Title: High-Intensity Interval Training as an Exercise Intervention for Intermittent Claudication, A Systematic Review.

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Abstract

Background and Objectives: Intermittent claudication (IC) is the most common symptom of peripheral arterial disease, which significantly affects walking ability, functional capacity and quality of life. Supervised exercise programmes (SEP) are recommended as first line treatment, but recruitment and adherence rates are poor. The time required to complete a SEP is the most common barrier to participation cited by patients who decline. High-intensity interval training (HIIT) is more time efficient than current SEP's and therefore has the potential to overcome this barrier.

We conducted a systematic review to appraise the evidence for HIIT programmes for IC.

Data Sources and Review Methods: MEDLINE, Embase and CENTRAL databases were searched for terms related to HIIT and IC. Randomised and non-randomised trials that investigated HIIT for the treatment of IC were included, with no exclusions based on exercise modality, protocol or use of a comparator arm. Outcome measures were walking distances, peak oxygen uptake, recruitment and adherence rates and quality of life. Risk of bias was assessed using the Cochrane tool and study quality using a modified PEDro scale.

Results: 9 articles reporting 8 studies were included in the review. HIIT appears to improve walking distances and oxygen uptake in relation to controls, with improvements attainable in just 6 weeks. When HIIT was compared to low-intensity exercise, it appeared that longer low-intensity programmes were required to obtain similar benefits to those from short-term HIIT.

Conclusion: Initial evidence suggests that HIIT may provide benefits for IC patients. initially, pilot studies of low-volume, short-term HIIT versus usual SEP's are required. This will allow for larger randomised controlled trials to be appropriately designed and adequately powered to further explore the potential benefits of HIIT in IC.

Key Words: High-intensity interval training, peripheral arterial disease, intermittent claudication, exercise.

Introduction

Peripheral arterial disease (PAD) occurs when arteriosclerosis reduces the blood supply to the lower limbs[1]. PAD is common with global prevalence estimates of 10-20% in the population > 70 years[2]. Intermittent claudication (IC), the most common symptom of PAD, is a reproducible cramping, ischaemic muscle pain precipitated by exertion and relieved by rest[3, 4]. IC often significantly impairs walking ability, functional capacity and quality of life (QoL), and is associated with an increased mortality risk[3, 5-8].

In the UK, the National Institute of Health and Clinical Excellence (NICE) recommend cardiovascular risk management and a supervised exercise programme (SEP) as the first-line treatment for IC. The SEP should include a minimum of 2 hours / week of supervised exercise for a 12 week period, whereby patients are encouraged to walk to the point of maximal pain[9]. The evidence for SEP's for IC is conclusive. A recent Cochrane review clearly demonstrated significant improvements in both pain-free and maximum walking distances[10]. However, SEP design is relatively poorly reported which limits replication and guideline development[11]. Furthermore, SEP recruitment and completion rates vary, but can be as low as 30% and 75% respectively and only 42% of NHS vascular units have access to a SEP[12, 13]. Clearly, there is the need to develop a more universally acceptable SEP for IC.

High-intensity interval training (HIIT) results in similar or superior physical fitness benefits and is more time efficient than lower-intensity alternatives in both healthy and clinical populations e.g. coronary artery disease patients[14-19].

Therefore, the aim of this review is to appraise the current evidence base to assess the acceptability and efficacy of HIIT as a treatment modality for patients with IC. An additional aim of this review is to provide standards that could be adopted for future HIIT studies.

Methods

A systematic review, adopting the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[20], of randomised and non-randomised clinical trials assessing HIIT as a treatment for IC was performed.

Search Strategy

The search was conducted from database inception to February 2018 using the MEDLINE, Embase, and CENTRAL databases. Only full-text articles published in English and relating to adults (>18 years old) were included. Titles and abstracts were independently screened for inclusion by two reviewers (S.P. and J.P.) and any disagreement resolved by a third (A.E.H.). Full texts of any potentially eligible articles were then independently screened against the inclusion criteria. Reference lists of identified studies were also hand searched for other relevant papers. Search terms included “Intermittent claudication” [OR] “Peripheral Arterial Disease” [AND] “High intensity interval training” [OR] “HIIT” [OR] “High intensity exercise”, the full search strategy is shown in appendix 1.

Inclusion Criteria

We included both randomised and prospective non-randomised studies that investigated HIIT in patients diagnosed with IC (Fontaine II/Rutherford 1-3). Studies that included patients with asymptomatic PAD were excluded. Similar to a recent systematic review in the cardiac population, HIIT was defined as an interval approach conducted at ≥85% peak heart rate (HRPeak) or another surrogate measure (i.e. ≥80% maximal exercise capacity or peak oxygen uptake [VO_{2Peak}] or a rating of perceived exertion ≥15)[21]. There was no exclusion based on programme duration, frequency, protocol (i.e. ratio between length of exercise and rest periods) or the use of a comparator arm.

Data Extraction

Data extraction was performed using a standardised form and inputted into Microsoft Excel (Microsoft, 2010, Redmond, WA, USA). The data extraction included information on study characteristics (to assess quality), sample size, inclusion/exclusion criteria, intervention components, outcome measures and main findings. The primary outcome measure was maximum walking distance or time (MWD/T), and secondary measures included pain-free walking distance or time (PFWD/T), QoL, VO_{2Peak} and recruitment and adherence rates. For key outcome measures, such as walking distance and VO_{2Peak} (where reported appropriately), mean difference (MD) and between group effect sizes (ES) were calculated and adjusted for small sample-sizes using Hedges bias-correction [22]. These effect sizes were interpreted as small (≥0.20 - <0.50), moderate (≥0.50 - <0.80) and large (≥0.80) [23]. Where necessary, study authors were contacted for more information to allow computation of effect sizes.

Risk of Bias

Studies were independently assessed by two reviewers (S.P and J.P) using the Cochrane Collaboration tool [24]. This consists of three-grades; low, unclear or high risk of bias. Disagreement was resolved by discussion or by a third reviewer (A.E.H).

Quality Assessment

Quality assessment was conducted using a modified version of the Physiotherapy Evidence Database (PEDro) scale. The PEDro scale awards a score out of 10 based on criteria described elsewhere [25]. As supervision is considered a vital element of exercise programmes for IC this was added as an extra quality criterion as previously described [26], leading to a total score out of 11 [26, 27].

Results

Search Results

The search yielded a total of 2023 results. A total of nine articles [28-36], reporting eight studies, were ultimately included in this review as shown in figure 1.

Included Trials

Trails included compared outcomes between HIIT and a low-intensity SEP or between HIIT and an "unsupervised" control group who were medically managed and given exercise advice without any supervised exercise intervention.

Two studies compared HIIT with low-intensity exercise [31, 33], two included three arms and investigated two HIIT groups versus an unsupervised control group [28-30]. Of the remaining studies, one included high-intensity resistance training versus low-intensity resistance training versus an unsupervised control group [32], and the other three compared HIIT to an unsupervised control group [34-36]. Studies are summarised in table I.

The total number of recruited patients within the studies was 350. HIIT programmes varied widely between studies and included treadmill walking [31, 33, 34, 36], upper limb or lower limb cycling [28, 30], plantar flexion [35] or resistance training [32]. The frequency, intensity and duration of programmes also varied and were generally completed 2-3 times per week for 12 to 40 minutes per session, for a period of six weeks to six months. HIIT intensity also ranged from 80% to 100% of maximal workload achieved at baseline.

All but one study included walking distance as an outcome measure. However, reporting was not consistent with the expression of walking distance in either meters or seconds. Maximal distance was also measured via various testing methods including a graded treadmill protocol [31, 34-36], the incremental shuttle walk test [28, 30], or the six-minute walk test [32]. The one study that did not include walking measurements reported time-to-exhaustion from a treadmill test [33]. However, the authors did not state whether *exhaustion* constituted maximum claudication pain, therefore this study was not included in the analysis of walking distances. VO_{2Peak} was included in six studies and measured via graded [31, 34-36] or stepwise rank [33] treadmill tests, or a cycle ergometer [28, 30].

Generic and disease-specific QoL was reported in three studies [28, 29, 31], using a combination of the Medical Outcomes Study Short-Form 36 (SF-36) and the walking impairment questionnaire (WIQ).
Follow-up ranged from six to 72 weeks and intention-to-treat analysis was used in only one study [29, 30].

Quality assessment and risk of bias

Risk of bias summary is shown in figure 2 and study quality in table II. The mean score on the PEDro scale was 5.67 ± 1.41. In all studies there was a lack of allocation concealment, limited blinding of outcome assessors and patients and / or limited use of intention-to-treat analysis. Future studies could benefit from adopting bias reduction methods such as using a central allocation system and ensuring that outcome assessors are blinded to the allocated treatment groups. In addition, when these methods are adopted, it is imperative that they are appropriately reported.

Due to the limited number of studies, no publication bias assessment was made.

Walking Performance

Maximum walking distance or time (MWD/T)

Three trials reported MWD in meters [28, 30, 32] and three trials reported MWT in seconds [34-36]. The results suggest that all modes of exercise significantly improved MWD/T. Two trials reporting the effect of upper and lower limb HIIT on MWD demonstrated significant improvements from baseline (both p = <0.05) [28, 30], with one of these studies reporting that the changes were significantly greater than controls [30]. For two trials reporting treadmill HIIT, both demonstrated significant improvements in MWT (p = <0.05). The improvement reported by Helgerud *et al* (2009) was significantly greater than the unsupervised control group, with moderate ES (p = <0.05, MD = 200s, ES = 0.60) [34]. Wood *et al* (2006) demonstrated a 45% improvement but this did not reach statistical significance versus the unsupervised control group (p = 0.059, MD = 220s, ES = 0.31) [36]. Wang *et al* (2008) reported the effect of plantar flexion HIIT on MWT and demonstrated a significant improvement versus baseline (p = 0.009), which was also significantly greater than controls (p = <0.05, MD = 173s, ES = 0.53) [35]. Finally, Parmenter *et al* (2013) reported the effect of a resistance-based HIIT programme on MWD and demonstrated a significant improvement versus baseline (p = 0.05), which was also significantly greater than the control group (p = 0.009, MD = 69.8m, ES = 0.74) [32]. Full detail in table I.

Gardner *et al* (2005) reported the effect of a 6-month high versus low-intensity treadmill programme on MWD and showed that both groups had significant improvements in MWD (p

= <0.01), and the change was similar between groups (*p* = >0.05; MD = 14m, ES = 0.06, favours high intensity; table I) [31]. Parmenter *et al* (2013) also reported the effect of a high versus low-intensity resistance-based programme on MWD [32], with the HIIT group demonstrating a significant improvement (*p* = 0.05), whilst the lower intensity group had a reduction of -12% (between group MD = 68.7m, ES = 0.53, difference in change between groups *p* = 0.002) [32].

Pain free walking distance or time (PFWD/T)

Three trials reported PFWD in meters [28, 30, 32], and one trial reported PFWT in seconds [36]. The results from two trials suggest that both upper and lower limb HIIT significantly improve PFWD (both *p* = <0.01) [28, 30], with one study reporting that the change was significantly greater than an unsupervised control group. The remaining study reporting PFWD demonstrated a non-significant increase following resistance-based HIIT [32]. For the one study reporting PFWT following treadmill-based HIIT, there was a non-significant improvement following the exercise programme [36]. The two non-significant findings may have been affected by the small samples given that the effect sizes for each training group versus control were large (MD = 121.9m, ES = 1.32) and moderate (MD = 150s, ES = 0.60) respectively.

Two trials also reported PFWD for HIIT versus a low-intensity group (table I) [31, 32]. A six month resistance-based programme elicited a 77% improvement in the HIIT group and a 2% reduction in the low-intensity group. The improvement in the HIIT group was not significant, nor was it significantly greater than the low-intensity group. However, this may have been effected by the small samples as there was a moderate effect size (0.58, MD = 80.2) [32]. Finally, a six month treadmill programme elicited significant improvements in both groups (*p*

= <0.01), with the magnitude of change being similar between groups (*p* = >0.05, MD = 24m, ES = 0.18, favouring high-intensity).

Peak oxygen uptake (VO_{2peak})

Four studies reported the effect of a HIIT programme on VO_{2Peak} versus a control group (table I) [30, 34-36]. A six month upper or lower limb cycling HIIT training programme improved VO_{2Peak} compared to unsupervised controls (both *p* = <0.01), in both exercising groups [30]. An eight week plantar flexion HIIT programme resulted in a 12% increase in VO_{2Peak} (*p* = 0.002 versus baseline and <0.05 versus control, MD = 2.4 $ml \cdot kg^{-1} \cdot min^{-1}$;ES = 0.54) in the training group [35]. Two studies utilised a treadmill HIIT protocol with equivocal results. Following six weeks of HIIT treadmill training, there was a non-significant increase in VO_{2Peak} in the exercise group (*p* = 0.069), with a small ES (0.18, MD = 1 $ml \cdot kg^{-1} \cdot min^{-1}$) [36]. However, an eight week treadmill programme resulted in a significant (10%) improvement in VO_{2Peak} (*p* = <0.05 versus baseline and controls, MD = 2.8 $ml \cdot kg^{-1} \cdot min^{-1}$, ES = 0.59) [34].

Two studies also reported the effect of HIIT or low-intensity exercise on VO_{2Peak} (table I) [31, 33]. An eight week treadmill HIIT programme resulted in a significantly greater improvement in VO_{2Peak}, compared to the low-intensity group (16% versus 9%, *p* = <0.05). In contrast, a six month programme induced significant changes in VO_{2Peak} for both groups (*p* = <0.05), and the between-group change was similar (*p* = >0.05, MD = 0.2 $ml \cdot kg^{-1} \cdot min^{-1}$ ES = 0.05 favouring low-intensity).

Quality of life

Two studies of upper and lower limb cycling HIIT used the SF-36 questionnaire to assess QoL versus a control group [28-30]. Following a six week programme, there were significant improvements in physical functioning and role limitation physical domains (*p* = <0.05) for both exercise groups, with no changes occurring in the other six domains. There were also no changes in any domain in the control group [28]. Following 24 weeks of training, there was a significant mean difference in the upper limb cycling group versus the control group for the vitality, general health, physical functioning, bodily pain and mental health domains (p = <0.05), with no changes in the other 3 domains [29, 30]. Conversely, the lower limb cycling group only demonstrated a significant mean difference in relation to controls for the vitality and general health domains, with no changes in the other six domains. These significant mean differences were maintained at 72 week follow-up with the exception of the improvement in vitality scores in the lower limb group.

Zwierska *et al* (2005) also used the WIQ; with both exercise groups demonstrating significant improvement compared to the control group after 24 weeks in the domains of calf pain, walking speed and stair climbing. The upper limb group also demonstrated a significant improvement compared to controls in the domain of walking distance, which was not apparent in the lower limb group [29, 30]. These improvements were not maintained at 72 week follow-up in the lower limb group, but were maintained for stair climbing and walking distance domains in the upper limb group [29]. Full detail in table I.

Recruitment and adherence

One study reported the number of patients screened to allow for calculation of recruitment rate, which was approximately 20% [29]. Completion rates were mostly in the region of 80-90%, with one study reporting a slightly lower rate of 70% and two reporting 100%. Adherence rates were also reported in the majority of studies and were generally >90%. One study reported rates that were slightly lower at 74-80% [31], whilst one study reported that the participants in the exercise group completed all planned training sessions [35].

Effect of programme duration and modality

The HIIT programmes varied in duration between trials, ranging from 6 weeks to 6 months, providing differing levels of improvement.

Two six week programmes elicited improvements of between 61-122% and 32-50% in PFWD/PFWT and MWD/MWT respectively [28, 36]. Two 8 week HIIT trials reported improvements of ~15% in MWT but did not report PFWT [34, 35]. The remaining trials adopted six month programmes and elicited improvements of between 51-109% and 19-63% in PFWD/PFWT and MWD/MWT respectively[30-32].

Benefits were also obtainable from a number of modalities with improvements in PFWD/PFWT and MWD/MWT ranging from 57-93% and 31-50% following lower limb cycling respectively 51-122% and 29-47% following upper limb cycling respectively, 61-109% and 15-63% following treadmill walking respectively and 77% and 19% following resistance training respectively. Plantar flexion HIIT also resulted in a 16% improvement in MWT.

Discussion

Recent evidence supports the effectiveness of HIIT in a number of clinical populations [14-17]. This review aimed to appraise the evidence base for HIIT as a treatment option for IC and provide standards for future HIIT studies in this population. Although the evidence base was limited, these preliminary results show that HIIT improves a number of important outcomes in patients with IC including walking distances, VO_{2Peak} and QoL.

Improvements in walking distances

All studies that compared HIIT to a control group demonstrated significant improvements in MWD/T [28, 30, 32, 34-36], with changes occurring in as little as six weeks [28, 36]. In addition, the majority of studies demonstrated significantly greater improvements than the control group, with moderate between-group effect sizes [32, 34, 35]. Only two studies considered HIIT versus a low-intensity exercise group, however, one adopted a resistance only based programme, which is not routinely used for SEP's in the IC population [32]. The other study compared a 6 month high versus low-intensity walking programme, similar to that adopted in most SEP's, with both groups demonstrating similar improvements in walking distances [31].

These results perhaps demonstrate that although low-intensity programmes do elicit comparable changes in walking distance, the six month duration of the programme suggests this may be gradual and takes longer than a high-intensity course of exercise, which elicited improvements in just six weeks [31, 36]. However, no trial has considered the effect of shorter term HIIT and low-intensity exercise programmes.

A key benefit of HIIT, as these results demonstrate, is that it may be more time efficient, thus benefitting both patients (reducing the burden of attending sessions) and providers (cost reduction). These results suggest that HIIT can provide the same benefit to walking distances in half the amount of time currently recommended by UK guidelines [36].

Peak Oxygen Uptake (VO_{2peak})

VO_{2Peak} is considered to be the gold standard measure of cardiorespiratory fitness [37], and is a strong independent predictor of all-cause mortality [38, 39]. The results suggest that a HIIT programme can elicit significant improvements in VO_{2Peak}, that are also superior in comparison to controls [30, 34, 35]. One study however, did not reach statistical significance for the improvement VO_{2Peak} with a mean difference of 1 $ml \cdot kg^{-1} \cdot min^{-1}$ [36]. Although this mean difference appears small, it may still be clinically meaningful. In a cohort study of cardiac patients undergoing cardiac rehabilitation, each 1 $ml \cdot kg^{-1} \cdot min^{-1}$ increase in VO_{2Peak} was associated with a ~15% decrease in all-cause mortality, meaning that this relatively modest mean difference in VO_{2Peak} improvement may still provide a protective mortality effect for the HIIT group [40].

The studies that considered changes in VO_{2Peak} for HIIT versus low-intensity groups provided conflicting results [31, 33]. A short-term 8 week HIIT programme resulted in significantly greater improvements in VO_{2Peak} compared with the low-intensity programme[33]. Conversely the longer six month programme led to significant but similar benefits in both the HIIT and low-intensity groups [31]. As previously mentioned, the similar benefits obtained across both groups may have been obscured by the longer duration of the exercise programme. This lends us to believe that improvements in the HIIT group may have occurred much sooner but this was masked by the longer programme duration. This is evidenced by the fact that the lower intensity group were required to complete a longer duration of 3-5minutes per session, translating to an extra 9-15minutes per week and 4.6 hours over the course of the programme.

A recent meta-analysis in patients with coronary artery disease demonstrated that HIIT significantly improved VO_{2Peak}, with benefits being obtained in as little as four weeks [14]. Furthermore, a recent study considered an eight week intervention of two low-volume HIIT protocols (<30minutes a week) versus a moderate-intensity continuous exercise protocol (76minutes a week) for previously sedentary individuals [19]. The results showed that although all three groups demonstrated improvements in VO_{2Peak}, the HIIT protocols induced a 4-11% greater improvement, required 60% less time commitment and had a substantially lower drop-out rate compared with the moderate intensity group [19]. Similarly, in the study of Slørdahl *et al* (2005), included in this review, the HIIT group demonstrated a significant improvement in VO_{2Peak} with an exercise time of just 16minutes per 40minute session, and a programme duration of eight weeks [33].These studies suggest that shorter-term, low volume

HIIT protocols may be beneficial to induce improvements in VO_{2Peak}, thus again reducing patient burden and improving adherence. This needs to be evidenced in patients with PAD using randomised trials that consider shorter term, low volume HIIT programmes versus usual care exercise programmes.

Quality of Life

There was limited consideration of QoL amongst the included studies and was reported in just three. A six week upper or lower limb HIIT programme elicited significant improvement in the physical functioning and role limitation physical domains of the SF-36 [28], whereas a longer, 24 week programme elicited a greater improvement in relation to controls in the majority of the SF-36 and WIQ domains [29, 30]. Although this may suggest that longer HIIT programmes are more beneficial for improvements in QoL, a six month treadmill programme elicited more modest improvements, with significant changes only occurring in two SF-36 domains and one WIQ domain [31]. These equivocal results suggest that more research into the effects of HIIT on QoL would be beneficial in determining the true benefits of this exercise method. QoL should be included as an outcome measure in all future studies considering both HIIT and usual care SEP's for the treatment of IC, as a recent Cochrane review of exercise for IC noted that QoL was only reported in two of the 32 included studies [10].

Recruitment and adherence

Only one study reported recruitment rates, which were slightly lower than that previously reported at 20% [13, 29]. However, this may have been affected by the programme length of 6 months. Therefore, it is important that future trials report the number of patients who were screened, to allow for identification of recruitment rates.

However, completion rates were generally higher than the previously reported 75% for SEP's [13], with two studies reporting 100% completion rates in the exercise groups. In addition, adherence rates for exercise sessions were reported in all but one study and were generally >90%. Only one study, which compared HIIT with low-intensity exercise, reported rates that were lower than this, but there was no significant difference between the two groups [31]. It is also worth noting that the age of patients initially recruited and subsequently randomised to the HIIT or comparator groups was comparable to that previously reported for SEP's [10]. It is therefore unlikely that HIIT recruitment and adherence is influenced by age, nor is it preferred by a younger patient group.

Therefore, considering these completion and adherence rates, that are at least comparable to SEP's, it appears that HIIT is exceptionally well tolerated and acceptable in this population.

Future Directions

Although the results suggest that HIIT may provide improvements in walking distances, VO_{2Peak} and QoL, five of the eight included studies compared HIIT with either unsupervised exercise advice or a sedentary control group, whilst all HIIT groups were supervised. Given that SEP's are recommended as first line treatment in the UK and that intensity of supervision is related to improvements in walking distance, these groups may not provide a valid comparator [9, 41]. Considering the overwhelming evidence for SEP's it may be unsurprising that supervised HIIT is more beneficial than these comparator groups, suggesting that any exercise is better than none at all. In addition, there is a lack of standardisation with regards to the HIIT protocol, with varying modalities, intervals and intensities, though this is also the case for usual SEP's despite the substantial evidence base [11, 12]. The data suggests that benefits between different HIIT modalities are comparable, which is congruent with SEP's in the UK that adopt either aerobic exercise or aerobic exercise in combination with resistance training [12]. The data also suggests that short-term HIIT can provide comparable benefits to longer-term protocols, but the most effective protocol is currently unknown. We therefore recommend that future randomised controlled trials (RCTs) use the most pragmatic modality available and adopt short-term, low-volume HIIT at an appropriate intensity (i.e. ≥85% HRPeak) and tolerable interval (i.e. short work-to-rest ratio), in comparison to an appropriate control group (i.e. usual SEP's), to provide a homogenous evidence base which can identify whether HIIT can accrue superior benefits or if it is indeed more time-efficient. Although this future evidence may show that short-term, low-volume HIIT is more time-efficient, it is important to recognise that it will still require a significant time commitment for patients. However, it is much less burdensome than current SEP's and is therefore likely to be more attractive to patients, healthcare professionals, employers and insurance providers.

There is also a lack of long-term follow-up for patients undergoing any form of exercise for IC in the literature. It is important that these patients are followed-up for longer periods to demonstrate and support self-monitored compliance with a healthy, active lifestyle following the initial intervention. We therefore recommend that any exercise trial in the IC population, especially the aforementioned RCTs, adopt a longer-term follow-up in the protocol (i.e. 1 and 5 years).

Limitations

There are a number of limitations of this review that limit the conclusions that can be drawn from it. Firstly, most studies had unclear risk of bias for a number of criteria and also included small sample sizes, with one study recruiting only 13 patients. There was also considerable heterogeneity between studies with outcome measures differing between studies, especially with regards to walking distance which was recorded using both over ground and treadmill walking, whilst also being reported in different ways such as MWD or MWT. There is a need within the literature for a standardised protocol for testing and reporting walking distance in IC patients to allow for more comparable results. In addition, the intervention protocols differed vastly between studies, in terms of the frequency, intensity, duration and type of exercise that was undertaken, making it difficult to implement a HIIT exercise programme in a real-world setting based upon findings from the current literature.

Conclusion

On the basis of the evidence in this review, HIIT cannot yet be incorporated into exercise management protocols for IC and the authors recommend that where possible, usual SEP's continue to be provided. However, this review provides initial evidence to suggest that HIIT can elicit improvements in walking distances and VO_{2Peak} whilst also potentially improving QoL in patients with IC. In addition, the completion and adherence rates suggest that HIIT is tolerable and acceptable in this population. HIIT may also provide the same symptomatic benefit to patients in a shorter duration, limiting the burden for both the patient and the provider. The results also suggest that these benefits are obtainable across a variety of different exercise modalities.

At present however, there is insufficient evidence available to draw robust conclusions on the role of HIIT in IC patients due to the heterogeneity of the interventions and small sample sizes of the included studies. The heterogeneous data will also preclude accurate power calculations for future studies. Therefore, initial pilot RCTs comparing HIIT, designed based on our aforementioned recommendations, to usual SEP's, including physical and QoL outcome measures, with longer-term follow-up are required. This will then allow for future RCT's to be appropriately designed and adequately powered to further explore the potential benefits of HIIT protocols in the PAD population.

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