, exercise, radiological and surgical intervention are all valuable therapies, but morbidity and mortality rates from this disease are increasing [3, 5, 6]. Due to the nature of the disease, exercise tolerance can be limited by performance status. Invasive procedures carry with them significant risks, and patients with diffuse disease are often not suitable for revascularisation [7].

Maximal medical and surgical therapy has been shown in the past to be augmented by the use of medical devices such as intermittent pneumatic compression [8]. Electronic muscular stimulation (EMS) and neuromuscular stimulation (NMES) devices can cause contraction of the leg muscles in similar ways to IPC, and may have similar beneficial effects. The supporting evidence for neuromuscular stimulation in peripheral arterial disease is variable in scientific and clinical content or relevance, and prompted further exploration.

This review aims to identify and analyse studies of non-invasive haemodynamic devices applicable to this cohort, and extrapolate evidence with a view to modulating current clinical practice. This is also relevant in the light of recent technological advances of electrical stimulation devices, becoming more portable, affordable, and accessible to health professionals.

2 Methods

A systematic review of Embase and Medline was undertaken, with the search string:

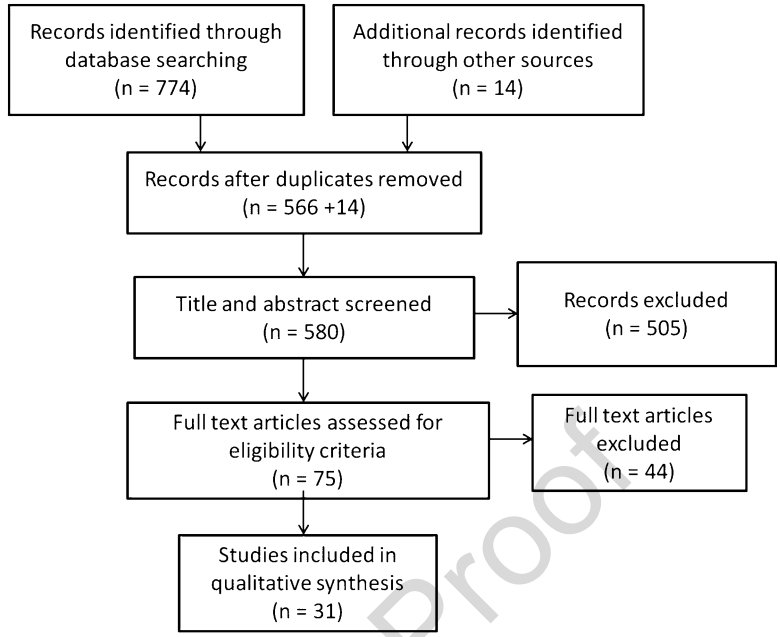

Fig. 1 PRISMA diagram

("device" OR "electric" OR "stimulation" OR "pneumatic" OR "compression" OR "IPC") AND ("peripheral arterial diseas*" OR "isch*" OR "peripheral vascular diseas*" OR "claudication") AND ("leg" OR "limb" OR "foot") (No Related Terms)

The search was performed on 8th July 2013 and repeated by the Royal College of Surgeons of England library. A PRISMA diagram shows the paper selection process (Fig. 1).

Abstracts were screened and included or eliminated by title, abstracts and full texts were screened for the peripheral use of non-invasive medical devices in humans for the management of lower limb peripheral arterial disease.

Inclusion criteria were clinical or haemodynamic data related to the device use. Exclusion criteria were animal studies, studies pertaining to epidemiology, diagnosis or pure imaging. Non-electrical devices were excluded (e.g. vascular closure devices), as were invasive therapies such as endovascular intervention, spinal cord/epidural stimulation, and extracorporeal limb perfusion. Functional electric stimulation for spinal cord injury was excluded.

3 Results

Thirty-one papers met criteria for inclusion and were grouped according to indication for use. Despite multiple devices, protocols and trial designs, inferences have been drawn. Table 1 details the studies, with numerical results data given where possible. Meta-analysis has not been performed.

4 Devices

4.1 Intermittent Pneumatic/External Compression

Six external compression devices were reported: five pneumatic (Circulator Boot, Circulator Boot Company, the AV Impulse, Novamedix Ltd, the DVT-30, Huntleigh Healthcare, the Art Assist 1000, ACI Medical, the ArterialFlow, DJO), and one which uses an external compressive band (FM220™, FlowMedic, Israel). Pressure settings varied from very low (55 mmHg in Circulation Boot) to high (120 mmHg in ArtAssist).

t.1 **Table 1** Results of systematic review grouped according to indication

t.2 Device	Paper	Year	Setting/program	Subject profile	N (PAD/control)	Outcome measure	Outcome time period	Finding
t.3 **Stable claudicants**								
Circulator boot	Dillon [9]	1980	Combination of laboratory studies and case series	Claudicants, severe PAD non-reconstructable	29/6	Lab – subcutaneous pO_2, pulse volume, ABPI	40 mins	Oscillometry readings from the leg increased during therapy in normal and diseased limbs after one session, changes more pronounced after series of treatment. $TcPO_2$ increased in diseased limbs during treatment
t.5						Clinical – ulcer healing, presence rest pain, ICD		
t.4			Reclining, applied to whole leg. 55–80 mmHg applied in late diastole. One 40 min session for lab study,					22/25 severe legs benefitted clinically from therapy (claudication distance, ulcer healing, rest pain). Best results in 3–4 sessions/day for >1 week. Two stopped therapy due to pain
t.6								
ArtAssist	Eze [10]	1996	Alternatively foot +/− calf, sitting position, 120 mmHg 10 s 2/min	Stable claudicants, SFA occlusion	10/22	Laser Doppler (great toe)	Mean of 6 IPC cycles	Flux (PAD/healthy) 288/428 % of baseline with combination IPC
t.7						Duplex popliteal artery		Arterial flow (PAD/healthy) 150/273 % of baseline with combination IPC
t.8								Combination IPC more effective than IPC calf/ft alone
t.9								

t.10	ArtAssist	Delis [11]	2000	Recovery position, IPC foot, 1–120 mmHg, 4 s, 3/min, 5 mins on, 10 min rest, 5 mins on etc.	Claudicants (fontaine 2)	40/25	Duplex popliteal artery velocities and flow	Lab	Mean popliteal artery flow 211 % $p < 0.001$ in healthy, 151 % $p < 0.001$ in PAD
t.11									Mean popliteal artery velocity 215 % $p < 0.001$ in healthy, 149 % $p < 0.001$ in PAD
t.12									Post compression baselines of both were significantly higher than pre-compression
t.13	ArtAssist	Delis [12]	2000	Sitting position, IPC foot/calf/combination, 1–120 mmHg, 4 s, 3/min, 5 mins on, 10 min rest, 5 min on etc.	Claudicants (fontaine 2)	31/25	Duplex popliteal artery velocity and flow	Lab	IPC combination mean velocity 263 % ($p < 0.001$) in controls, 170 % ($p < 0.001$) in PAD
t.14									IPC combination volume flow 278 % in ($p < 0.01$) controls, 174 % ($p < 0.001$) in PAD
t.15									IPC combination was more effective than IPC foot or IPC calf in PAD
t.16	ArtAssist	Delis [13]	2000	Device versus no device. Sitting position, 1–120 mmHg, 4 s, 3/min, >4 h/day	Claudicants (fontaine 2) stratified for smoking and diabetes	25/12	ICD, ACD, ABPI rest and post-exercise, duplex popliteal artery flow	4.5 months treatment, follow-up at 12 months	No improvement in parameters for those randomised to no device
t.17									Popliteal artery flow 136 % of week 0 baseline at 4.5 months
t.18									IPC foot at 4.5 m – ICD 246 % baseline, AWD 206 % ($p < 0.001$ for both)

(continued)

t.20 **Table 1** (continued)

t.21 Device	Paper	Year	Setting/program	Subject profile	N (PAD/control)	Outcome measure	Outcome time period	Finding
								ABPI (pe) significantly greater than control group at 4.5 and 12 m. Significant benefit over controls persisted at 12 m
ArtAssist	Delis [14]	2002	Sitting position, IPC calf/ft/combination, 1–120 mmHg, 4 s, 3/min, 5 mins stim, 10 min rest, 5 min stim etc.	Stable claudicants	22 IC, 36 bypass	Laser Doppler great toe	Minutes, unspecified	IPC increases limb skin blood flux in controls and claudicants
								IPC combination and IPC foot produced the biggest flux differences over IPC calf ($p < 0.004$)
ArtAssist	Ramaswami [15]	2005	Device versus no device	Stable claudicants (matched for smoking, diabetes)	15/15	ICD, AWD, ABPI	12 months	ICD compared to baseline (device/no device) at 4, 6 and 12 months was 237/102 %, 241/103 %, and 250/104 %
			Sitting, IPC foot + calf, 120 mmHg, 3/min, 1 h twice a day					AWD was 184/102 %, 196/105 %, and 201/106 % (difference $p < 0.01$ for all)
								No significant change in ABPI shown in either group

t.26	ArtAssist	Delis [16]	2005	Device versus no device	Stable claudicants (AWD 35–350 m)	20/21	ICD	17 months	ICD IPC at 5 months 197 % ($p < 0.005$), BMT no significant difference
t.27				Sitting, IPC foot and calf, 1–120 mmHg, 4 s, 3/min, 3+ h/day			AWD		AWD IPC at 5 months 212 % ($p < 0.005$), BMT no difference
t.28							ABPI (rest and post-exercise)		Resting ABPIs not changed either group
t.29							US popliteal artery volume flow		pe-ABPI IPC higher at 5 months ($P < 0.005$), BMT no difference
t.30							QoL (SF-36)		No significant resting artery flow volume changes either group
t.31							Compliance		Improved quality of life in IPC group at 5 months, BMT unchanged
t.32									All reported gains with IPC sustained 12 months after treatment
t.33									85 % compliance with home IPC (defined as ≥2.5 h/day)
t.34	DVT-30	Morris [17]	2002	Supine, unilateral, thigh and calf, 60 mmHg, 10 s, 1/min	Stable claudicants	11/18	Duplex common femoral artery frequency	10 min	PAD subjects arterial frequency 94 %/129 % of baseline during compression/deflation. Controls 85 %/121 % of baseline
t.35							Temperature limb		Hallux temperature changes −0.1 °C for controls and +2.2 °C PAD

(continued)

t.36 **Table 1** (continued)

t.37 Device	Paper	Year	Setting/program	Subject profile	N (PAD/control)	Outcome measure	Outcome time period	Finding
AV impulse	Morgan [18]	1991	Seated, non-weight bearing, 100 mmHg, 3 s, 3/min	Claudicants	10/12	Doppler popliteal artery flow	Lab	Flow 193 % and 184 % of baseline in healthy and PAD ($p < 0.0001$ and $p < 0.03$)
								Increase reduced by supine position and limb cooling
								Flow increase more persistent in PAD
								Contralateral limb flow not affected
FM220 (IMC)	de Haro [19]	2010	Calf	Stable claudicants	14/16	ICD, AWD and ABPI (pre- and post- exercise)	3 months	ICD 185 %, ($p = 0.002$), ACD 176 % ($p = 0.002$), in IMC group, no significant changes in controls
			65 mmHg for 3 s, 3/min			Compliance		ABPI (pe) 197 % ($p = 0.003$) in IMC group, no significant changes in controls
								Changes sustained after 3 months
								Compliance with device 78 %
IPC (unspecified)	Anthonysamy [20]	2012	10 mins, settings not specified	Stable claudicants (fontaine 2)	15/0	Duplex popliteal artery peak systolic flow	Lab	Flow with IPC 175 % of baseline ($p < 0.05$)
NMES	Loubser [21]	1988	Unilateral, common peroneal nerve	Stable claudicants	8/8	BP, HR	60 min	BP and HR changes not significant for either group
			2 Hz, intensity to produce muscle contraction, 60 mins			Hallux photoplethysmographic waveform		Hallux photoplethysmographic waveform significant change in PAD, not control
						Skin temp		Skin temperature significant rise in PAD, not controls

t.50	NMES (Medicompex)	Tsang [22]	1994	NMES versus sham (TENS)	Stable claudicants, ABPI < 0.9, AWD < 500 m, peABPI drop > 30 mmHg	13/13 sham	Treadmill ICD/AWD	8 weeks	ICD with NMES 126 % of baseline ($p < 0.003$), control 122 %, at 8 weeks
t.51				Popliteal and anterior tibial nerves, 8 Hz, 350 microsecs			ABPI,		AWD with NMES 134 % ($p < 0.004$), control 127 % at 8 weeks
t.52							Ankle flexion fatigue index		Differences between control and IPC not significant after 4 weeks therapy cessation
t.53									Neither group improved ABPI
t.54									Fatigue index improved in both groups, NMES more than sham, but returned to baseline after treatment cessation
t.55	NMES (Medicompex)	Hudlicka [23]	1994	Unilateral, tibialis anterior and gastrocnemius muscles	Claudicants	12/12 sham	AWD	4 weeks	AWD with 4 weeks NMES 161 % baseline ($p < 0.05$), sham 102 % (ns)
t.56				8 Hz, 330 microsecs, voltage to produce muscle contraction. 20 mins, 3/day, 28 days			ABPI		Fatigue index NMES 200 % baseline ($p < 0.05$), sham 111 % (ns)
t.57							Ankle flexion fatigue index		ABPI did not change significantly in either group
t.58	EMS (MediCompex)	Anderson [24]	2004	EMS versus sham (TENS)	Stable claudicants, pe-ABPI < 0.8, AWD 50–350 m	15	Leucocyte activation, vascular permeability,	4 weeks	No evidence of activated neutrophils, increased vascular permeability, or increased cardiovascular event incidence
t.59				Unilateral gastrocnemius			ICD/AWD		ICD EMS/sham 182 %/ 208 % of baseline ($p < 0.01$)

(continued)

t.61 **Table 1** (continued)

t.62 Device	Paper	Year	Setting/program	Subject profile	N (PAD/control)	Outcome measure	Outcome time period	Finding
t.60			250 microsecs, 100 V, 6 Hz, 20 mins. 3/day, 7/week			Compliance		AWD 250 %/163 % ($p < 0.05$)
t.61								95 % compliance
EMS (Veinoplus)	Abraham [25]	2013	Gastrocnemius and soleus	Claudicants (Fontaine 2)	15	Duplex SFA,	Baseline, during, 10 mins after	Flow 240 % baseline with stimulation at 100 bpm ($p < 0.01$) but wide variation
t.62			Rectangular pulse <25 micro C, 50 Vpeak, 1–250 Hz, max duration 240 microsecs, 20 mins increasing contraction rates 60–100 bpm	Most symptomatic leg		NIRS TcO_2		No change in NIRS or O_2Hb signal with stimulation
t.63						O_2Hb		No induction of ischaemic pain
t.64						(compared to treadmill test)		
t.65								
t.66 **Critical limb ischaemia**								
Circulator Boot	Dillon [26]	1997	Reclining. Cardiosynchronous end-diastolic single chamber pneumatic compression boot, 55–80 mmHg	Limb lesions (peripheral arterial, venous, diabetic, and neuropathic disease)	1517	Healing rate	Variable	80.5 % healed or improved
t.67								
t.68						Relapse rate		Relapse rate of 21.6 %
t.69								Smoking and distance of home from treatment centre sig affected healing rates
Circulator Boot	Dillon [27]	1997	Reclining. Cardiosynchronous end-diastolic single chamber pneumatic compression boot, 55–80 mmHg	CLI for limb salvage	2/0	Limb salvage	Variable	Limb salvage described in both PAD cases, also diabetes and osteomyelitis. Intensive treatment regime using injected antibiotics, soaks, dressings and boot Tx. Reversal of peripheral neuropathy loosely described
t.70								

t.71	Circulator boot (then home programme)	Vella [28]	2000	No unified protocol.	CLI, non-reconstructable with ischaemic ulcers	98/0	Ulcer healing, ulcer size (static or smaller), amputation rate, mortality	Average 40 days	79 % "favourable outcome" (ulcer decrease in size, complete healing, revascularised)
t.72				Circulator boot – 55–80 mmHg timed with end-diastole, 45 mins, 1–2/day					83 % limb salvage (15 major amputations, 2 deaths)
t.73				Home boot – foot +/− leg, 100 mmHg 3 s, 3/min, 2–6 h/day, mean duration 8 weeks					Authors claim can be used to bridge to revascularisation or skin grafting
t.74	ArtAssist	Louridas [29]	2002	Not specified	CLI	25/0	Ulcer healing	Mean 3 month	26 % ulcers healed
t.75							Rest pain		
t.76							Amputation rate		Rest pain improved in 40 %
t.77							Toe pressures		
t.78							Mortality		58 % limb salvage
t.79									Toe pressures improved $p = 0.03$
t.81									Mortality rate 12 %
t.82	ArtAssist	Labropoulos [30]	2005	Foot and calf IPC. Semi-erect, 120 mmHg, 3 s, 3/min	CLI (fontaine 3–4)	20/0	Duplex flow volume popliteal, medial gastrocnemius, genicular collateral artery	5 IPC cycles	Popliteal – 205 % of baseline ($p < 0.01$)
t.83									Gastrocnemial–170 % of baseline ($p < 0.01$)
t.84							Laser doppler foot		Collateral – 156 % of baseline ($p < 0.01$)
t.85									Laser Doppler flux increased significantly with IPC use ($p < 0.03$)
t.86									
t.87	ArtAssist	Sultan [31]	2011	Upright. 0–120 mmHg, 4 s, 3/min, 2 × 3 h/day, 3 months	CLI (Rutherford ≥ 4)	171/0	Ulcer healing	3 months, repeated for 18 %	94 % clinical improvement (Rutherford 4 -- > 3), 30 % at 3 years
t.88				Protocol repeated if of significant benefit			Limb salvage	Median F/U 13 months	Rest pain resolved in all over treatment period
t.89							Mortality		

(continued)

t.91 **Table 1** (continued)

t.92 Device	Paper	Year	Setting/program	Subject profile	N (PAD/control)	Outcome measure	Outcome time period	Finding
								94 % resolution of ulcers and limb salvage at 3.5 years, median amputation-free survival 18 months
						Doppler popliteal arterial flow		30-day mortality 0.6 %. All-cause survival 31 % at 4 years
						Toe pressure		Toe pressures 146 % of baseline ($p < 0.0001$), sustained at 12 m
						QoL		Popliteal artery flow 158 % of baseline ($p < 0.0001$), sustained at 12 m
						Cost-effectiveness		Regression showed DM, chronic renal failure, and hypercholesterolemia had no significant effect on limb salvage
								Cost per quality-adjusted life year for IPC was €2953
Arterial flow, DJO	Kavros [32]	2008	IPC calf, 85–95 mmHg, 2 s, 3/min, 3 × 2 h/day	CLI (non-reconstructable)-non-healing ulcer or amputation wound	24/24	Limb salvage, wound healing	18 m	58 % (IPC) vs 17 % (control) had complete healing and limb salvage ($p < 0.01$)

t.97	IPC (unspecified)	Montori [33]	2002	Home use, 6 h/day	CLI non-healing wounds	107/0	Wound healing, amputation rate	Median 6 m	Wound healing seen with 40 % patients $TcPO_2 < 20$, 48 % in osteomyelitis/active infection, 46 % in IDDM, 28 % with a previous amputation
t.98									7 patients discontinued use due to pain
t.99	IPC (unspecified)	Beirne [34]	2009	Not specified	CLI	149/0	Limb salvage, mortality.	30 days, 90 days, 6 m intervals (mean 18 m)	72 % "Sustained clinical improvement"
t.100							Limb digital pressure measurement		3 % amputation rate
t.101									21 % mortality
t.102	NeuroTrac 3 TENS (Verity Medical, UK)	Seenan [35]	2012	TENS versus sham	Tourniquet induced ischaemic pain in healthy legs	13	Time to pain threshold, pain tolerance, total pain endurance	To maximal pain able to be endured	Time to pain threshold ($p < 0.05$), tolerance ($p = 0.002$) and total endurance ($p = 0.003$) increased with device compared to sham controls
t.103				Unilateral			Reported pain (21-NRS, McGill Pain Questionnaire)		Reported pain lower with device compared to sham
t.104				Gastrocnemius					
t.105				200 msecs biphasic pulses, 120 Hz, in a continuous pattern					
t.106	**Post revascularisation**								
t.107	AV impulse	White [36]	1996	IPC foot. 50–200 mmHg, 3 s, 3/min. 7 post-operative days, 4–6 h/day	Post ischaemic leg reconstruction (femorotibial bypass)	5/5	Calf and ankle circumference	7 days	Significantly less swelling in experimental patients compared to controls, which peaked on day 5 (no figure given)
							Duplex femoral/popliteal venous velocity		Significant increase in experimental patients' femoral and popliteal

(continued)

t.109 **Table 1** (continued)

t.110 Device	Paper	Year	Setting/program	Subject profile	N (PAD/control)	Outcome measure	Outcome time period	Finding
t.108								venous velocities (no figure given)
t.109								Cessation of treatment to less than 4 h per day led to recurrence of symptoms, oedema, and a worsening of ulcers
ArtAssist	Delis [14]	2002	Sitting position, IPC calf/ft/combination, 1–120 mmHg, 4 s, 3/min, 5 mins stim, 10 min rest, 5 min stim etc.	Infra-inguinal arterial revascularization	36/20	Laser Doppler great toe	Minutes, unspecified	IPC increases limb skin blood flux in controls and grafted arteriopaths ($p < 0.001$), although no difference between these groups
t.110								IPC combination and IPC foot produced the biggest flux differences over IPC calf ($p < 0.004$)
t.111								
t.112 **Misc**								
Galvanic electrical stimulation (Micro Z)	Peters [37]	1998	Device on diabetics, with and without impaired TcO_2 ft	Diabetics	11/8	Laser Doppler foot TcO_2 ft	1 day	No difference in fluximetry readings, either group
t.113			Unilateral, 100 Hz (twin peak monophasic), delivered via a silver nylon mesh stocking, 4 × 60 mins. No muscle contraction	(Foot $TcO_2 < 40$ mmHg)				Oxygen perfusion rose with stimulation during first 5 mins ($p < 0.04$). No changes in controls. No significant difference from baseline after cessation of device
t.114								

t.115	Galvanic electrical stimulation (Micro Z)	Peters [38]	2001	Device to placebo	Diabetics with foot ulcers	20/20	Healing rate	12 weeks	No significant differences in wound healing rate between groups
t.116				50 V, twin peak monophasic pulses, pulse width 100 microsecs, delivered via a silver nylon mesh stocking. 8 h, delivered at night. Alternating 10 min 80 Hz, 10 min 8 Hz, 40 min no stimulation	(TcO_2 > 30 mmHg)		Complete wound healing		Device/sham total wound surface area healed 86.2 %/71.4 % (ns)
t.117							Complications		Complete healing 13/7 subjects (ns)
t.118							Compliance (>20 h/ week)		Time to complete healing 6.8/6.9 weeks (ns)
t.119									One amputation, in sham group
t.120									70 % device compliance

t.121 *PAD* peripheral arterial disease, *ICD* intermittent claudication distance, *AWD* absolute walking distance, *$TcPO_2$* transcutaneous oxygen, *SFA* superficial femoral artery, *IPC* intermittent pneumatic compression, *ABPI* ankle brachial pressure index, *pe* post-exercise, *US* ultrasound, *NIRS* near-infrared spectroscopy, *CLI* critical limb ischaemia, *DM* diabetes mellitus

All applied pressure anatomically to the calf, some additionally to the foot or thigh.

4.2 Electrical Stimulators

A mixture of transcutaneous electrical stimulators were reported. The Veinoplus™ (Adrem Tech, France) delivers electricity to the gastrocnemius muscle (1–250 Hz, 50 V, pulse width 240 ms), whilst the three NMES/TENS machines can operate at variable settings and be placed over muscles or nerves (Medicompex™, Medicompex SA, NeuroTrac ™ TENS, Verity Medical Ltd, TENS SM1, Schwa-Medico). The Micro-Z™, Prizm Medical Inc is a galvanic electrical stimulator (50 V, pulse width 100 μs, sub-threshold for sensation and muscle contraction). Direct current is applied to a specific body area by a conducting garment, with contact aided by an electrolyte solution.

5 Evidence by Indication

5.1 Intermittent Claudication (Also Described as "Stable Claudicants", or Fontaine Stage 2)

The immediate effect of IPC devices is to increase popliteal artery velocity (49–70 %) [11, 12] and flow (49–84 %) [10–12, 18, 20] when compared to baseline levels. When used for a prolonged period of time they have also been shown to improve popliteal artery flow by 3–36 % [13, 16]. Electrical stimulation of the gastrocnemius has been shown to increase superficial femoral artery flow by 140 %, although there were a wide range of flow changes in the small cohort study [25].

There were a wide variety of protocols, however over the course of 4.5–6 months IPC was shown to increase ICD (97–150 %) and AWD (84–112 %) by clinically significant distances, with the benefits persisting over 12 months [13, 15, 16]. External compression of the calf achieved an increase of 85 % and 76 % in ICD and AWD, which was significant when compared to negative controls, and sustained at 3 months [19]. NMES of the calf muscles, using the Medicompex, increased ICD and AWD by 82 % and 61–150 % over 4 weeks [23, 24], and 26 % and 34 % over 8 weeks [22]. These trials were small, but results were significant when compared to a sham device group.

Delis et al. showed an increase in quality of life at 5 months with IPC therapy, whilst the best medical therapy groups scores were unchanged [16]. These gains were sustained at 12 months post-treatment.

5.2 Critical Limb Ischaemia

Studies suggest that IPC reduces rest pain in 40–100 % [29, 31]. One trial evaluated the effect of high frequency TENS on the relief of laboratory-induced tourniquet ischaemic pain [35]. The blinded use of the TENS machine delayed the onset of pain, reduced pain levels, and increased endurance of pain over a period of several minutes. This was significant when compared to sham-placebo. However, the feasibility of clinical use of TENS in peripheral arterial disease does not appear to have been explored.

IPC treatment was shown to have ulcer healing rates of 26 % [29]. Vella et al. offer a 79 % "favourable outcome" at 40 days, a loose term which covers decreased ulcer size, complete healing, or improved sufficiently to allow revascularisation [28]. Blood flux to the skin of the foot, as evidenced by laser Doppler, was increased significantly over 5 IPC cycles in a cohort of 20 subjects [30].

IPC had an early limb salvage rate of 58–83 % at 1–3 months, and 58–94 % at 1.5–3.5 years [28, 29, 31, 32, 39]. Beirne et al. quoted an amputation rate of 3 % at 18 months, and a mortality rate of 21 %, but do not compare to controls [34].

No studies have reported the use of EMS or NMES in the management of CLI.

5.3 Post Revascularisation

Two IPC devices have been investigated for their utility in circulatory support after surgical revascularisation. Application to the foot for 7 days after femorodistal bypass in 5 subjects led to reduced swelling and increased haemodynamic parameters in the femoral and popliteal vessels over controls not treated with IPC [36]. No numerical data to support this is given, and conflicts of interest have not been declared. The 2002 paper looks at grafted arteriopaths (femoropopliteal and femorodistal bypass) approximately 18 months post-operation, and shows that a single treatment with IPC increases foot skin blood flux from baseline equally to controls, during device operation [14].

5.4 Galvanic stimulation - a special mention

There were few published clinical studies using galvanic electrical stimulation in peripheral arterial disease. Peter et al. investigated subjects who had impaired peripheral perfusion and microvascular insufficiency, as measured by laser Doppler and transcutaneous oximeter [37]. He demonstrated an increase in skin blood flux and oxygen tension in 11 diabetic patients with impaired microcirculation after 5 mins of stimulation, which dropped back to baseline after stimulation ceased. Another study of 40 randomised and controlled subjects looked at the healing of diabetic neuropathic foot ulcers when subjected to a nocturnal program of galvanic skin stimulation over 12 weeks [38]. There was no significant difference in wound healing rate, time to complete healing, or limb salvage between test and control groups.

6 Discussion

There is evidence to support the use of IPC in the management of intermittent claudication, with clinically important changes in treadmill distances seen with regular use. The greatest volume of published supporting research lies behind the ArtAssist device. The benefit of linking compressions to cardiac cycle, such as with the Circulator Boot, has not been shown to be clinically important at this point in time.

This review suggests that long term EMS or NMES can positively affect clinical parameters of symptomatic peripheral arterial disease. It remains to be seen how effective long term NMES is for treating symptomatic intermittent claudication, and if this is equivalent to supervised exercise training, or a useful adjunct. NMES may have additional benefits over exercise alone. There is evidence in animal models that changes in muscle stimulation can affect muscle fibre differentiation, although this has not been replicated in adult humans [40]. Nerve cross-union experiments have shown the ability of fast and slow twitch muscles to change their contraction times and metabolic activity, according to changes in innervation [40, 41]. Forst et al. showed a positive effect on diabetic microvascular disease, with NMES able to increase foot temperature, but this was blunted in cases of peripheral neuropathy [42]. High level evidence will only be provided by an adequately powered comparative clinical trial.

The evidence presented here suggests that IPC reduces pain and increases limb salvage in critical limb ischaemia, and that this would be directly applicable to the clinical management of these patients were revascularisation is not possible.

Electrical stimulation devices have evolved significantly since their initial introduction as a simple pair of electrodes attached to a generator box, with significant safety concerns – they had been known to cause burns at the interface site, or explode in the operating theatre [43]. They are decreasing in size and cost, some are portable and do not interfere with mobilisation. The duration and length of NMES protocol remains contentious, with some advocating three 20 min stimulation sessions per day, others 1 h continuous stimulation per day. However, results in these small studies do appear to be both beneficial and similar [44]. There is no general

consensus as to an ideal protocol, which may be best explored in a combination of laboratory and clinical trials.

TENS machines have been used in the management of pain, and are thought to work through a gating mechanism, effectively switching off downstream pain signals by providing an alternative stimulus. This can be used in the treatment of pain symptoms of any cause, and do appear to be effective in the short-term treatment of ischaemic pain. Conclusions beyond this are not supported by the literature.

There is little evidence to support the use of galvanic stimulation in this patient cohort.

7 Conclusion

There are many devices that are clinically relevant to the vascular specialist managing patients with peripheral arterial disease. A working knowledge of available devices, especially IPC and NMES, expands the range of therapies available for management of symptomatic disease, and may be of special benefit to those with limited exercise capacity. The use of IPC in non-reconstructable critical limb ischaemia is particularly useful for limb salvage.

Medical devices for the assistance in management of all forms of PAD are emerging as important non-invasive tools. If they are to cement their roles in this management strategy, more robust research in the form of randomised controlled studies will be required to add to their evidence base.

Declarations of Interest None declared

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