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ORIGINAL ARTICLE

Effectiveness of Early Mobilization in Prevention and Rehabilitation of Functional Impairment After Myocardial Revascularization Surgery: A Systematic Review

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Abstract

Introduction: Myocardial revascularization surgery is associated with high morbidity and mortality, due to factors like the general anesthesia and the surgical procedure itself. Physiotherapy, combined with early mobilization (EM), can provide the patient with better functional parameters.

Objective: To review, identify and describe the effectiveness of EM in the prevention and rehabilitation of functional parameters of coronary artery bypass graft surgery.

Methodology: This is a systematic review conducted between February 2020 and 2021 of randomized clinical trials (RCTs) published in the Cochrane databases Library, LILACS, Scielo and Medline / PubMed. The Physiotherapy Evidence Database (PEDro) scale was used for assessment of the methodological quality of studies included.

Results: Four studies were reviewed. Two articles assessed functional capacity, one using the cycle ergometer and one with inspiratory muscle training (IMT) together with active exercises and early walking. One article reported a reduction in the incidence of atelectasis and pleural effusion with EM and one article reported improvements in the alveolus-artery gradient and inspiratory muscle power using an inspiratory muscle trainer combined with EM.

Conclusion: EM is effective in the prevention and rehabilitation of functional parameters after CABG surgery, by improving functional capacity, respiratory muscle power, quality of life and gas exchange, and reducing the incidence of atelectasis and pleural effusion.

Keywords: Myocardial revascularization; Early mobilization; Rehabilitation.

Introduction

Cardiovascular diseases are the main causes of death in the world, mainly in low- and middle-income countries. In Portuguese-speaking countries with a high sociodemographic index, risk factors such as dyslipidemia and hyperglycemia have a great influence on mortality from cardiovascular diseases, particularly from ischemic heart disease (IHD).[1-3]

Coronary artery obstruction due to accumulation of atheromatous plaques often requires a coronary artery bypass graft (CABG) surgery. It is important to highlight that this procedure is associated with a high rate of morbidity and mortality due to impacts on pulmonary, renal and cardiac function, caused by general anesthesia and the surgical procedure itself.[4-6]

In this scenario, physiotherapy combined with early mobilization (EM) plays an important role in reducing

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postoperative (PO) complications and functional limitations in these patients. EM is a simple intervention that reduces the time to wean from mechanical ventilation (MV) and helps in functional recovery of patients with cardiorespiratory instability.[7] The programs employ a multidisciplinary approach to progressively increase patient engagement in therapeutic activities such as bed mobility exercises, sitting at the bedside, transfer to the chair, standing position and ambulation.[7,8]

Exercise improves physical function and general health, and postponing its start contributes to aggravate patient's functional decline. Therefore, early intervention is necessary to prevent physical and psychological problems, prolonged hospitalization, and the risks associated with immobilization.[7]

In combination, EM and exercise may improve overall muscle strength, oxygen saturation (SpO_2),[8] and performance in functional tests.[9] . In addition, EM has been reported to reduce atelectasis and pleural effusion in patients undergoing CABG .[10]

In light of the above, the present study aims to systematically review, identify and describe the effectiveness of EM in the prevention and rehabilitation of functional impairments in patients undergoing myocardial revascularization surgery.

Materials and methods

This is a systematic review of the literature conducted according to the Preferred Reporting Items for Systematic reviews and Meta-Analysis Protocols (PRISMA-P, 2015). The study was registered at PROSPERO with registration number CRD42020186693.

Search strategies

The electronic search was performed in the following databases: Cochrane Library, Latin American and Caribbean Literature in Health Sciences (LILACS), Medical Literature Analysis and Retrieval System Online (MEDLINE / PUBMED) and Scientific Eletronic Library Online (SciELO) between February and March 2020, and again in February 2021. The following MeSH terms were used in the search: *" Early Ambulation"; "Ambulation, Accelerated"; "Ambulation, Early"; "Early Mobilization"; "Mobilization, Early"; "Coronary Artery Bypass"; "Artery Bypass, Coronary"; "Artery Bypasses, Coronary"; "Bypasses, Coronary Artery"; "Coronary Artery Bypasses"; "Coronary Artery Bypass Surgery"; "Bypass, Coronary Artery"; "Aortocoronary Bypass"; " Aortocoronary Bypasses"; "Bypass, Aortocoronary"; "Bypasses, Aortocoronary"; "Bypass Surgery, Coronary Artery"; "Coronary Artery Bypass Grafting"*, combined with the Boolean operators "*AND*" and "*OR*" of all the bases, as follows:

((((((("Early Ambulation") OR "Ambulation, Accelerated") OR "Ambulation, Early") OR "Early Mobilization") OR "Mobilization, Early")) AND (((((((((((("Coronary Artery Bypass") OR "Artery Bypass, Coronary") OR "Artery Bypasses, Coronary") OR "Bypasses, Coronary Artery") OR "Coronary Artery Bypasses") OR "Coronary Artery Bypass Surgery") OR "Bypass, Coronary Artery") OR "Aortocoronary Bypass") OR "Aortocoronary Bypasses") OR "Bypass, Aortocoronary") OR "Bypasses, Aortocoronary") OR "Bypass Surgery, Coronary Artery") OR "Coronary Artery Bypass Grafting")))))).

Eligebility criteria

The inclusion criteria were randomized clinical trials (RCTs) in English or Portuguese using passive mobilization, active exercises, positioning and progressions, and a cycle ergometer as the EM, combined or not with another technique in the PO period of CABG. There were no restrictions on the time of publication. Exclusion criteria were review articles and clinical trial protocols.

The articles were initially screened by reading the titles and abstracts, and those that met the eligibility criteria were selected for full-text reading.

The selected studies were entered in an Excel spreadsheet, and the outcomes of interest – study design, sample characteristics, intervention and control, analyzed outcomes and results – were extracted.

Assessment of the risk of bias

To assess the methodological quality of RCTs, the Physiotherapy Evidence Database (PEDro) scale was used. The scale is composed of 11 items, with a score of 0-10 (the first item is not included as it refers to external validity).

The titles and abstracts of the articles were evaluated by two independent reviewers and the full texts by one of the reviewers (Figure 1).

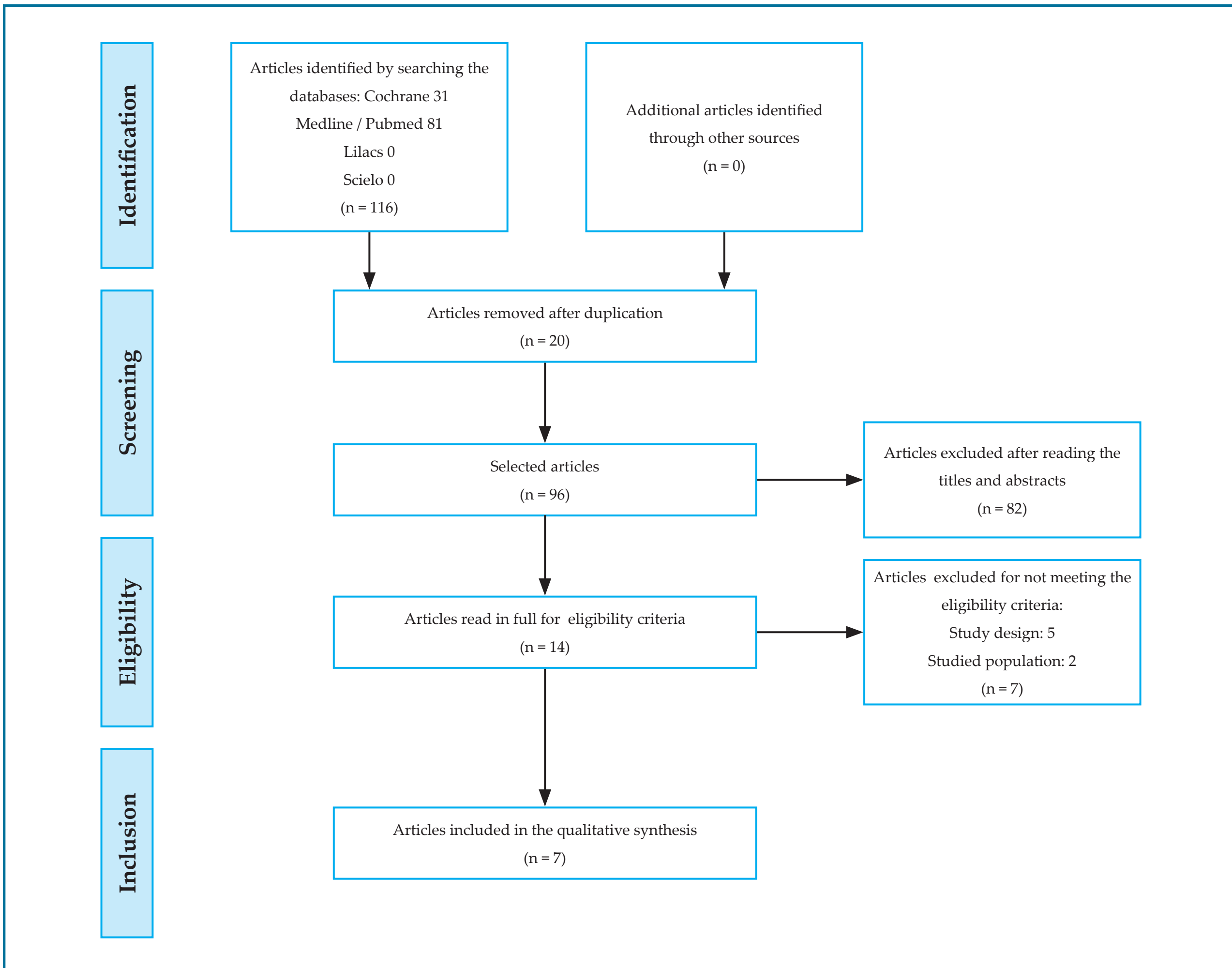

Figure 1 – Flowchart of article selection.
Source: Modified from Prisma, 2009.

Results

Initially, 116 articles were retrieved. After removing duplicates, 96 articles were screened for titles and abstracts, and 82 were excluded. To assess eligibility, 14 articles were selected for full-text reading, of which seven were excluded because they did not meet the inclusion criteria (Figure 1). Thus, seven[10-1,7] RCTs were included in the review.

Table 1 presents the characteristics of the studies, and description of the intervention and of methodological quality assessed using the PEDro scale. The years of publication ranged from 2012 to 2020; the study populations were adults and elderly men and women aged from 18 to 75 years undergoing CABG,[10,,11,13-16] –. A total of 697 participants were included, 350 in the intervention group (IG) and 331 in the control group (CG); the studies were conducted in Australia,[11] Iran,[10] Egypt,[12] Brazil,[13,15] China[14] and Germany.[16]

Functional capacity was assessed using different methods and measurements, including stationary cycling,[11] inspiratory muscle training (IMT) and early ambulation,[13] the six-minute walking (6MW) test, timed-up-and-go (TUG) test[15] and –the MacNew questionnaire,[16] and respiratory muscle strength combined with one-minute sit-to-stand test and intensive care unit (ICU) length of stay.[15] An article reported a reduction in the incidence of atelectasis and pleural effusion by EM,[10] and another study showed improvements of IMT and alveolar-arterial gradient by using a threshold load inspiratory muscle trainer (POWERbreathe) and EM resulted in improvement of inspiratory muscle power,

Table 1 – Characteristics of included studies

Author and year	Study design	Pedro scale	Sample	Intervention	Control	Analyzed outputs	Main results
Hirschhorn et al .[11] 2012	PROSPECTIVE SCREEN	9 /1 0	n = 64 (66 ± 9 years) IG: 32 CG: 32 Post-operative first CABG.	Cycle rgometer (power proportional to the square of the cycling speed) (2x / day) for 10′ with a BORG of 3 and 4 + breathing techniques and standard clinical musculoskeletal movements until hospital discharge.	Walking (2x / day) for 10′ with a BORG of 3 and 4 by the Modified Borg Scale + breathing techniques and standard clinical musculoskeletal movements until hospital discharge.	6MWA, 6MCA and SF-36v2.	There was no statistically significant difference between groups for the 6MWA tests (cyclists: 402 ± 93 m vs walkers: 417 ± 86 m, P = 0.803), 6MCA (cyclists: 15.0 ± 6.4) kJ vs walkers: 14.0 ± 6.3 kJ, P = 0.798) or health-related quality of life.
Moradian et al .[10] 2017	RCT	6/10	n = 98 IG: 49 (59 ± 10 years). CG: 49 (60 ± 11.3 years). Patients undergoing CABG.	1st POD sits in the beside with hangin legs for 15′. 2nd POD sits in the bedside for 5′ in addition of walk of 10 meters + Night walk of 30 meters. 3rd POD before and after removal of the chest tube walk 30 meters.	Routine hospital treatment. 3rd POD: mobilization after removal of the chest tube.	Presence of atelectasis and pleural effusion, SaO_2 and PaO_2.	The PaO_2 in 3DPO and percent SaO_2 in 4DPO were higher in the treatment group ($P < 0.05$). In general, the incidence of atelectasis and pleural effusion decreased in the treatment group.
Turky and Afify .[12] 2017	RCT	5/10	n = 40 participants IG: 20 CG: 20 Post-operative CABG	IMT (3x10′ 2x a day with a load of 30% of MIP with a pause of 30 to 60′′ between sets), the resistance was increased incrementally according to BORG. If < 5 the resistance would gradually increase by 2 cmH_2O or half a turn, or reduced 1 to 2 cmH_2O BORG case between 9 and 10 + EM (walking around the bed and along the corridors).	Routine respiratory physiotherapy and early mobilization (walking around the bed and through the corridors).	Arterial alveolar gradient and inspiratory muscle power.	The intervention group showed significant improvement ($P < 0.05$) in the alveolar gradients of arterial oxygen and inspiratory muscle power at all measurement points.

Zanini et al 2019.[13]	RCT	7/10	n = 40 participants divided into: G1 = 10 G2 = 10 G3 = 10 G4 or GC = 10 (18 to 70 years old). Submitted to CABG.	G1:IMT with a load of 20% of the MIP (10 x 10 breath), active training of the upper limbs and lower limbs and early walking (twice a day), conventional pulmonary therapy and Borg 11; G2: Same protocol that without IMT G1 (2x daily), CPT and Borg 11; G3: TMI with a load of 20% of the MIP (10 x 10 breath 2x daily) e CPT.	Conventional pulmonary therapy (THB, deep breathing and EPAP.	Functional capacity (6MWT).	G1 and G2 achieved a more effective recovery of FC on the 6th postoperative day, remaining greater 30 days after discharge. ($P < 0.001$ between groups).
Cui et al .[14] 2020	RCT	8/10	n = 194 participants GI = 89 GC = 89	Intervention – 1st POD transition sitting on the bed → chair at the bedside with hanging legs + 10'and can stand 3'-5' repeating 5x. 2POD equal to 1POD + minimum 20′ walk with incentive to ↑ intensity and ↑ frequency up to 5x. 3POD sit out of bed + 10', stand 5′ and walk minimum 20′ with help and incentive for ↑ intensity and ↑ frequency up to 5x. Turn back the lifestyle with walking + distant independently.	Walking on the second or third day after surgery	Post-operative hospital stay, postoperative complications and physiological and psychological functional return.	IG had ↓ postoperative hospital stay significantly compared to the CG ($P = 0.031$), with no significant difference in atelectasis and pulmonary infection ($P > 0.05$) between the two groups. Return physiological functional function + rapid evacuation to the IG compared to the CG $P < 0.001$ in addition to better PO_2 values between GI and GC $P = 0.001$. PTSD in the GI was ↓ than GC $P < 0.001$.

Steinmetz et al.[15] 2020 .	RCT	6/10	230 patients GI = 115 CG = 115 (age between 67.1 ± 8.4).	2 weeks of supervised preoperative exercise in exercise bike 3x weekly, with 70% of VO_2peak. Each session of training included 2 aerobic exercises and 15’ of light gymnastics between them. Start: 2 cycling sessions of 10'(1st session) up to 2 cycling sessions of 25' (6th session); (2nd and 3rd session: 2 × 15’, 4th and 5th session: 2 × 20’). Light gymnastics included breathing techniques and chair coordination exercises.	GC without preoperative training or additional information. Usual care provided by the patient's general practitioner. IG and GC participated in a 3-week post-cardiac rehabilitation program operative.	Baseline (T1), 1 day before surgery (T2), onset (T3) and end of cardiac rehabilitation (T4): cardiopulmonary exercise test, 6 'walk test (6MWT), timed - Up-and-Go (TUG) and QoL test (MacNew questionnaire).	171 patients (IG, n = 81; CG, n = 90) completed the study. Preoperative FC (6MWTIG: 443.0 ± 80.1 m to 493.5 ± 75.5 m, P = 0.003; TUGIG: 6.9 ± 2.0 s to 6.1 ± 1.8 s, P = 0.018) and QoL (IG: 5.1 ± 0.9 to 5.4 ± 0.9, P & lt ; 0.001) improved significantly more in the IG than in the CG. In addition to postoperative also in FC (6MWDIG: Δ-64.7 m, pT1 - T3 = 0.013; Δ + 47.2 m , pT1 - T4 & lt; 0.001; TUGIG: Δ + 1.4 s, pT1 - T3 = 0.003).
Windmoller et al.[16] 2020	RCT	6/10	n = 31 (40-75 years). GI = 15 GC = 16	Exercise bike + PEPPA (10cmH2O pressure), session single daily in 2POD (maximum length 20’), and 3POD 4POD (maximum 30’ each). Intensity estimated at up to 30 bpm of HRR; SpO2 up to 90% without oxygen therapy; and MBS between mild and moderate.	7 steps immediately for each POD gradually, with exercises between MI and MS. Evolution of positions: 1st POD lying down; 2nd POD sitting; 3rd POD to the 7th POD ambulation (between 35 and 200m). Stretches: 2nd POD (passive); 3rd POD to 7th POD (active). Up and down stairs: 4th POD and 7th POD (between 1 and 3 levels). Breathing exercises and flow stimulation: between 1st POD and 7th POD.	FC (6MWT); respiratory muscle strength and 1 ' test to get up and sit down; length of ICU stay.	FC ↓ in both groups, but IG was not significant (P = . 11); respiratory muscle strength and 1 'stand up and sit ↓ test on both the groups. Hospitalization time was ↓ in the IG (P = 0.50).

RCT: randomized clinical trial; PEDRO: Physiotherapy Evidence Database; MIP: maximum inspiratory pressure; IG: intervention group; CG: control group; CABG: coronary artery bypass surgery; IMT: inspiratory muscle training; BHT: bronchial hygiene therapy; PEPPA: positive expiratory pressure in the pathways air; 6MWT: six - minute walk test; 6MWA: distance walked on foot; 6MDC: duty cycle; SF-36: ***Short Form Health surve;*** **POD: postoperative day; EAP: early ambulation precision; PTSD:** ***Post traumatic stress disorder checklist; ‘: minutes; ’’: seconds; MBS: modified Borg scale; BPM: beats per minute; SPO2: Hemoglobin oxygen saturation; HRR: heart rate rest; LL: lower limb; UL: upper limb; FC: functional capacity;*** **CPT: Conventional pulmonary therapy. All selective articles used a statistical significance level of 5%.**

and oxygen saturation.[12] A study reported reduction in PO length of hospital stay and improvements in physiological and psychological symptoms with early ambulation.[14]

Post-traumatic stress disorder in patients undergoing CABG submitted to early ambulation (was lower (P < 0.001) compared to controls,[14] and significant improvements in functional capacity, TUG and quality of life of patients awaiting elective CABG undergoing anexercise-based prehabilitation program.[15] 'Also, patients receiving protocols combining active physical exercises and early walking experienced a more effective recovery of functional capacity, both before hospital discharge and 30 days after discharge.[13] On the other hand, there was no difference between the cycle ergometer and supervised walking in the recovery of functional capacity.[11] Most training programs were carried out twice a day, in the PO period until hospital discharge. The beginning of the interventions varied from the first PO day ,[14,15] the second PO day[10,12,13] to the third PO day,[11] and from baseline to the end of cardiac rehabilitation.[16]

Results of analysis of the methodological quality of the articles, using the PEDro scale, are shown in Table 2. The scores of all included studies were equal to or greater than five.

Discussion

The present systematic review demonstrated that EM techniques were effective in promoting rehabilitation and preventing functional decline of patients in the PO period of CABG surgery. Improvements in functional capacity, respiratory muscle power, quality of life, changes of arterial gases and in the alveolus-arterial gradient, and reductions in the incidence of atelectasis and pleural effusion and in hospital stay were reported in the studies included in the review.

Hirschhorn et al.[11] showed that both stationary cycling and moderate walking exercise were effective in recovering functional capacity in the immediate PO period of CABG. There was no difference in hospital discharge compared between groups in the 6MW test (P = 0.803) and in the 6-minute cycle work (P = 0.798). However, when compared to preoperative data, all patients obtained a significant reduction in the 6MWA and 6MCA tests (P < 0.001).

Regarding the subjective perception of effort, EM activities, according to BORG scale were between easy and slightly tiring, which is in accordance with the guidelines of the American college of sports medicine.[17] This may partially explain the positive results of EM on functional capacity.The level of effort perceived must be within acceptable levels to promote the best results, without presenting risks to patients.

Zanini et al.[13] evaluated different rehabilitation protocols after CABG. The CG that only received conventional pulmonary therapy, despite showing less recovery in functional capacity, obtained longer 6MW distance, reaching values similar to the preoperative ones. Interestingly, this study[13] did not assess subjective perception of effort during EM, which may have contributed to underestimating exercise capacity of patients, who were submitted to an amount of exercise that was less than necessary. In addition to the intensity, other exercise prescription parameters were not clear, such as time, and whether the active training of limbs

Table 2 – Methodological quality of the included studies

Author	1	2	4	3	5	6	7	8	9	10	11	Score 0/10
Hirschhorn et al.[11] 2012	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	9
Turky et al.[12] 2017	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes	5
Moradian et al.[10] 2017	Yes	Yes	Yes	Yes	No	No	No	No	Yes	Yes	Yes	6
Zanini et al.[13] 2019	Yes	Yes	Yes	Yes	No	No	Yes	Yes	No	Yes	Yes	7
Cui ***et al.***[14] ***2020***	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	8
Windmoller et al.[16] 2020	No	Yes	Yes	Yes	No	No	Yes	No	No	Yes	Yes	6
Steinmetz et al.[15] 2020	Yes	Yes	Yes	Yes	No	No	No	Yes	No	Yes	Yes	6

included resistance / calisthenic exercises focused on improving the resistance of patients (e.g., exercises with low load and greater number of repetitions).

In the study by Moradian et al.,[10] EM reduced the incidence of atelectasis and pleural effusion. This fact is relevant, as these conditions compromise gas exchange, reducing uptake and consequently the maximum oxygen consumption (VO2máx.), in addition to increasing dyspnea.[18] In fact, the mean PaO2 was 95 ± 2.5 mmHg in the IG and 93.5 ± 3 mmHg in the CG (P value = 0.01), with SaO2 of 92/3 versus 91% respectively (P value = 0.03). It is known that oxygenation, together with VO2max, is directly proportional to exercise capacity, and its elevations often correspond to an increase in the distance covered in tests such as the 6MW test.[17]

Corroborating with these findings, Hanada et al.[19] evaluated, in a retrospective study, the effectiveness of EM in preventing pulmonary complications in a group composed of 118 PO patients undergoing video-assisted thoracoscopic surgery. All participants underwent preoperative physiotherapy and EM in the PO period in the form of walking and activity of daily living without the assistance of the physiotherapist. The results showed a decrease in the incidence of PO pulmonary atelectasis (P <0.001).

Turky and Afify[12] (2017) evaluated changes in the arterial alveolus gradient and respiratory muscle power with IMT in the preoperative period and IMT and EM after surgery . After extubation, there was a progressive increase in the alveolar-arterial gradient , followed by a gradual decrease 24hrs (P <0.005), 48hrs (P <0.004) and at the end of the study (P = 0.02). The IMT through positive end-expiratory pressure provided the patient with alveolar expansion, improved gas exchange, oxygenation, right ventricular afterload , and in CABG, it may promote alveolar recruitment, reducing the incidence of atelectasis caused by prolonged time of extra-bodily circulation, surgical trauma and anesthesia.[20]Also, EM significantly improved respiratory muscle power measured by PImax, one day after extubation (P <0.001) and at the end of the study (P <0.001). Corroborating this, in a controlled study, Bonorino used the same IMT protocol (2x daily 3 series of 10 breaths) in the IG and found that preoperative training increased Plmax , resulting in a lower incidence of pulmonary complications.

A recently published clinical trial [14] showed significantly shorter hospital stay and faster physiological and psychological functional return in older adults after CABG, as well as better levels of arterial oxygenation with an accurate mobilization program. Exercise intensity was individualized based on age-predicted maximal heart rates. The use of these physiological parameters, compared with the CG (routine rehabilitation) allowed most of the intervention participants to complete the low-intensity exercises in a controlled manner, resulting in a lower incidence of post-surgical complications such as hypotension and orthostatic intolerance.[21] This allows greater safety for these older patients, considering that these complications have a significant positive association with falls.[22]

However, the study has low statistical power for secondary outcomes due to the small sample size, clinical limitations in early ambulation, high risk of bias due to the inclusion criteria of age and type of surgical procedure, and lack of blinding participants and therapists. This limits generalization or results to other hospitals that do not adopt the same interventions after CABG difficult.

Steinmetz et al.[15] aimed to determine the impact of an exercise-based pre-rehabilitation program (exercise bike and gymnastics), in the pre- and post-CABG on functional capacity and quality of life of elderly patients. The CG did not perform this program in the preoperative period and both groups performed cardiac rehabilitation in the PO period. The results of the pre- and post-CABG tests demonstrated that the individualized pre-rehabilitation program was efficient in improving functional capacity of the IG, in addition to positively influencing the cardiac rehabilitation in the PO period, even without affecting cardiopulmonary capacity.

The aforementioned results corroborate previous pilot studies that showed a significant difference in functional capacity with tests conducted before and after myocardial revascularization surgery, in addition to a reduction in the length of hospital stay (in the PO period) in patients who underwent pre-rehabilitation protocols before procedure.[23,24]

Windmoller et al.[16] evaluated the effects of two therapeutic interventions on rehabilitation of individuals in the PO period of cardiac surgery. One intervention was a standardized and progressive exercise protocol, which consists of an individualized physical therapy program. This protocol was compared with a new intervention that combined physical exercises in a cycle ergometer with continuous positive airway pressure (CPAP) and showed that the latter was safer and decreased the ICU length of stay. This result suggests a significant impact of the physical therapy intervention on hospital costs and on functional capacity of the individuals.

Although the two protocols presented in this study have shown benefits for the patients, the second has led to additional improvements. However, studies comparing the effects of the physical training on a cycle ergometer alone and the combination of this training with CPAP are still needed. Furthermore, this study had two main limitations, first, it was not possible to blind the subject or the physiotherapist for the type of treatment and, second, it was not possible to evaluate the subject in the immediate PO period to compare the outcomes between the pre- and post- periods.

The results of the present study corroborate those of the systematic review by Silva et al.[25] aimed to systematize EM in the ICU. The authors concluded that EM prevented neuromuscular disorders associated with a long length of stay in the ICU, and improved functional capacity, quality of life, and functional parameters such as peripheral and respiratory muscle strength. Although the populations of the two studies were different, we can somehow extrapolate the study result to patients with CABG, as both groups of patients (ICU and CABG) are exposed to the effects of immobilization during hospitalization.

It should be noted that EM provides the patient with significant gains in terms of functionality, quality of life, overall muscle strength, ICU length of stay and hemodynamic variables in the PO period. When administered and monitored by the physiotherapist, kinesiotherapy and cycle ergometer exercise are safe and can reduce the incidence of adverse effects. The presence of a multidisciplinary team is essential to make EM possible.[8]

Although the articles included had a PEDro scale score ≥ 5, the total number of articles is relatively small. This is a reflection of the low number of studies addressing EM alone in the PO period of CABG.

Conclusion

EM is effective in the prevention and rehabilitation of functional parameters after CABG. Especially when combined with other techniques, EM promoted an improvement in functional capacity, respiratory muscle power, gas exchange and quality of life, and a reduction in the incidence of atelectasis and pleural effusion.

Author Contributions

Conception and design of the research, analysis and interpretation of the data and writing of the manuscript: Das Judas MCL; acquisition of data: Das Judas MCL, Fontes RF, Dos Santos LLP; statistical analysis: Das Judas MCL, De Moura RF; critical revision of the manuscript for intellectual content: Fontes RF, De Moura RF, De Almeida MLO, Gomes VA.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This article does not contain any studies with human participants or animals performed by any of the authors.

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