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CONTEXT AND POLICY ISSUES:

Peripheral vascular disorders encompass a group of diseases that affect the blood vessels of the lower extremities, such as chronic venous insufficiency (CVI) and peripheral arterial disease (PAD). CVI can result from valvular incompetence/obstruction or deep vein thrombosis (DVT). Clinical manifestations include pain, edema, skin changes, venous ulceration, and the potential for acute DVT or pulmonary embolism (PE). PAD is a common, but underdiagnosed and undertreated, disorder associated with tobacco use, renal insufficiency, diabetes mellitus, hypertension, and hypercholesteremia. Clinical features include pain, intermittent claudication (i.e., pain on walking due to exercise-induced ischemia), arterial ulceration and most seriously, critical limb ischemia. Both CVI and PAD are associated with advancing age and comorbidities and are significant causes of morbidity and mortality.

Intermittent pneumatic compression (IPC) devices have been proposed for the treatment of CVI and PAD, namely for the prevention of DVT. IPC devices work by applying high pressure to the lower limbs in a synchronized manner via garments consisting of a sleeve or compression cuff containing one or more air bladders. In general, the garment(s) fit over the foot, the calf, or the calf and thigh and are connected via tubing to an air pump which intermittently inflates and deflates the air bladder according to preset specifications. In turn, the limbs are compressed and released; the inflation cycle aids venous return and the deflation cycle allows time for the veins to refill. Alternative therapies for these disorders are elevation of the affected limbs above heart level, exercise, graduated compression stockings, compression dressings for leg ulcers, pharmacologic therapy (including thromboprophylaxis for DVT or PE), and surgery.
The ArtAssist® (ACI Medical Inc., San Marcos, CA) is an IPC device indicated as adjunctive therapy for patients with ischemic disease of the lower limbs. Although it was developed as an arterial assist device, its use has expanded to ambulatory patients who suffer from CVI. It is contraindicated in patients with infected limbs, suspected DVT or arterial clots, inflammatory phlebitis or PE, or when increased venous and lymphatic return is undesirable (e.g., congestive heart failure). The device is portable and can be used by the patient in a home setting without the assistance of medical personnel. The ArtAssist® is factory pre-set to deliver 120 mmHg of pressure over a three second compression and 17 second non-compression cycle; the only setting that can be adjusted outside the factory is the amount of pressure which should only be done by a clinician. It is recommended that the device be used for one hour intervals, three to four times daily.

Due to our aging population and increasing prevalence of these disorders, there is a need to review the evidence supporting efficacy and harms of IPC devices. With a focus on the ArtAssist® device, this report will review the current evidence for clinical and cost-effectiveness of IPC therapy and current guidelines for use in the treatment of CVI and PAD, when used in non-surgical patients and in a non-hospitalized setting. The use of IPC therapy as a mechanical adjunct for thromboprophylaxis in surgical or trauma patients, post-thrombotic syndrome, or lymphedema is beyond the scope of this report. This report also updates and expands on information provided in a previous HTIS reference list on the same topic dated October 6, 2008.

RESEARCH QUESTIONS:

1. What is the clinical effectiveness of pneumatic compression devices for treatment of patients with peripheral vascular disorders?

2. What is the cost-effectiveness of pneumatic compression devices for treatment of patients with peripheral vascular disorders?

3. What are the guidelines for use of pneumatic compression devices for patients with peripheral vascular disorders, including treatment time?

METHODS:

A limited literature search was conducted on key health technology assessment resources, including PubMed, The Cochrane Library (Issue 4, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international HTA agencies, and a focused Internet search. Results include articles published between 2003 and November 2008, and are limited to English language publications only. No filters were applied to limit the retrieval by study type. The systematic reviews and randomized controlled trials (RCTs) included in this report were not limited by the type of IPC device; however, the included observational studies were limited to only those that specifically investigated the ArtAssist® device.

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews and meta-analyses are presented first. These are followed by RCTs, observational studies, economic evaluations, and evidence-based guidelines.
SUMMARY OF FINDINGS:

The literature search identified two systematic reviews, five RCTs, two observational studies, and four relevant guidelines. No health technology assessments or economic evaluations were identified.

Health technology assessments

No health technology assessments that specifically examined the non-surgical use of IPC were identified.

Systematic reviews and meta-analyses

A systematic review by Nelson et al. (2008)\(^\text{10}\) investigated whether IPC increases the healing of venous leg ulcers and impacts on health-related quality of life in patients of any age and level of mobility with venous leg ulcers. The intervention group included any type of IPC applied to the leg (e.g., below knee or thigh length, single or multicompartiment devices) irrespective of the duration or frequency of treatment. Control groups included sham IPC or no IPC (standard care). Studies comparing IPC treatment regimens were also included. A total of seven RCTs in 367 patients with venous insufficiency, irrespective of method of diagnosis, were included. Only one included trial reported both allocation concealment and blinded outcome assessment. In one trial (n=80) more ulcers healed with IPC than with no compression and dressings alone (62% vs 28%; P=0.002). Four trials compared IPC with compression against compression alone. The first of these trials (n=45) found increased ulcer healing with IPC plus compression compared to compression alone [relative risk (RR) for healing: 11.4 (95% CI: 1.6, 82)]. The remaining three trials (n=122) found no evidence of a benefit for IPC plus compression compared with compression alone. One small trial (n=16) found no difference between IPC (without additional compression) and compression bandages alone. One trial compared different methods of delivering IPC (n=104) and found that rapid IPC healed more ulcers than slow IPC (86% vs 61%; log rank P=0.003). The systematic review was limited by the small size and methodological shortcomings of included trials as well as the different types, frequency, and duration of IPC delivered. It was concluded that IPC may increase healing of venous leg ulcers compared with no compression, but that it is not clear if IPC increases healing when added to treatment with compression bandages/hosiery, or if it can be used instead of compression bandages/hosiery. Due to the limited data available, no conclusions were made regarding an impact of IPC on health-related quality of life in these patients.

Berliner et al. (2003), \(^\text{11}\) conducted a systematic review of the use of IPC for the treatment of CVI and venous ulcers on behalf of the US Centers for Medicare and Medicaid as part of a reconsideration of coverage policy. Studies were included if they investigated treatment with IPC as major therapy (not as an adjunct to surgery) in patients with CVI of the lower extremities or leg ulcer, used a compression pump (none were the ArtAssist®) in the home setting, and reported outcomes of reduction of edema or ulcer healing rate. Eight trials (n=431), four of which were RCTs and the remainder clinical controlled or cohort trials, were included. Most studies were small and may have been underpowered. Three studies supported that IPC could alleviate symptoms of CVI and the remainder either showed no difference or did not report statistical comparisons. No studies directly measured whether the devices could prevent recurrence of venous ulcers. Overall, the results among trials were conflicting and it was concluded that the available data cannot be relied upon to inform the optimal choice of compression therapy or the optimal protocol for patients with these conditions. Following consideration of these results, the Centers for Medicare and Medicaid decided that IPC will only...
be covered for patients with refractory edema with significant ulceration of the lower extremities after a 6-month trial of standard therapies, such as compression stockings, has failed.

**Randomized controlled trials**

Delis *et al.* (2005) evaluated the effects of IPC applied to the foot and calf (IPC<sub>foot+calf</sub>) on walking ability, peripheral hemodynamics, and quality of life in 41 patients with stable arterial claudication. Patients (57-82 years of age) were randomly assigned to receive IPC<sub>foot+calf</sub> delivered using the ArtAssist® AA-1000 and 75 mg/day aspirin or 75 mg/day aspirin alone in conjunction with unsupervised exercise. Outcomes assessed included initial (ICD) and absolute (ACD) walking distances on treadmill testing, resting (r-ABI) and post-exercise (p-eABI) ankle brachial indices, arterial calf inflow (Q), and quality of life at baseline, 1, 2, 3, 4, and 5 months. The ICD is the distance at which the patient feels pain or discomfort in the legs and the ACD is the distance at which the patient stops walking because the pain or discomfort becomes severe.

At five months, patients using IPC<sub>foot+calf</sub> returned the devices and continued with aspirin alone and were again assessed at 17 months (12 months post-treatment). At five months, ICD, ACD, r-ABI and p-eABI had increased from baseline by 197%, 212%, 17% and 64%, respectively, in patients receiving IPC<sub>foot+calf</sub> and aspirin (P<0.001), but little had changed in patients receiving aspirin alone (P>0.1). When the two groups were compared, IPC<sub>foot+calf</sub> and aspirin treated patients had improved ICD, ACD, r-ABI and p-eABI compared to patients treated with aspirin alone (P<0.01). Inter- and intragroup popliteal artery flow differences were small (P>0.1). Quality of life measured by the SF-36 questionnaire at five months improved significantly from baseline with IPC<sub>foot+calf</sub> and aspirin (P<0.001) but not with aspirin alone, and was also improved significantly with IPC<sub>foot+calf</sub> and aspirin compared to aspirin alone (P<0.01). IPC<sub>foot+calf</sub> was well tolerated and complication-free and compliance (>2.5 h/day) was >85% at three and five months. When patients who received IPC<sub>foot+calf</sub> were assessed 12 months post-treatment, ICD, ACD, r-ABI and p-eABI were not different from that at the end of active treatment. The authors concluded that IPC<sub>foot+calf</sub> improved walking ability and pressure indices in stable claudication with a durable outcome that was also associated with improvement in quality of life. Despite some limited benefit noted in some patients, unsupervised exercise had a nonsignificant impact.

The above study has been criticized for being small, unblinded, and lacking an appropriate placebo comparison group. Given that IPC is a mechanical therapy, blinding of patients is not practical, but no attempt was made to blind those administering the treadmill tests. It was also noted that the control group in the study had no change in walking distances from baseline whereas in large placebo-controlled, double-blind studies of pharmacologic therapy for intermittent claudication, a substantial placebo effect (i.e., increase in maximal walking distance) has previously been observed.

Kakkos *et al.* (2005) compared the effects of unsupervised exercise, supervised exercise, and IPC<sub>foot+calf</sub> on ICD, ACD, r-ABI, resting hyperaemic calf arterial inflow, and quality of life in 34 patients with stable intermittent claudication. Patients (mean age 66.5 years) were randomized to IPC<sub>foot+calf</sub> (n=13 at 3 h/day for six months using the ArtAssist® AA-1000), supervised exercise (n=12 at 3 h sessions/week for six months), or unsupervised exercise (n=9). Outcomes were assessed before and six weeks, six months, and one year after randomization. Quality of life was assessed using the SF-36 questionnaire, the walking impairment questionnaire (WIQ), and intermittent claudication questionnaire (ICQ). Compared to baseline, both IPC<sub>foot+calf</sub> and supervised exercise increased ICD and ACD up to 2.83 times (P<0.05) whereas there was no change in the unsupervised exercise group. Compared with unsupervised exercise, both IPC<sub>foot+calf</sub> and supervised exercise significantly increased ACD at six months (P<0.05). IPC<sub>foot+calf</sub> increased resting arterial inflow by 28% at six weeks (P<0.05) while supervised exercise...
resulted in a decrease. \( \text{IPC}_{\text{foot+ calf}} \) decreased the reactive hyperaemic flow rate at six weeks and six months (P<0.05), while exercise had no effect. Supervised exercise decreased arterial inflow and increased r-ABI (P<0.05 at six months) and although an increase was observed in the \( \text{IPC}_{\text{foot+ calf}} \) group, it did not reach statistical significance. Unsupervised exercise had no effect on arterial inflow or r-ABPI. Significant improvements in the physical health domain of the SF-36 were observed in the \( \text{IPC}_{\text{foot+ calf}} \) group for role-physical and general health scores at 12 months only, although a significant improvement in walking speed score at six months was observed with the WIQ. The clinical effectiveness of supervised exercise and \( \text{IPC}_{\text{foot+ calf}} \) appeared to be largely preserved after one year. Similar to the previous study,\(^1\) this study was small, unblinded, and outcomes in control patients (unsupervised exercise) did not practically change from baseline. The study is also compromised by a high patient withdrawal rate (24%). Compliance in the \( \text{IPC}_{\text{foot+ calf}} \) group ranged from 7 to 70% (median 35%) of the expected use (548 h) and attendance rates for supervised exercise ranged from 12.8 to 100% (median 60.3%) of expected attendance (72 days). It was concluded that the improvement in walking distance with \( \text{IPC}_{\text{foot+ calf}} \) was comparable with supervised exercise.

Ramaswami \textit{et al.} \((2005)^{15}\) conducted an open-label pilot study to investigate \( \text{IPC}_{\text{foot+ calf}} \) in 30 male patients (mean age 70.7 years) with stable intermittent claudication. Patients (n=15 each) were randomized to \( \text{IPC}_{\text{foot+ calf}} \) using the ArtAssist\textsuperscript{®} device for one hour twice daily and advised to exercise, or to the control group, which was advised exercise alone. All patients received aspirin and were followed up at 1, 2, 3, 4, 6, and 12 months at which times ICD, ACD and ABI were measured. The percent change from baseline (mean ± SD) for ICD/ACD in the control group was 2.2 ± 18/2.3 ±18.5 at four months, 2.9 ± 17.5/5.2 ± 20.2 at six months, and 3.6 ± 18.3/5.8 ± 20.4 at 12 months. Corresponding changes in the \( \text{IPC}_{\text{foot+ calf}} \) group were 137.1 ± 128.0/84.3 ± 81.7 at four months, 140.6 ± 127.0/96.4 ± 105.7 at six months, and 150.8 ± 123.7/101.2 ± 103.7 at 12 months (all P<0.001 for difference between treatment and controls). Although ABI increased in the treatment group, it did not reach statistical significance compared with baseline. The study was compromised by a high drop-out rate (63% by 12 months). The authors conducted an analysis of walking distance data at six months in patients in the treated group that dropped out, which found that the patients were overachievers with a 298% (ICD) and 229% (ACD) increase from baseline, thus it was assumed that these patients did not feel the need to attend further follow-up. Dropouts from the control group showed either no improvement or slight deterioration from baseline. It was concluded that \( \text{IPC}_{\text{foot+ calf}} \) improves walking distance in patients with stable intermittent claudication, with significant increases in ICD and ACD at four and six months of treatment with improvement sustained at one year.

Grieveson \textit{et al.} \((2003)^{16}\) evaluated the effects of different combinations of IPC pump settings on ankle edema using the Flowpac pump by Huntleigh Healthcare Ltd. among 27 patients with CVI. Patients (22-96 years of age) were randomly assigned to treatment with IPC or control (i.e., elevation of both lower limbs for 45 minutes). IPC was administered in three stages during which pressure settings, inflation, and deflation times varied. The average difference in limb volumes (calculated on the basis of four measurements and leg circumference) for each pump setting was compared to changes in limb volume in the control group. The highest mean reduction in limb volumes was recorded for a pressure of 40 mmHg (P=0.02), 10 second deflation time (P=0.0002), and 15 second inflation time (P=0.0096). Other statistically significant results were obtained at different pressures or inflation/deflation times; however, for the majority (84%) of setting combinations, no significant differences were observed between the intervention and control groups. IPC was well tolerated and patients felt more comfortable after treatment with the exception of the 60 and 70 mmHg inflation pressures. Limitations of the study are its small size, unblinded design, and the use of a specific IPC pump as other pumps may have a different range of settings. It is also possible that the optimum combination of settings may have been missed as this study only explored 43 of 1805 possible pump settings. The
majority of patients were physically disabled (i.e., 67% required a wheelchair for mobility). Overall, it was concluded that lower pressures together with shorter inflation/deflation times appears to be more efficient than higher pressures and long inflation/deflation times with no significant further reductions in edema at pressures > 40 mmHg.

An abstract for a RCT by Louridas (2006) was identified on the ArtAssist® website. The study was a randomized, placebo-controlled, single-blind study in 84 patients with critical limb ischemia (99 ischemic limbs) and non-reconstructable vessels. Of these, 28 patients had renal failure (34 ischemic limbs). The experimental group received IPC to the foot, calf, and ankle via the ArtAssist® (120 mmHg of pressure) whereas the control group used a placebo device that delivered low pressure (20 mmHg) slowly over the inflation time. The devices were self-applied by the patients at home for one hour, three times a day. Patients were followed for 24 months and assessed using toe pressures, ABI, and transcutaneous oxygen pressures (TcPO₂) in both supine and sitting (dependant) positions. Results indicated that non-renal failure patients in the experimental group had a limb salvage rate of 86% compared with 32% in the control group (P=0.014). In patients with renal failure, the limb salvage rates were 67% in the experimental group and 30% in the control group (P=0.54). It was concluded that IPC significantly improves the limb salvage rate in non-renal failure patients with non-reconstructable chronic, critical limb ischemia. Limbs with TcPO₂ values that increased at least 15 mmHg from supine to sitting had the best prognosis for limb salvage. This summary reflects the extent of information available as it does not appear that this RCT has been published in the peer-reviewed medical literature to date.

Observational studies

Delis and Knaggs (2005) carried out a prospective, cross-sectional study to determine the duration and amplitude decay of acute arterial leg inflow enhancement with IPC delivered to the foot, calf, and both combined, in the sitting position in patients with intermittent claudication compared with healthy controls. The findings were cross-correlated with the features of three implicated physiologic mechanisms: 1) increase in the arteriovenous pressure gradient, 2) suspension of peripheral sympathetic autoregulation, and 3) enhanced release of nitric oxide with flow and shear-stress increase. A total of 24 patients with claudication (26 limbs) with superficial femoral artery occlusion or stenosis (>75%) and 20 healthy controls (24 limbs) matched for age and sex had their popliteal volume flow and pulsating index (peak-to-peak velocity/mean velocity) measured with duplex scanning at rest and upon delivery of IPC. The three IPC methods were applied according to a crossover design using the ArtAssist® device.

Results demonstrated that the median duration of flow enhancement in patients with claudication exceeded 50 seconds with IPCfoot, IPCcalf, and IPCfoot+calf but was shorter (32.5 to 40 seconds) in the controls (P < 0.001). Among the three IPC modes, the duration of flow enhancement differed (P < 0.05) only between IPCfoot and IPCfoot+calf. After reaching its peak within five seconds of IPC, flow enhancement declined thereafter. The percentage rates of volume flow decay (determined at nine consecutive time segments lasting five seconds each) demonstrated a significant declining ‘trend over time’ (P<0.05). Baseline and peak flow with all IPC modes was similar between the two groups. Pulsatility index attenuation (an estimate of peripheral resistance) in claudicating limbs lasted a median 32.5 seconds with IPCfoot, 37.5 seconds with IPCcalf, and 40 seconds with IPCfoot+calf. The duration of pulsatility index attenuation was shorter in the control limbs, but differences were not significant. In addition, there were no significant differences among the three IPC modes. It was concluded that following IPC, leg inflow enhancement was longer in patients with claudication than controls. It was also concluded that the data support that all implicated physiologic mechanisms (1, 2, and 3) are likely active immediately after IPC delivery (0 to 20 sec) and all but nitric oxide are
effective in the mid time period (20 to 35 seconds). As the pulsatility index has returned to baseline, the late phase of flow enhancement (35 to 50 seconds) could be attributable to the declining arteriovenous pressure gradient alone.

Labropoulous et al. (2005)\textsuperscript{19} conducted a prospective case-series study to measure the hemodynamic effects of IPC in the systemic, muscular, and collateral circulation as well as in the foot skin blood flow in patients with critical limb ischemia. The limbs of 20 patients (20 limbs; mean age 74 years) were evaluated with duplex ultrasound or laser Doppler fluxmetry in the semi-erect position before, during, and after IPC delivered using the ArtAssist® device. One pneumatic cuff was applied on the foot and the other on the calf. Fourteen limbs were characterized as inoperable, and six were considered marginal for reconstruction. Flow volumes were measured in the popliteal, medial gastrocnemial, and a genicular collateral artery. Skin blood flux was measured on the dorsum of the foot at the same time. Results demonstrated significant flow increases during IPC in all three arteries (18/20 limbs) compared with baseline values (P <0.02). The highest change was seen in the popliteal, followed by the gastrocnemial and the collateral arteries. After the cessation of IPC, the flow returned to baseline. This was attributed to the elevation of time average velocity, as the diameter of the arteries remained unchanged. The skin blood flux increased significantly as well (P <0.03). In the two limbs without an increase in the arterial or skin blood flow, significant popliteal vein reflux was found. Both limbs were amputated shortly after. All patients tolerated the IPC well with the exception of one that could not tolerate the foot component of the pump due to severe pain. It was concluded that IPC increases axial, muscular, collateral, and skin blood flow in patients with critical limb ischemia and may be beneficial to those who are not candidates for revascularization. Patients with significant venous reflux may not benefit from IPC. This supports the theory that one of the mechanisms by which IPC enhances flow is by increasing the arteriovenous pressure gradient.

The two studies above are limited by their non-randomized and unblinded designs. Due to lack of a control group in the study by Labropoulous et al., it is not possible to know if the observed results were due to the device and not placebo effects. In neither study was the effect of patient position during the test analyzed to see what extent of improvement was due to position. In addition, neither study reported clinical outcomes, nor included any patient follow-up to assess the clinical impact of the observed hemodynamic responses attributed to IPC treatment.

**Economic evaluations**

No economic evaluations of IPC devices in any patient group were identified.

The ArtAssist® device is available for purchase directly from the manufacturer at a cost of US$4,800 for the single limb type and US$4,900 for the two limb (bilateral) type.\textsuperscript{20} The device can also be rented at a cost of US$1,200 for a 3-month rental plan and then US$400 monthly thereafter. A monthly rental plan is also available to US residents only.

Cost-effectiveness of the ArtAssist® device was considered in two of the included RCTs.\textsuperscript{12,14} In the study by Kakkos et al. (2005),\textsuperscript{14} the cost of a six month exercise course per patient was estimated to be £1000. The rental cost of the IPC device for the same period of time was £1263. The authors calculated (data not shown) that the improved results in the IPC group at six months favours IPC at a cost per metre of walking distance gained to be approximately £5 compared to £13 in the patients allocated to supervised exercise. Delis et al. (2005)\textsuperscript{12} suggest that an IPC foot+calf unit at a cost of $4,900 could be used by four patients with claudications annually over a number of years, assuming three months of treatment per patient and equipment serviceability, thus offering effective treatment at small fraction of the minimal cost of a treatment strategy involving bypass surgery and balloon angioplasty.
Guidelines

In 2008, the Australia and New Zealand Working Party on Prevention of VTE issued updated guidelines on VTE prophylaxis in both surgical and medical patients. The Working Party was comprised of surgeons, vascular surgeons, hematologists, internists, and general physicians. Recommendations were based on the International Union of Angiology and American College of Chest Physicians (ACCP) consensus statements adapted to Australian and New Zealand conditions. In clinical situations where the literature provided little information, recommendations were based on expert judgment and experience. The guidelines recommend that in high-risk medical patients with no contraindications to mechanical prophylaxis (e.g., severe PAD, recent skin graft, severe peripheral neuropathy, severe leg deformity), graduated compression stockings (GCS) or IPC should be considered. In low-risk medical patients with no contraindications, GCS or IPC should be considered if there are additional risk factors (e.g., immobility, thrombophilia, estrogen therapy, pregnancy or puerperium and strong family history of VTE and/or obesity).

In 2008, the International Compression Club, an ad hoc group of clinicians involved in the management of patients with venous diseases and technical specialists from companies manufacturing IPC devices issued a consensus statement on the indications for compression therapy in venous and lymphatic disease. In developing the statement, the group reviewed the published medical literature and their own collections to identify experimental findings concerning clinically relevant effects of compression therapy and RCTs of compression used for various clinical indications. The strength of the recommendations from RCTs was based on the scoring criteria from the international GRADE group. For IPC, the present level of evidence for its use in ulcer healing was determined to be weak; however, strong levels of evidence support use of IPC for thrombosis prevention after surgery and in the treatment of post-thrombotic syndrome and lymphedema.

The Wound, Ostomy and Continence Nurses Society (WOCN) issued an updated guideline (2008) for the management of wounds in patients with lower extremity arterial disease. Guideline development involved review of the published literature and weighting of the strength of the evidence according to a rating scheme. The guidelines recommend that arterial flow augmentation (IPC) should be considered as adjunctive therapy for individuals with intermittent claudication and limb-threatening arterial disease for whom vascular reconstruction is not feasible.

In 2004, guidelines for the prevention of VTE were developed under the auspices of the 7th American College of Chest Physicians (ACCP) Conference on Antithrombotic and Thrombolytic Therapy. Guideline development was according to the ACCP model for developing evidence-based guidelines and included grading the level of evidence for each recommendation. Although the guidelines consider both surgical and medical patients, a general recommendation was made pertaining to mechanical prophylaxis. The guidelines recommend that mechanical methods of prophylaxis such as IPC be used primarily in patients who are at high risk of bleeding, or as an adjunct to anticoagulant-based prophylaxis. It is further recommended that careful attention be directed toward ensuring the proper use of, and optimal compliance with, the mechanical device.

Limitations

Only two systematic reviews evaluating IPC for CVI or venous ulcers and none evaluating IPC for PAD or intermittent claudication were identified. In the systematic reviews that examined IPC use in CVI or venous ulcers, the numbers of included studies were few and of small size and
low methodological quality (i.e., unblinded, single-centre, allocation concealment unclear or not used, etc.). Furthermore, included studies were conducted in a wide range of patient groups and differed in the type, frequency, and duration of IPC delivered, which does not allow the results to be easily compared, nor make the results generalizable to any specific patient group. Tolerability or compliance with the recommended IPC regimen was not considered as an outcome in any of the systematic reviews.

The RCTs identified also suffer from similar limitations as the systematic reviews. In contrast to the systematic reviews, three of the five RCTs were conducted in patients with intermittent claudication, whereas the other two included patients with CVI and critical limb ischemia, respectively. As a whole, the RCTs are limited by small size, short duration, low methodological quality, and the lack of reporting of meaningful clinical endpoints such as rates of DVT or PE. The only report of limb salvage was from an unpublished abstract on the ArtAssist® website of a RCT in patients with critical limb ischemia; however, detailed information about the study design and results were lacking. Generally, studies did not report any harms data and only two studies reported on compliance with the IPC device.

The identified observational studies were limited by their non-randomized and unblinded designs and lack of a control group in one study. Neither study reported clinical outcomes, nor included any patient follow-up to assess the clinical impact of the observed hemodynamic responses that were attributed to IPC treatment.

The timeline for the literature search for this report encompassed only the last five years. As a result, there may be some studies and systematic reviews of IPC published in the 1990s that are not included in this report.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

The available evidence in support of the clinical effectiveness of IPC therapy in CVI and PAD is inconclusive. Overall, the evidence is limited by the small size, short duration, and low methodological quality of studies that have examined this technology. No head-to-head comparison of IPC therapy with another active treatment (e.g., graduated compression stockings) was identified.

Although there is literature evidence to support a benefit of IPC compared to no compression, there is no evidence that IPC is superior to other methods of applying compression for treating CVI and its complications. There is evidence to support that IPC therapy produces similar improvements in walking distance as supervised exercise in patients with intermittent claudication and perhaps may be superior to unsupervised exercise in this setting. A recent systematic review of exercise for intermittent claudication by Watson et al. (2008) found that exercise programs were of significant benefit compared with placebo or usual care in improving walking time and distance in these patients. This systematic review included only one trial [Kakkos et al. (2005)] that compared IPC and exercise so no conclusions were drawn on the relative effectiveness of IPC compared to exercise.

None of the included studies in this HTIS review reported an impact of IPC therapy on hard clinical outcomes (e.g., reduction in rates of DVT, PE, or amputation). Only one unpublished abstract of a RCT in patients with critical limb ischemia reported a significant effect of IPC in improving limb salvage rate in patients without renal failure; however, caution is warranted in the interpretation of these data due to the lack of study details.
No health technology assessments or cost-effectiveness studies were identified. As a result, no information is available to assess whether or not IPC is cost-effective compared to other treatment alternatives (e.g., graduated compression stockings, exercise, pharmacologic therapy or surgery).

No studies or guidelines addressed the optimal length of IPC therapy. Active IPC treatment in included studies ranged from five to 12 months. Comments on cost-effectiveness in two studies were based on the assumption of three to six months of IPC therapy.

Advantages to IPC therapy are that it can be self-administered in the patient’s home without need for medical personnel. It is portable and can be initiated at a time that is most convenient for the patient. Nonetheless, one must consider that IPC therapy requires that the patient sit for three or four one hour sessions every day.

In order to better inform decision or policy making pertaining to IPC devices such as the ArtAssist®, well-designed RCTs and economic evaluations that directly compare IPC with other active treatment alternatives are needed to provide compelling evidence of the clinical and cost-effectiveness of this technology for the management of CVI, PAD and their related sequelae.

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APPENDIX 1: Coverage Policies for IPC Devices in the United States

The search of the grey literature for this review identified a number of US payors that provide reimbursement for IPC devices. Specific policies and criteria for coverage of IPC therapy can be found at the websites indicated below.

A. **Aetna**


B. **Blue Cross BlueShield of Alabama**


C. **Centers for Medicare and Medicaid Services**


D. **CIGNA**


E. **Empire BlueCross BlueShield**


F. **Excellus Health Plan**


G. **Oxford Health Plans**


H. **Regence Group**