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Review

# Eccentric exercise in ischemic cardiac patients and functional capacity: A systematic review and meta-analysis of randomized controlled trials

C. Karagiannis [a,*], C. Savva [a], I. Mamais [a], M. Efstathiou [b], M. Monticone [c], T. Xanthos [d]

[a] European University of Cyprus, School of Sciences, Department of Health Sciences, Nicosia, Cyprus
[b] University of Nicosia, Department of Life and Health Sciences, Nicosia, Cyprus
[c] University of Cagliari, Department of Public Health, Clinical and Molecular Medicine, Cagliari, Italy
[d] European University of Cyprus, School of Medicine, Nicosia, Cyprus

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ABSTRACT

*Background:* Eccentric (ECC) exercise is an "economical" type of exercise with low energy requirements and does not cause early fatigue. Therefore, it is used for cardiac patients, who have low physical activity and exercise intolerance, as an easier kind of training.
*Objective:* This systematic review aimed to investigate the efficacy of ECC exercise for functional capacity (FC) in patients with ischemic heart disease.
*Design:* Systematic review.
*Methods:* MEDLINE via PubMed and EBSCO databases were searched for articles of randomized controlled trials of adults with ischemic heart disease who underwent ECC training as compared with other forms of exercise (concentric exercise) or no exercise and assessed FC. The methodologic quality of studies was assessed by the PEDro scale. A meta-analysis was performed with sufficient homogeneity between at least 2 studies in the pre-defined comparisons.
*Results:* Four studies, investigating a total of 99 subjects, met the inclusion criteria. The results of the studies did not clearly indicate whether ECC exercise could improve FC better than traditional forms of exercise. However, the small number of studies and their methodologic weaknesses do not allow for drawing firm conclusions.
*Conclusions:* We found contradictory results about the effectiveness of ECC as compared with concentric exercise in terms of FC in ischemic cardiac patients. Further investigation with well-designed randomized trials is needed to determine the effectiveness of this kind of exercise for FC in such patients.
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## 1. Introduction

Functional capacity (FC) is the ability to perform daily activities [1]. In most cardiac patients, FC is reduced with the occurrence of cardiac symptoms such as early fatigue, dyspnea and angina pectoris during activities [2]. Moreover, the progressive skeletal muscle wasting and weakness increase functional limitations in patients with chronic heart failure [3,4]. Therefore, ischemic cardiac patients became functionally disabled, because many patients (e.g. New York Heart Association class-IV patients) are unable to perform any physical activity without discomfort, and symptoms are present even during rest [2].

Ischemic heart disease (IHD) is the primary cause of death worldwide according to the World Health Organization (WHO). Specifically WHO statistics show that 7.4 million people died because of IHD in 2012 [5]. IHD is the end effect of coronary artery disease (CAD), but many cases of IHD result in heart failure [6,7].

Aerobic exercise is a cornerstone of cardiac rehabilitation programs and can improve FC in ischemic cardiac patients [8]. In recent years, there has been some interest in another form of exercise for rehabilitation, namely, eccentric (ECC) exercise [9–15]. Muscle contraction with ECC exercise is defined as the contraction of the muscle while it is elongated. This type of muscle contraction results in greater increases in muscle strength because of the production of greater torque; at the same time, oxygen requirement and cardiovascular stress are reduced as compared with concentric (CON) exercise [16–19]. Thus, ECC exercise seems to be an "economical" type of exercise that has the results of regular exercise (i.e. muscle strengthening) but without causing

* Corresponding author. 12, Isthmion Street, 3083 Limassol, Cyprus.
*E-mail addresses:* C.karayiannis@euc.ac.cy, xristos_fys@hotmail.com (C. Karagiannis).

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early fatigue and is easily afforded by patients with exercise intolerance. Moreover, ECC exercise is an integral part of daily human activities because it occurs in such activities as walking downhill or descending stairs. In cardiac patients, ECC exercise is not performed solely for a certain muscle but is a general low-intensity exercise for lower limbs.

A randomized clinical trial (RCT) revealed that this type of exercise in coronary patients could significantly improve maximum oxygen uptake ($VO_{2peak}$) as well as other parameters as compared with typical CON exercise [9]. However, the effectiveness of ECC exercise for FC remains debatable because in another study of ischemic cardiac patients, $VO_{2peak}$ did not show any significant improvement with ECC exercise [15].

To our knowledge, no other study has systematically examined the effect of ECC exercise on FC. This review aimed to explore its efficacy for FC as compared with the standard form of aerobic exercise (CON) in ischemic cardiac patients.

## 2. Methods

PRISMA guidelines were used for this systematic review [20,21]. We searched for articles published in English from inception to July 2016 in the electronic databases PubMed and all EBSCO Host databases (including Academic Search, CINAHL, Health Source, SportDiscus) with keywords related to both IHD (CAD, heart failure, coronary patients, cardiovascular disease, ischemic heart disease, cardiorespiratory disease, cardiorespiratory patients, myocardial infarction) and ECC exercise (eccentric exercise, eccentric training, eccentric endurance, downhill walking, downhill running, stair descending, negative work) (Appendix 1). Articles retrieved were perused for other relevant references.

The search yield was initially screened by 2 assessors (CS, ME) to remove duplicates and to independently assess titles and abstracts of potentially relevant articles, then the full-text article was retrieved. Disagreements were discussed to reach consensus, and if necessary, with a third reviewer (IM).

### 2.1. Inclusion criteria

We included articles following the PICOS model:

- men and women over 18 years old, with a diagnosis of IHD (e.g. CAD, heart failure, myocardial infarction) (patients who had undergone heart surgery such as coronary artery bypass grafting or percutaneous coronary intervention could also be included);
- any form of ECC exercise training program;
- comparing no exercise or other forms of exercise programs (e.g. traditional aerobic exercise);
- FC assessed by maximal or submaximal tests;
- and a RCT.

#### 2.1.1. Quality evaluation of studies

The quality of the studies was assessed by methodological and statistical criteria (e.g. randomization, blinding, data comparison before and after the intervention and between groups). The quality of each study was assessed independently by 2 investigators (CK, IM) who used the PEDro scale, which is based on the Delphi List criteria [22] and is considered valid and reliable [23,24]. High quality was considered a score $\geq$ 7/10; intermediate quality, a score 4 to 6; and poor quality, a score $\leq$ 3.

#### 2.1.2. Statistical analysis

A meta-analysis was performed if sufficient homogeneity existed between at least 2 studies in the pre-defined comparisons. For articles that did not contain numerical data, the authors were contacted for the data. Meta-analyses of the results are presented as pooled mean differences for continuous data, comparing treatment and control groups with a random-effects model. The existence of statistical heterogeneity between the included studies was assessed by the $Chi^2$ test and $I^2$. Two-sided $P < 0.05$ was considered statistically significant. Analysis involved use of RevMan 5.0 [25].

## 3. Results

During the initial research, 173 articles were found. After removing duplicates and non-relevant articles, 8 articles remained. Only 4 studies met all inclusion criteria and comprised the necessary data to investigate the effectiveness of eccentric exercise for FC of ischemic cardiac patients (Fig. 1) (Appendix 2).

### 3.1. Methodological quality of studies

The quality of the studies was moderate: scores ranged from 5 to 7/10 on the PEDro scale (Table 1). All studies were referred for evaluation of the outcome measures before and after the intervention and also between the 2 evaluation groups. Two of these trials involved no form of blindness (by participants, researchers or examiners) [9,12], whereas in the other trials, only assessors were blinded [13,15].

### 3.2. Characteristics of participants, disease, surgery, and medications

The studies included 13 to 42 patients for a total of 99 patients. Most patients were males ($n$ = 85). The mean age was 57 $\pm$ 8 years old. Participant characteristics are in Table 2.

In 2 of the studies, the participating patients had CAD [9,13], whereas in the other 2 studies, patients had chronic heart failure [12,15]. In all studies, an inclusion criterion was that the patients with cardiac disease were in stable status, and the patients with CAD should have > 45% ejection fraction. In studies including CAD patients, 89% of patients (24/27) had previously had acute coronary syndrome; 21 had undergone percutaneous coronary intervention and 3 coronary artery bypass graft.

The main medication for patients was beta-blockers (95%), antiplatelet agents (87%), statins (82%), angiotensin-converting enzyme inhibitors (81%) and diuretics (40%). Receipt of diuretics was more frequent for patients with chronic heart failure than CAD.

### 3.3. Characteristics of exercise programs

In all studies, the sample was divided into 2 groups, one group following an ECC exercise training program and the other a typical CON aerobic exercise program. None of the studies had a no-exercise group. In all trials, a cycle ergometer was used for the exercises.

Studies differed regarding the parameters of the exercise programs. The total duration of the programs ranged from 5 to 8 weeks. In all studies, the protocol was 3 exercise sessions per week. The total length of each session of the actual duration of an eccentric or a concentric exercise (except for warm-up, rest and recovery time) ranged from 25 to 30 min.

Various factors were used to determine exercise intensity. In some studies, metabolic rate (%) of $VO_{2peak}$ [9], ventilation threshold (VT) [12,13,15] or maximum heart rate (HR) were used [9,12]. In some other studies, subjective symptoms considered were rate of perceived exertion (RPE), used to determine the intensity [12,15]. In 3 studies, the intensity was determined by number of revolutions per minute combined with an adjusted

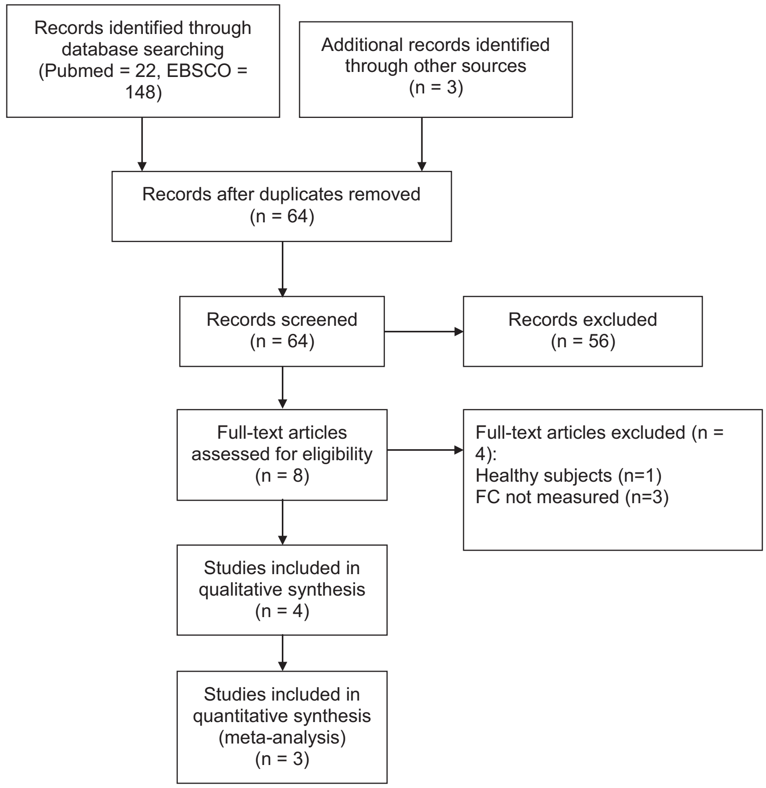


**Fig. 1.** Selection of articles in the study. FC: functional capacity.

**Table 1**
Quality of the studies (based on PEDro scale).

| Author | Criterion 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | PEDro score |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Meyer et al. (2003) [9] | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 1 | 1 | 1 | 6 |
| Gremeaux et al. (2010) [13] | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 7 |
| Besson et al. (2013) [12] | 1 | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1 | 1 | 5 |
| Casillas et al. (2016) [15] | 1 | 1 | 0 | 1 | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 7 |

Criterion 1: eligibility criteria specified (this criterion is not used to calculate the PEDro score); Criterion 2: random allocation of participants; Criterion 3: allocation concealed; Criterion 4: groups similar at baseline regarding the most important prognostic indicators; Criterion 5: participants blinded; Criterion 6: therapists blinded; Criterion 7: assessors blinded; Criterion 8: measures of key outcomes obtained from more than 85% of subjects; Criterion 9: data analyzed by intention to treat; Criterion 10: between-group statistical comparisons were conducted; Criterion 11: point measures and measures of variability were provided.

**Table 2**
Characteristics of participants and exercise programs.

| Author/country | Criteria | Exercise interventions: Type | Session duration | Intensity | Frequency | Total duration |
|---|---|---|---|---|---|---|
| Meyer et al. (2003) [9] Switzerland | Male Stable CAD | Eccentic ergometer ($n$ = 7) | 30 min | 60% $VO_2$peak and/or 85% $HR_{max}$ | 3 × week | 8 weeks |
| | | Standard cycle ergometer ($n$ = 6) | 30 min | 60% $VO_2$peak and/or 85% $HR_{max}$ | 3 × week | 8 weeks |
| Gremeaux et al. (2010) [13] France | Male Stable CAD | Eccentic ergometer ($n$ = 7) | 30 min | HR corresponding to VT 20 rpm | 3 × week | 5 weeks |
| | | Standard cycle ergometer ($n$ = 7) | 30 min | HR corresponding to VT 50 rpm | 3 × week | 5 weeks |
| Besson et al. (2013) [12] France | Male or female Stable CHF | Eccentric ergometer ($n$ = 15, 4F) | 25 min | HR corresponding to VT 15 rpm | 3 × week | 7 weeks |
| | | Standard cycle ergometer ($n$ = 15, 4F) | 25 min | < 80% $HR_{max}$, 9–11 RPE 60 rpm | 3 × week | 7 weeks |
| Casillas et al. (2016) [15] France | Male or female Stable CHF | Eccentric ergometer ($n$ = 21, 3F) | 25 min | 9–11 RPE 15 rpm | 3 × week | 7 weeks |
| | | Standard cycle ergometer ($n$ = 21, 3F) | 25 min | HR corresponding to VT 60 rpm | 3 × week | 7 weeks |

CAD: coronary artery disease; CHF: chronic heart failure; F: female; HR: heart rate; $HR_{max}$: maximum heart rate; RPE: rate of perceived exertion; RPM: revolutions per min; $VO_{2peak}$: maximum oxygen uptake; VT: ventilation threshold.

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**Table 3**
Results of functional capacity before and after testing.

| Author | | $VO_2$peak (ml/kg/min) | | 6-min walk test (m) | | $VO_2$ at last 3'' (ml/kg/min) | | First VT (ml/kg/min) | | 200-m fast walk (sec) | | Symptom limited $VO_2$ (ml/kg/min) | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | ECC | CON | ECC | CON | ECC | CON | ECC | CON | ECC | CON | ECC | CON |
| Meyer et al. (2003) [9] | Pre | NR | NR | | | | | | | | | | |
| | Post | NR[a] | NR | | | | | | | | | | |
| Gremeaux et al. (2010) [13] | Pre | | | 495 (74.2) | 508.4 (58.3) | | | | | 107.7 (14) | 108.6 (15.2) | 24.8 (0.8) | 26.4 (5.1) |
| | Post | | | 557.1 (17.7)[a] | 559.9 (50.3)[a] | | | | | 101.7 (5.7) | 99.6 (14.4) | 28.3 (4.1)[a] | 27.6 (5.8)[a] |
| Besson et al. (2013) [12] | Pre | | | 440.5 (97.4) | 454.9 (98.5) | 14.9 (4.9) | 14.2 (5) | | | | | | |
| | Post | | | 493.6 (109.5)[a] | 487.5 (80.6)[a] | 15.5 (4) | 16 (4.8)[a] | | | | | | |
| Casillas et al. (2016) [15] | Pre | 16.6 (4.8) | 17.3 (4.6) | 441 (89) | 456 (90) | 14.3 (3) | 13.8 (4) | 12.4 (2.9) | 12.4 (3.4) | | | | |
| | Post | 18.5 (4.7) | 19.3 (4.7)[a] | 483 (100)[a] | 492 (82)[a] | 15.3 (3.4) | 15.9 (4)[a] | 13.7 (3.3) | 14 (3.6)[a] | | | | |

Data are mean (SD). CON: concentric exercise group; ECC: eccentric exercise group; NR: not reported in numbers; $VO_2$: oxygen uptake; $VO_{2peak}$: maximum oxygen uptake; VT: ventilation threshold.
[a] $P < 0.05$ comparing pre- vs. post-data.

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workload leading to an HR or RPE target [12,13,15]. Finally, in the Gremeaux et al. study [13], the power output had to be self-adjusted for patients by visual feedback on a computer screen while cycling. In all studies, intensity gradually increased. In one study, the intensity increased gradually up to the fifth week, with no further increase for the rest of the study [9]. In studies using metabolic parameters (such as HR) to determine intensity, the increase in exercise intensity needed to be controlled to not differentiate these parameters. The characteristics of the exercise programs are in Table 2.

### 3.4. Compliance, complications, attrition

Patient compliance with the exercise program was reported in 3 studies, showing that all patients who participated fully complied with the exercise program [12,13,15].

Overall, 13 patients left the research process before it was completed. In the study of Gremeaux et al. [13], one of the patients left the study due to re-hospitalization for a psychiatric problem. Moreover, in the other studies, patients from each group were excluded because of adverse events. One patient with ECC exercise was excluded for non-medical reasons and 4 patients because of severe pain in the knee and thigh muscles. In all, 7 patients with CON exercise did not complete training because of diffuse muscle pain (1), acute decompensate heart failure (3), painful inguinal hernia (1) and non-medical reasons (2) [12,15].

Generally, studies contained no reports of deterioration of disease or any other serious adverse complications that could lead to hospitalization or death.

### 3.5. FC assessment

FC was assessed by several outcome measures. Two studies assessed $VO_{2peak}$ during cardiopulmonary exercise testing [9,15]. The 6-min walk test was an FC outcome in 3 studies [12,13,15]. In 2 of these, the authors also examined $VO_2$ at the last 30'' of the 6-min walk test [12,15]. Results of the 6-min walk test and $VO_2$ during the test underwent meta-analysis. Other outcome measures of FC were first VT [15], time to perform a 200-m fast walk test [13] and symptom limited $VO_2$ [13] (Table 3).

#### 3.5.1. $VO_{2peak}$

In 2 studies that assessed $VO_{2peak}$, exercise groups did not differ. However, in the Meyer et al. study [9], $VO_{2peak}$ showed a significant improvement with ECC exercise [9], whereas in the other study $VO_{2peak}$ improved significantly with CON exercise [15].

#### 3.5.2. 6-min walk test

All studies assessing the 6-min walk test revealed significant improvement between pre- and post-values with both exercises [12,13,15]. None showed any significant difference between groups. Meta-analysis showed a slight dominance with ECC exercise but without significance (Fig. 2).

#### 3.5.3. $VO_2$ at the last 30'' of the 6-min walk test

$VO_2$ was increased within the 6-min walk test but only with CON exercise. The increase was significant [12,15]. No study revealed a significant difference between exercises. Meta-analysis did not show a significant difference between exercise types in this factor (Fig. 3).

#### 3.5.4. Other FC variables

First VT was improved significantly only with CON exercise [15]. The time to perform the 200-m walk test was reduced with both exercise groups as compared with initial values, but findings were not significantly different within or between exercise groups [13]. Finally, a symptom-limited $VO_2$ test showed a significant increase within both groups but without significant difference between groups [13].

## 4. Discussion

The aim of this review was to investigate the potential effectiveness of ECC exercise in FC in patients with IHD. The results of this review did not clearly indicate if ECC exercise could improve FC better than the traditional forms of exercise. In most submaximal tests of FC, significant improvements were shown only within groups [12,13,15], whereas improvements in others (such as VT and $VO_2$ during the 6-min walk test) occurred only with CON exercise [12,15]. None of the studies revealed a significant difference between groups in FC variables.

The major assessment method of FC is the measurement of maximal oxygen uptake ($VO_{2max}$ or $VO_{2peak}$) during a cardiopulmonary exercise test [1]. Different results occurred in 2 studies that assessed $VO_{2peak}$. In the first, $VO_{2peak}$ seemed to improve significantly only with ECC exercise [9], whereas in the other study, it improved significantly with CON exercise [15]. This difference is probably attributed to how the intensity of the exercise was determined by the 2 researchers. In the Casillas et al. study [15], the intensity of the ECC exercise was lower than that with the CON exercise (15 vs. 60 revolutions per min), whereas in the Meyer et al. study [9], the intensity was calculated by $VO_{2peak}$ and was similar for both exercise groups (60% $VO_{2peak}$). However, intensity at the

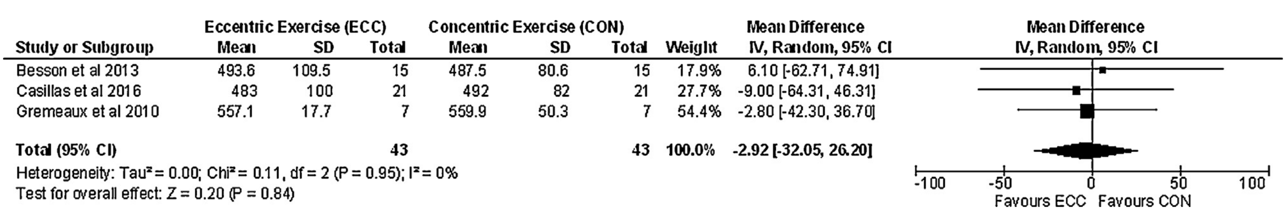


**Fig. 2.** Meta-analysis of the results of the 6-min walk test.

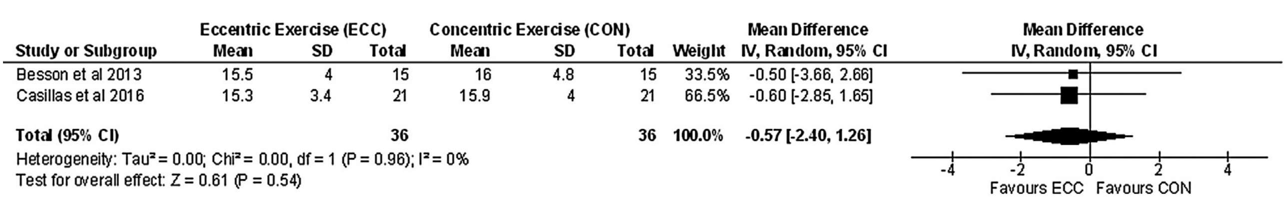


**Fig. 3.** Meta-analysis of the results of $VO_2$ at the last 30 sec of the 6-min walk test.

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same $VO_{2peak}$ level requires more mechanical power and more cardiovascular work during ECC than CON exercise [26,27]. Therefore, training was performed at a higher intensity with ECC than CON exercise [9].

Of note, most daily activities did not require maximal effort. Therefore, FC was also assessed by submaximal tests, such the 6-min walk test or VT [1]. These tests can also provide validated and reliable results [28–30]. Another way of assessing FC was a symptom-limited exercise test. Submaximal tests have a pre-determined endpoint (e.g. 70% of maximum heart rate), whereas symptom-limited tests are designed to continue until the appearance of certain signs or symptoms [31]. However, this test can also give useful information for FC [32]. The distance covered in the 6-min walk test and symptom-limited $VO_2$ was improved significantly with ECC and CON exercise [12,13,15]. However, $VO_2$ during the 6-min walk test and first VT improved significantly only with CON exercise [12,15]. Meta-analysis of the 6-min walk test and $VO_2$ during the 6-min walk test did not reveal any significant difference between exercise groups perhaps because in all studies using submaximal tests, intensity was lower with ECC than CON exercise (Table 2).

The results of this systematic review cannot be generalized because of some quantitative and qualitative limitations of the studies reviewed. First, we found only 4 research studies, with meta-analysis conducted for the results of 3 of them, which seems insufficient to give clear results. Moreover, the 3 studies were conducted in the same centre by the same group of researchers [12,13,15] which may be a limitation of the generalization of the meta-analysis.

The qualitative deficits of the research mainly pertain to their methodological design. The studies were of moderate quality and assessors were blinded in only 2 studies. In studies in which researchers were not blinded, their personal beliefs in favor of or against an intervention can alter the results (information bias-systemic error) [33,34].

Another limitation is that the samples consisted of patients who were in a stable condition and most were male (85 men vs. 14 women). Therefore, because sample does not fully reflect the entire cardiac patient conditions presented clinically, we cannot generalize the results to the relevant population. In addition, 2 studies involved ischemic patients without ventricular dysfunction [9,13], whereas the other 2 studies were of chronic heart failure patients (with ventricular dysfunction) [12,15]. Although the results did not differ between exercise groups in these studies, variations of ventricular function may alter the results of FC. Further studies in both populations are still needed to generalize results.

Also, from the results, the long-term effect of ECC exercise cannot be known because all researchers had one final re-evaluation at the end of the exercise program. There were no reassessments of the results, so questions may be raised regarding the long-term effectiveness of the ECC intervention.

Beyond the limitations in methodological design, differences seem to exist regarding the dosage of exercise among the studies. For example in the Meyer et al. study [9], the total intervention lasted 8 weeks, whereas in the Gremeaux et al. study [13], the intervention lasted only 5 weeks. Moreover, the calculation of the intensity of exercise differed between studies and groups (Table 2). In general, equalizing intensity between ECC and CON exercise is difficult for various reasons. First, determining the intensity in the same mechanical work has resulted in much lower metabolic requirements (expressed by $VO_2$) with ECC than CON exercise [26,35]. However, if the intensity is determined on the same $VO_2$ level, mechanical work is increased more in ECC exercise [26,27]. For example, in the Meyer et al. study [9], an approximately four-fold greater muscular stress occurred with ECC than CON exercise but without a greater increase in central hemodynamics or metabolic responses. Second, training in the same revolutions per minute seems inadequate because it is not tolerated by participants and can cause muscle damage [36,37]. Therefore, in 3 of the studies, researchers chose lower revolutions per minute for patients with ECC than CON exercise [12,13,15]. Therefore, we cannot be sure about how intensity can be calculated to be equal and also which dosage of exercise will bring better outcomes for these patients.

## 5. Conclusions

This systematic review has shown moderate to weak evidence of the effectiveness of ECC for FC for ischemic cardiac patients. However, this type of exercise may be an alternative form of exercise for these patients because it can lead to positive effects in certain cases. Further research in well-designed randomized studies is needed to conclude on the efficacy of this method for FC.

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## Disclosure of interest

The authors declare that they have no competing interest.

## Acknowledgements

None declared.

## Appendix 1. Search strategy

| # | KeyWords | PubMed (Title/Abstract | EBSCO (Abstract) |
|---|---|---|---|
| #1 | ((coronary artery disease) OR heart failure) OR chronic heart failure) OR CHF) OR coronary patients) OR CAD) OR cardiovascular disease) OR ischemic heart disease) OR cardiorespiratory patients) OR myocardial infarction)) | 420,206 | 1,254,891 |
| #2 | ((eccentric exercise) OR ECC) OR eccentric training) OR eccentric endurance) OR eccentric endurance training) OR eccentric resistance exercises) OR downhill walking) OR downhill running) OR stair descending) OR negative work)) | 5239 | 40,184 |
| #3 | ((RCT) OR Randomized controlled) OR Randomly) OR Randomized) OR CT) OR Clinical Trial) | 905,577 | 2,915,740 |
| #4 | #1 AND #2 AND #3 | 22 | 148 |

## Appendix 2. Articles in EBSCO databases

| EBSCO Databases | Articles per database |
|---|---|
| Medline | 56 |
| Medline Complete | 56 |
| Academic Search Complete | 15 |
| CINAHL Plus with full text | 11 |
| Health Source: Nursing/Academic Edition | 5 |

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**Appendix 2** (*Continued*)

| EBSCO Databases | Articles per database |
|---|---|
| SPORTDiscus with full text | 3 |
| Physiology and Behavioral Sciences Collection | 1 |
| Education Research Complete | 1 |
| Total | 148 |

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