Arab Journal of Nutrition and Exercise

ISSN:2518-6590 Published on 31st August, 2017

High intensity interval training or moderate intensity continuous exercise in patients with myocardial infarction?

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A**bstract**

Objectives: To determine the effects of high intensity interval training (HIIT) or moderate intensity continuous exercise (MICE) in patients with myocardial infarction (MI).

Background: Cardiovascular diseases are the leading cause of mortality and morbidity globally causing a significant reduction in the quality of life of these patients. Participation of these patients in rehabilitation programs which involve a significant component of exercise seems to help by improving functional capacity and quality of life (QoL). Despite the beneficial effect of exercise, the type of exercise that yields the best results is yet to be determined.

Methods: Three databases (MEDLINE, CINHAL and SportDirect) were searched in May-June 2017 for original articles regarding the effect of two types of exercise in patients with myocardial infarction. Randomized control trial studies which enrolled patients with myocardial infarction and studied the effects of HIIT and/or MICE, were included in this review. Data were extracted and summarised and all studies were assessed for bias.

Results: Both forms of exercise seem to improve the relevant outcome measures such as functional capacity, QoL, walking distance, fatigue and function of the left heart. However HIIT seemed to be better in comparison with MICE in improving these outcomes. Several limitations and risk of bias have been identified and reported.

Conclusion: Both HIIT and MICE are recommended for patients with MI. Further research is required to conclusively support the superiority of HIIT over other types of exercise.

Introduction

According to World Health Organisation (2014) chronic diseases are among the primary causes of global mortality. The most common causes of mortality in 2012 were: cardiovascular diseases (46.2% of all deaths), cancer (21.7%), respiratory diseases (10.7%) and diabetes (4%) (Alwan, A. WHO, 2014).

Several studies show that frequent physical exercise helps in the prevention of several chronic diseases and reduces the mortality rate from all causes, including cardiovascular diseases (Blair et al, 1995; Lee, Hsieh & Paffenbarger, 1995; Pollock et al, 1998; Hulens et al, 2002; Bauman, 2004; Lebrun et al, 2006). Aerobic exercise is extremely important for patients with CHD with or without MI (Barboza, Rocha, Caperuto, Irigoyen and Rodrugues, 2013). Taylor and colleagues (2004) report that rehabilitation programs based on aerobic exercise have reduced the total mortality rate by 20% and the cardiovascular disease mortality rate by 26% and they have helped in reducing risk factors such as hypertension, hypercholesterolemia, diabetes, and obesity in patients with MI, angina and CHD (Taylor et al., 2004).

In addition exercise improves well-being and QoL (Kruk, 2007). Exercise is important especially for patients with coronary heart disease (CHD) (Perk et al., 2012) because it improves functional capacity, reduces coronary ischemia and angina and improves endothelial function (Thompson, 2005). However benefits from exercise rehabilitation programs depend heavily on the parameter of the program most notably the intensity and volume of exercise (Azevedo & Santos, 2014). Studies show that perhaps interval exercise especially with high intensity might be superior in comparison with other forms of exercise in improving cardiac function, functional capacity and

ultimately QoL in patients with CHD especially after myocardial infarction (Meyer et al., 1998; Nilsson, Westheim & Risberg, 2008a; Nillson, Westheim & Risberg, 2008b; Moholdt, Madssen, Rognmo & Aamot, 2014).

Methods

Search strategy

The following electronic databases were searched from March until June 2014: Science Direct, MEDLINE and Cumulative Index to Nursing and Allied Health Literature [CINAHL]. The medical subject headings (MeSH) "myocardial infarction", "coronary heart disease'', "high intensity interval training'' AND "moderate intensity continuous exercise" were used alone or in combination. Each specific phrase was combined with the Boolean operator to limit the search and make it more specific. Additional searches were carried out by scanning the reference lists of related articles in order to maximize the amount of investigations involved in the current review.

Study criteria and selection

In order to define and frame the research questions the Population(s), Intervention(s), Comparator(s), Outcome(s) and Study Design (PICOS) were used (O'Connor, Green & Higgins, 2011). The titles and abstracts of all records were screened initially against the basic initial eligibility criteria. A single failed eligibility criterion was sufficient for a study to be excluded from a review (Higgins & Deeks, 2011). Moreover, the records that remained after initial eligibility screening, were therefore screened against the full eligibility criteria outlined in **Table 1**.

Table 1- Full eligibility screening criteria

Inclusion Criteria	Exclusion Criteria	PICOS
Was the study a RCT?	Study designs other than RCT Quasi experimental studies, pilot studies	Study
Was the study published in English?	Duplicates Abstract and pilot-studies publications	
Did the study include males and females with CHD and MI?	Included subjects with disease risk factors	Population
Was the intervention HIIT or MICE and was it combined with another type of exercise?	Not HIIT or MICE Not specified	Intervention
Were the outcomes measures relevant?	Not relevant outcomes measures	Outcomes
Were the interventions compared with another type of exercise, or placebo or non therapy?		Comparison

Outcome measures

All relevant outcome measures were considered. Specifically measures such as QoL, VO2peak, functional capacity, fatigue or perceived rate of exertion, left ventricular function, and exercise time were considered relevant.

Data extraction and assessment of risk of bias

For each RCT included, data were extracted regarding: first author, year of publication, study outcomes, groups and exercise parameters, and assessed for bias using the Cochrane risk of bias tool. The quality assessment was performed to identify the quality of papers. Trials should provide full details of the randomisation process, allocation concealment or blinding of outcome assessment to be considered high quality. The quality of included studies was assessed using the

Jadad scale (Jadad et al. 1996), a three-point questionnaire form. Each question was to be answered with a *yes* and score a single point, or a *no* and scored zero points.

Results

Identification of records and study selection

The search strategy from the three databases identified a total of 1095 records. An initial screen of the article title resulted in exclusion of 830 papers. Three hundred and sixty five studies were assessed for eligibility using the inclusion and exclusion criteria of **Table 1**. Following this process of the eligibility criteria, 352 records were excluded, due to reason described in detail in **Figure 1**. The remaining 13 records met the eligibility criteria and were included in the final review.

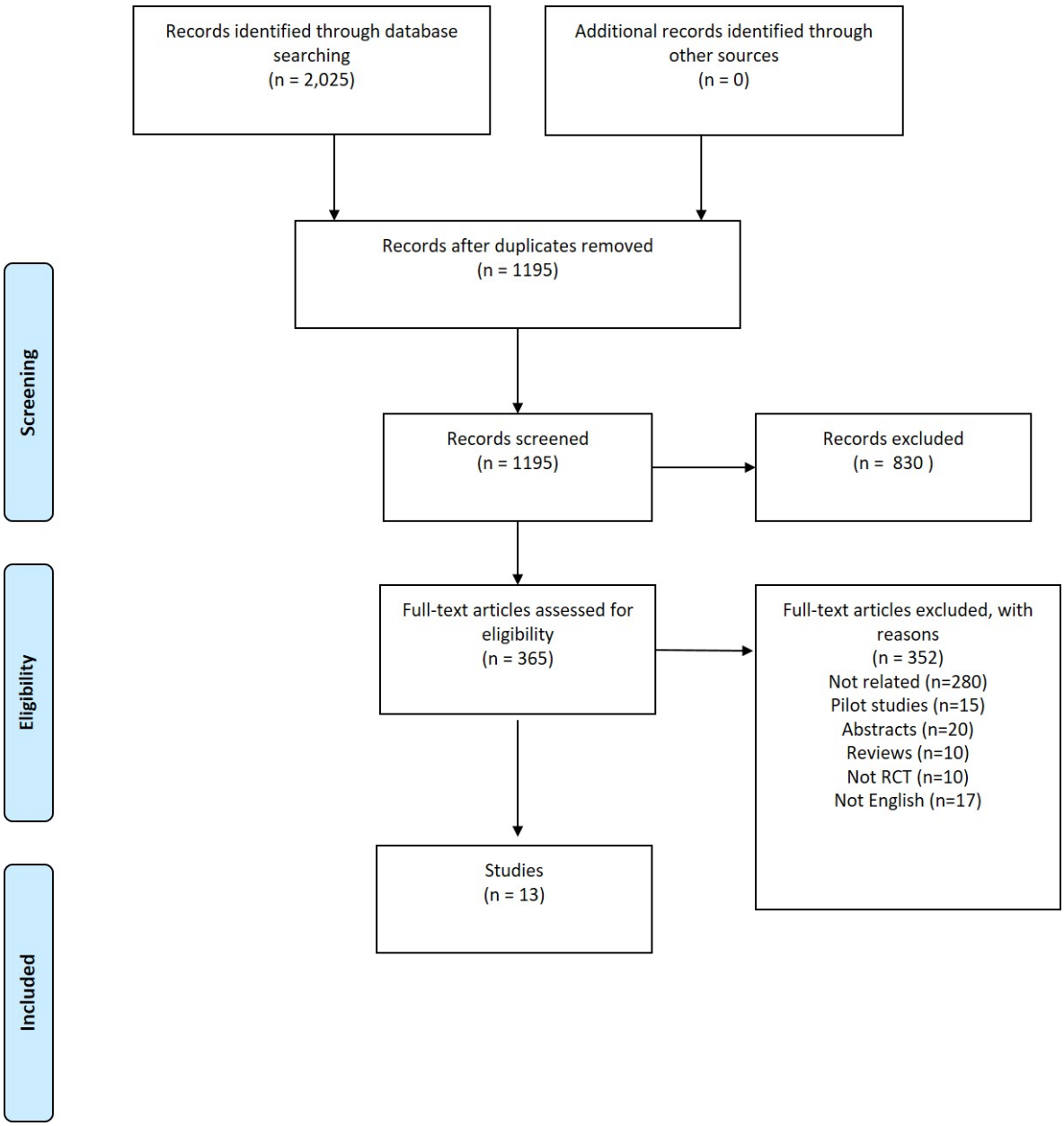

Figure 1. PRISMA diagram for included studies (Moher et al., 2009)

Description of included studies

Thirteen studies were included in this review. A summary of the studies' characteristics is presented in **Table 2**. Eight of the studies (Cardozo et el. 2015, Currie et al. 2013a, Currie et al. 2013b, Guiraud et al. 2011, Moholdt et al. 2009, Wisløff et al. 2007, Warburton et al. 2005,

Rognmo et al. 2004) compared HIIT with MICE alone or in combination with a control group, whereas the remaining studies (Nlisson et al. 2008a, Nlisson et al. 2008b, Moholdt et al. 2011a, Moholdt et al. 2011b, Conaards et al. 2015) examined only HIIT or MICE in relation to another type of exercise.

Six of the studies (Warburton et al. 2005, Rognmo et al. 2004, Wisløff et al. 2007, Guiraud et al. 2011, Currie et al. 2013a, Currie et al. 2013b) had a small sample (below 30) and the rest had sample that varied from 59 to 200 participants. Most of the studies used an exercise program of 10-16 weeks with a frequency of 2-3 times per week, however one study used a program of four week with a higher frequency (5times/week) and one study used a 1-year program of 2 sessions per week.

Generally both forms of exercise seemed to improve QoL, maximum aerobic capacity, functional capacity and left ventricular function. HIIT and MICE were superior to control intervention in two of the studies that had a control group (Cardozo et el. 2015, Wisløff et al. 2007) in terms of aerobic capacity, functional capacity and QoL. In addition HIIT was superior to a control group in another two studies (Nlisson et al. 2008a, Nlisson et al. 2008b) in terms of functional capacity, QoL and exercise time. HIIT was also superior in improving VO2peak compared to aerobic exercise (no further information regarding parameters) in two additional studies (Moholdt et al. 2011a, Moholdt et al. 2011b). No study compared MICE with a control group only. From the eight studies that examined both HIIT and MICE, five favoured HIIT (Warburton et al. 2005, Rognmo et al. 2004, Wisløff et al. 2007, Moholdt et al. 2009, Guiraud et al. 2011) in at least one outcome measure or one time point, while 3 studies (Currie et al. 2013a, Currie et al. 2013b, Cardozo et el. 2015) showed no differences between the two forms of exercise.

ISSN:2518-6590 Published on 31st August, 2017

Table 2. Summary of the studies included in the review

Authors	Sample size/Groups	Duration / Frequency	Equipment	Exercise protocol	Outcome measures
Rognmo et al. (2004)	21 participants IT/MICE	10 weeks 3days/week	Treadmill	**IT group** 4×4min at 80-90%VO2peak [33min] **MICE group** 50-60%VO2peak [41min]	IT group had greater ↑ of VO2peak compared to MICE group
Warburton et al. (2005)	14 participants IT/MICE	16 weeks 2days/week Additional 3days/week	Treadmill, Stair-climber, Combined arm and leg cycle ergometer	**IT group** 40%VO2reserve (2 min) with intervals at 90%VO2reserve (2 min) [30min] 65% VO2reserve [Resistance exercise, 30min] **MICE group** 65% VO2reserve [30min] 65% VO2reserve [Resistance exercise, 30min]	IT and Mice groups had similar ↑of VO2 Peak IT group had greater ↑ of AT

Authors	Sample size/ Groups	Duration/ Frequency	Equipment	Exercise protocol	Outcome measures
Wisløff et al. (2007)	27 participants IT/MICE/CONTROL	12 weeks 3days/week	Treadmill	**IT group** 50–60% HRpeak (3 min) with intervals at 90–95% HRpeak (4 min) [38min] **MICE group** 70% HRpeak [47min] **CONTROL group** (Walking and counseling) 70% HRpeak [47min]	IT group had greater ↑ of LV remodeling, VO2peak and endothelium function compared to MICE and CONTROL groups. QOL improved both after IT and MICE exercise. No changes occurred in the CONTROL group regarding the QOL.
Nlisson et al. (2008a)	80 participants IT/CONTROL	16 weeks 2days/week	Aerobic dance movements (with music) and involved the use of both upper and lower extremities, including endurance, strength, and stretching exercises	**IT group** 3×5–10 min at RPE = 15–18 [50min] **CONTROL group** Without exercise	Greater ↑ of functional capacity, workload (watts), exercise time (seconds) and QOL significantly improved for the exercise group.
Nlisson et al. (2008b)	80 participants IT/CONTROL	1year 2days/week	Aerobic dance movements (with music) and involved the use of both upper and lower extremities, including endurance, strength, and stretching exercises	**IT group** 3×5–10 min at RPE = 15–18 [50min] **CONTROL group** Without exercise	Greater ↑ of functional capacity, workload (watts), exercise time (seconds) and QOL significantly improved for the exercise group.

Authors	Sample size/ Groups	Duration/ Frequency	Equipment	Exercise protocol	Outcome measures
Moholdt et al. (2009)	59 participants IT/MICE	4weeks 5days/week	Treadmill	**IT group** 4×4min intervals at 90% HRmax with active pauses of 3min of walking at 70%HRmax **MICE group** 70%HRmax [46min]	↑ Of VO2peak in both groups after 4 weeks. After 6 months IT group significantly improved VO2peak compared to MICE group. QOL significantly ↑ at 4weeks and 6months, with no significant difference between the groups. No changes occurred at 4 weeks regarding the blood markers and LV function. However,there was a change at 6 months on both groups.
Guiraud et al. (2011)	20 participants IT/MICE	2 sessions 2 weeks difference	Cycle ergometer	**IT group** 2sets of 10min composed of repeated phases of 15s at 100% PPO, interspersed by 15s of passive recovery **MICE group** 70% PPO **AEROBIC group** N/A	IT protocol resulted in lower mean ventilation for a small difference in metabolic demand. Participants preferred the IT mainly because the perceived exertion measured by the Borg scale was lower.

Authors	Sample size/ Groups	Duration/ Frequency	Equipment	Exercise protocol	Outcome measures
Moholdt et al. (2011a)	107 participants IT/AEROBIC	12 weeks 2daysç/week	Treadmill Aerobic exercises	**IT group** 4×4min intervals at 85–95% HRmax with active pauses of 3min of walking at 70% HRmax [38min] **AEROBIC group** N/A	IT group had greater ↑ of VO2peak. ↔ Improvement of endothelial function, QOL and blood markers between the groups.
Moholdt et al. (2011b)	107 participants IT/AEROBIC	12 weeks 2days/week Measurement at 6 and 30 months	Treadmill Aerobic exercises	**IT group** 4×4min intervals at 85–95% HRmax with active pauses of 3min of walking at 70% HRmax [38min] **AEROBIC group** N/A	After 6 and 30 months, VO2peak in both groups declined. At 30 months the improvement of VO2peak in IT group, was still significant.
Currie et al. (2013a)	22participants IT/MICE	12 weeks 3days/week	Cycle ergometer	**IT group** 10minX 1-min cycling intervals at 89% PPO separated by 1-min intervals at 10% PPO **MICE group** 58% of PPO [50min]	↔ Improvement of endothelial function, between the groups. No change in HR recovery or variability following 12 weeks of exercise

Authors	Sample size/ Groups	Duration/ Frequency	Equipment	Exercise protocol	Outcome measures
Currie et al. (2013b)	14 participants IT/MICE	12 weeks 2days/week	Cycle ergometer	**IT group** 10minX 1-min cycling intervals at 88% PPO separated by 1-min intervals at 10%PPO	. FMD was increased post-training with no differences between groups. There was a significant improvement in cardiorespiratory fitness following both training programs, with no group differences.
				MICE group 60% of PPO [50min]	
Cardozo et el. (2015)	71 participants IT/MICE/CONTROL	16 weeks 3days/week	Treadmill	**IT group** Alternation of 90% HRpeak and 60% HRpeak every 2min [30min]	IT group had greater ↑ of O_2P slope. No changes of VE/VCO_2 slope and OUES occurred between groups.
				MICE group 70–75% HRmax [30min]	
				CONTROL group Without exercise	

Authors	Sample size/ Groups	Duration/Frequency	Equipment	Exercise protocol	Outcome measures
Conaards et al. (2015)	200 participants IT/CONTINUOUS	12 weeks 3days/week	Cycle ergometer	**IT group** 4×4min at 90–95% HRpeak with active pauses of 3min of 50–70% HRpeak **CONTINUOUS group** 70-75% HRpeak	↔ Improvement of endothelial function, cardiovascular risk factors and QOL.

✱ **Abbreviations:** OUES:oxygen uptake efficiency slope; HRpeak: heart rate peak; IT: interval training; MICE: moderate intensity continuous training; LV Funtion: left ventricle function; QOL: quality of life; HR: heart rate; VO2: oxygen consumption; AT: anaerobic threshold; O_2P slope: oxygen pulse; ↔: Similar improvement; ↑: Greater improvement; ↓: Reduction.
FMD: Flow mediated dilation.

ISSN:2518-6590 Published on 31st August, 2017

Risk of bias assessment

The Jadad score ranged between 0 and 3 out of 5 (**Table 3**). One study scored 0 (Guiraud et al., 2011); two studies scored 1 (Warburton et al., 2005, Cardozo et al., 2015), four studies scored 2 (Wislof et al., 2007, Currie et al., 2013a; 2013b, Conraads et al., 2015) and six studies scored 3 (Rognmo et al., 2004, Nisson et al., 2008a; 2008b, Moholdt et al., 2009; 2011a; 2011b). These scores indicated that approximately half of the studies were low quality. This is due to the fact that the double-blinding criterion is not feasible in these kind of RCT within exercise intervention. On the Jadad scale 40% of the score accounts for the double-blinding criterion (Hempel et al., 2011).

ISSN:2518-6590 Published on 31st August, 2017

Table 3. Assessment of the methodological quality of the studies using the Jadad score.

	Potential Score			
JADAD SCORING CRITERIA	**Rognmo et al. (2004)**	**Warburton et al. (2005)**	**Wislof et al. (2007)**	**Nisson et al. (2008a)**
1. The study described as randomized?	**1**	**0**	**1**	**1**
2. Was the method of randomization described and appropriate to conceal allocation?	**1**	**1**	**1**	**1**
3. Was there a description Of withdrawals and drop outs?	**1**	**0**	**0**	**1**
4. Was the study described as Double-blinded?	**0**	**0**	**0**	**0**
5. Was the method of blinding inappropriate?	**0**	**0**	**0**	**0**
FINAL SCORE (0 – 5)	**3/5**	**1/5**	**2/5**	**3/5**

	Potential Score			
JADAD SCORING CRITERIA	**Nisson et al. (2008b)**	**Moholdt et al. (2009)**	**Moholdt et al. (2011a)**	**Moholdt et al. (2011b)**
1. The study described as randomized?	**1**	**1**	**1**	**1**
2. Was the method of randomization described and appropriate to conceal allocation?	**1**	**1**	**1**	**1**
3. Was there a description Of withdrawals and drop outs?	**1**	**1**	**1**	**1**
4. Was the study described as Double-blinded?	**0**	**0**	**0**	**0**
5. Was the method of blinding inappropriate?	**0**	**0**	**0**	**0**
FINAL SCORE (0 – 5)	**3/5**	**3/5**	**3/5**	**3/5**

	Potential Score				
JADAD SCORING CRITERIA	**Guiraud et al. (2011)**	**Currie et al. (2013a)**	**Currie et al. (2013b)**	**Cardozo et al. (2015)**	**Conraads et al. (2015)**
1. The study described as randomized?	**0**	**0**	**0**	**1**	**0**
2. Was the method of randomization described and appropriate to conceal allocation?	**0**	**1**	**1**	**0**	**1**
3. Was there a description of withdrawals and drop outs?	**0**	**1**	**1**	**0**	**1**
4. Was the study described as Double-blinded?	**0**	**0**	**0**	**0**	**0**
5. Was the method of blinding inappropriate?	**0**	**0**	**0**	**0**	**0**
FINAL SCORE (0 – 5)	**0/5**	**2/5**	**2/5**	**1/5**	**2/5**

All the included studies were evaluated in terms of its risk of bias (**Table 4**). Major sources of the risk of bias were related to allocation concealment, blinding study subjects or research personnel and blinding of outcome assessment. Risk of reporting bias was low in general. Therefore, a high risk of bias might be introduced in most of the RCTs included.

	1	2	3	4	5	6	7
Rognmo et al. (2004)	-	-	+	+	-	+	+
Warburton et al. (2005)	+	?	-	-	+	+	+
Wislof et al. (2007)	+	+	+	-	+	+	+
Nilsson et al. (2008a)	+	+	+	-	+	+	+
Nilsson et al. (2008b)	+	+	+	-	+	+	+
Mohold et al. (2009)	-	?	+	-	+	+	+
Moholdt et al. (2011a)	+	-	+	-	+	+	+
Moholdt et al. (2011b)	+	-	-	-	+	+	+
Guirad et al. (2011)	-	-	-	-	+	+	+
Currie et al. (2013a)	-	-	-	-	-	+	+
Currie et al. (2013b)	+	-	-	-	+	+	+
Cardozo et al. (2015)	-	-	-	-	+	+	+
Conraads et al. (2015)	-	+	+	+	+	+	+

+ Low risk of bias - High risk of bias? Unclear risk of bias

Table 4. Risk of bias assessment. 1, Random sequence generation (selection bias); 2, Allocation concealment (selection bias); 3 Blinding of participants and personnel (performance bias); 4, Blinding of outcome assessment (detection bias); 5, Incomplete outcome data (attrition bias); 6, Selective reporting (reporting bias); 7, Other bias.

Limitations

Jadad et al. (1996) reported that RCTs of high quality, must score between 3 and 5 points on the above scale. The quality assessment of the papers demonstrated that only six studies reached the minimum score to be considered of adequate quality. However, none of the records were excluded based on the score. Therefore, a high risk of bias exists in most studies.

The comprehensive search strategy was performed in order to minimise publication bias. Nevertheless, it may not have been sufficient to prevent bias, as identifying and improving potential biases is not easy (Sterne, Egger & Moher, 2011). The exclusion of non-English language records may have introduced language bias, and this is another limitation of this review. The search of the records was updated during the process of the review, to prevent any time-lag biases; however it is impossible to exclude such biases. In addition, the review included only thirteen studies and most of them had a small sample. This makes the interpretation and generalisation of the results difficult.

Conclusion

Despite the limitations in the studies, HIIT and MICE both improve QoL and functional capacity of patients with MI and therefore are recommended. However there seems to be a slight advantage of HIIT over MICE but this is not a universal finding. Obviously there is significant heterogeneity in methodologies among the different trials. Despite this, the findings of this review suggest that HIIT is safe and may improve QoL in patients with MI. However, additional studies with higher sample sizes and improved methodological quality are required to confirm these findings. In light of the limitations that have been reported, the results must be interpreted with caution.

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