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Efficacy of Prehabilitation Before Cardiac Surgery

A Systematic Review and Meta-analysis

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Objective: Patients awaiting cardiac surgery seem to benefit from exercise-based prehabilitation, but the impact on different perioperative outcomes compared with standard care is still unclear.

Design: Eligible nonrandomized/randomized controlled studies investigating the impact of exercise-based prehabilitation in adults scheduled for elective cardiac surgery were searched on December 16, 2020, from electronic databases, including MEDLINE, CENTRAL, and CINAHL. The data were pooled and a meta-analysis was conducted.

Results: Of 1490 abstracts, six studies (n = 665) were included into the review and meta-analysis. At postintervention interval and at postsurgery interval, 6-min-walking distance improved significantly in exercise-based prehabilitation group compared with controls (mean difference, 75.4 m; 95% confidence interval, 13.7 to 137.1 m, P = 0.02, and 30.5 m, 95% confidence interval, 8.5 to 52.6 m, P = 0.007, respectively). Length of hospital stay was significantly shorter in exercise-based prehabilitation group (mean difference, −1.00 day; 95% confidence interval, −1.78 to −0.23 day, P = 0.01). Participation in exercise-based prehabilitation revealed a significant decrease in the risk of postoperative atrial fibrillation in patients 65 yrs or younger (risk ratio, 0.34; 95% confidence interval, 0.14 to 0.83, P = 0.02).

Conclusions: The participation in exercise-based prehabilitation significantly improves postintervention and postsurgery 6-min walking distance, length of hospital stay, and decreases the risk of postoperative atrial fibrillation in patients 65 yrs or younger compared with controls.

Key Words: Cardiothoracic Surgery, Preoperative Exercise Training, Systematic Review, Meta-analysis

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What Is Known

- Prehabilitation before cardiac surgery is associated with reduced time to extubation, lower risk of postoperative pulmonary complications, and reduced length of hospital stay (LOS).

What Is New

- The participation in exercise-based prehabilitation before cardiac surgery significantly improves postintervention and postsurgery 6-min walking distance and LOS and decreases the risk of postoperative atrial fibrillation in patients 65 yrs or younger compared with controls.

In older patients undergoing cardiac surgery, a high prevalence of frailty, multiple comorbidities, and postoperative complications have been reported.[1–6] Exercise-based prehabilitation (EBPrehab) could be effective to ameliorate negative effects.

Until now, only few randomized controlled studies evaluated the effect of EBPrehab on various perioperative outcomes in patients undergoing cardiac surgery.[6–11] Four published systematic reviews[5,12–14] include studies with nonexercise-based prehabilitation, with EBPrehab and breathing exercises. These reviews found prehabilitation before cardiac surgery to be associated with reduced time to extubation, lower risk of postoperative pulmonary complications, and reduced length of hospital stay (LOS).[5,12–14]

The effect of EBPrehab on postoperative functional capacity, various outcomes of postoperative recovery status, quality of life, exercise capacity, and cost effectiveness is not well evaluated. The aim of this systematic review and meta-analysis was to evaluate the effect of EBPrehab, explicitly focused on the exercise modalities, on preoperative and postoperative functional status measured by 6-min walking distance (6MWD), Timed Up and Go (TUG) time, 5-meter gait speed, or Short Physical Performance Battery (SPPB). Furthermore, we analyzed the impact of EBPrehab on postoperative recovery status, quality of life, exercise capacity, and cost effectiveness.

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The results had been presented as an E-Poster at the 45th Annual Meeting from the German Society for Prevention and Rehabilitation of Cardiovascular Diseases, Berlin, Germany, June 24, 2022.

BBW, CS, and CW designed this systematic review. CS and CW performed the systematic literature search. BBW, CS, and CW selected and evaluated retrieved studies. BBW, CS, and CW extracted the data and assessed the risk of bias. CS, CW, and TFS computed the meta-analysis and analyzed the data. CS, CW, and BBW drafted the manuscript, and TFS and TW critically revised it. All authors gave their final approval and agreed to be accountable for all aspects of work ensuring integrity and accuracy. The manuscript had been read and approved by all authors.

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METHODS

Protocol, Registration, and Study Eligibility Criteria

This systematic review was conducted according to the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (see Supplementary Checklist, Supplemental Digital Content 1, http://links.lww.com/PHM/B799).[15] The study protocol has been published previously in the PROSPERO (International prospective register of systematic reviews) registry (CRD42020213207). Inclusion criteria are listed in Table 1.

Data Sources, Search Strategies, and Identification of Studies

We developed search strategies based on the Population Intervention Control Outcome model (BBW, CS, CW). A systematic literature search was performed on December 16, 2020, using MEDLINE, CENTRAL, and CINAHL. We supplemented the initial results of the systemic database search by manual searches using reference lists of other reviews and articles.[11] Details of all search strategies are documented in the Supplementary Material (Supplemental Digital Content 2, http://links.lww.com/PHM/B800).

Outcomes Definition

The preoperative and postoperative functional status measured by 6MWD, TUG time, 5-meter gait speed, or SPPB was defined as the primary end point. Predefined secondary end points were postoperative recovery status measured by postoperative surgical complications (length of stay at intensive care unit [ICU], LOS, time to extubation, and postoperative complications as pneumonia, atelectasis, and atrial fibrillation [AF]). Additional predefined secondary end points were cardiovascular events (mortality and stroke), preoperative and postoperative quality of life measured by SF-36, MacNew questionnaire or other validated questionnaires, preoperative and postoperative exercise capacity (measured by peak oxygen consumption [VO_{2peak}] or peak work load), and cost effectiveness.

Study Selection and Data Extraction

We used EndNote X9 (Clarivate Analytics, 2018, Philadelphia) system for reference management. Three reviewers (BBW, CS, and CW) independently screened all articles by titles and abstracts. Full text of potentially suitable studies was evaluated by the three reviewers according to a predefined scheme based on Population Intervention Control Outcome criteria (Table 1). Final selection of studies was discussed by all authors (BBW, CS, CW, TFS, and TW) and in case of disagreement ruled by majority vote (Fig. 1).

Data were extracted from full texts of the eligible publications into a standardized data extraction form (CS; Table 2) and entered into Review Manager 5.4.1 (The Cochrane Collaboration, 2020; London) by CS. Primary reasons for study exclusion at the Population Intervention Control Outcome selection level are listed in Figure 1.

Assessment of Risk of Bias Domains

The Cochrane Collaboration tool was used to assess the risk of bias for all included randomized controlled studies.[16] Two reviewers (CS, CW) rated the risk of bias, and in case of disagreement, a third reviewer (BBW) made a final determination.

TABLE 1. Inclusion criteria for literature selection

Population	
Age	≥18 yrs
Type of surgery	Patients before nonurgent cardiac surgery: Index event is cardiac surgery: CABG surgery; heart valve surgery: aortic, pulmonary, tricuspid or mitral valve replacement or repair; combined heart valve and CABG surgery and transcatheter aortic valve implantation
Intervention	(a) Any form of formal structured exercise intervention (e.g., aerobic exercise training, resistance training or endurance-resistance training) alone or in combination with comprehensive intervention (e.g., education, psychological support); (b) The exercise program should meet the following requirements: minimum cumulative duration of training interventions of 90 mins/wk; Minimum of 2-wk training program duration; minimum of 6 training sessions in consumption; clear documentation of type of exercise, number of sessions, program duration, and intensity
Control	Standard care without exercise-based prehabilitation program
Reported follow-up	The follow-up period must be ≥4 wks postoperative
Accepted study designs	Randomized controlled trials; controlled nonrandomized trails addressing a possible risk of bias by adequate statistical methods; postintervention, postoperative outcomes documented; published in English or German; peer reviewed
Primary outcome	Preoperative and postoperative functional status measured by 6MWD, TUG time, 5-meter gait speed, or SPPB
Secondary outcome	(a) Postoperative recovery status measured by postoperative surgical complications (length of ICU, LOS, time to extubation and additional postoperative complications as pneumonia, atelectasis, and AF) and cardiovascular events (mortality, stroke); (b) Preoperative and postoperative quality of life measured by SF-36, MacNew questionnaire, or other validated questionnaires; (c) preoperative and postoperative exercise capacity (VO_2peak or Wattpeak); (d) cost effectiveness (costs in reduction of in-hospital stay minus costs of prehabilitation)
Publication year	Studies published in 2000 or later.

SF-36, Short-Form 36 questionnaire; Wattpeak, peak maximum workload.

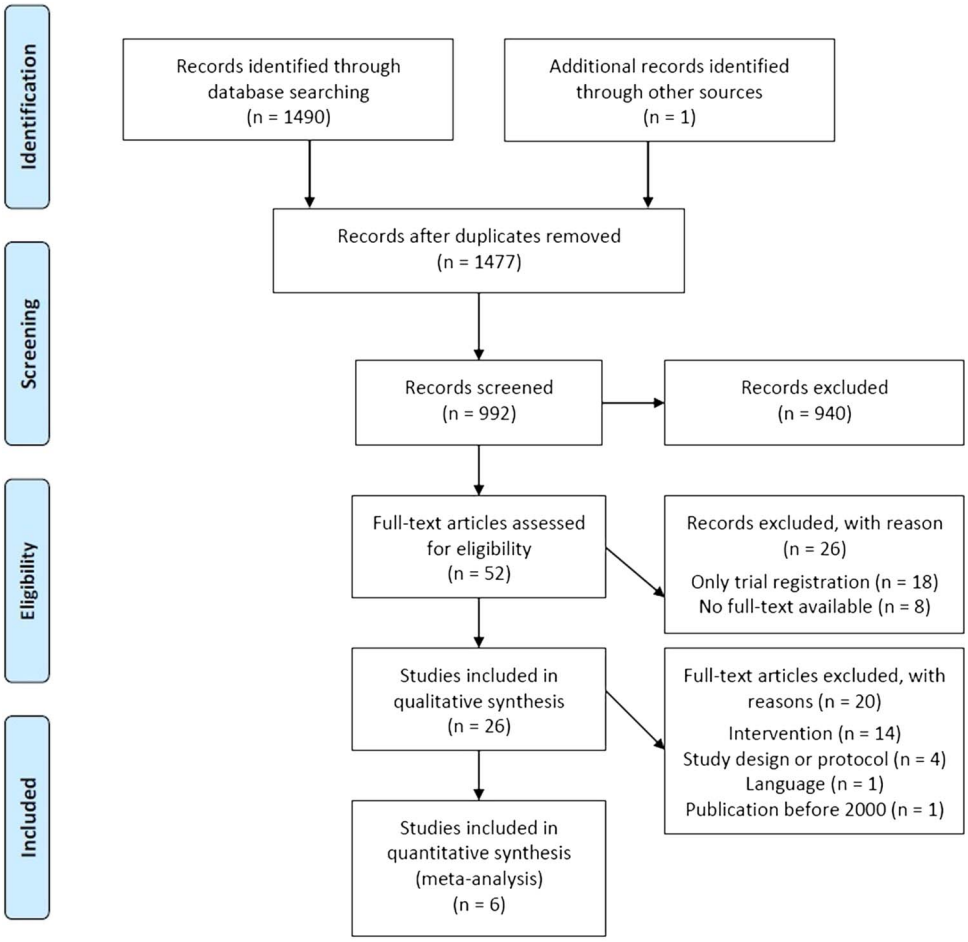

FIGURE 1. Flow diagram of study inclusion and exclusion process.

Statistical Analysis and Data Synthesis

To analyze the data and to perform a meta-analysis the STATA Software SE16 (StataCorp LLC, 2019, TX) and Review Manager 5.4.1 (The Cochrane Collaboration, 2020) were used. Where studies applied the same type of intervention and comparator, we pooled the results using a random-effect meta-analysis with hazard ratios for time-to-event outcomes. In addition, we assessed standardized mean differences for continuous outcomes and risk ratios for binary outcomes. For each outcome, 95% confidence interval and two-sided *P* values were calculated as well. Peto odd ratio was estimated for perioperative mortality. This method for estimating relative effects is recommended for binary end points with rare events.[17] As a random-effect model, the "DerSimonian and Laird approach" was applied because clinical heterogeneity and methodological heterogeneity were expected between the studies. This method is the most frequently used approach for estimating the between-study variance.[18] Some studies calculated only medians and interquartile ranges instead of means and standard deviations. For these, we approximated mean and standard deviation as proposed by Wan et al.[19] When possible, we performed subgroup analyses comparing age (≤65 vs. >65 yrs) and surgery type (coronary artery bypass graft [CABG] surgery or valve surgery versus combined valve and CABG surgery). Heterogeneity between the studies in effect measures was assessed using both the χ^2 test and the I^2 statistic.

RESULTS

Study Characteristics

Initial systematic search of literature identified 1490 articles. After the review of titles and abstracts, 52 publications remained for full-text evaluation. Finally, six studies fulfilled all criteria and were selected for this analysis (Fig. 1).

Table 2 provides a detailed overview of all included studies. Five studies[6–10] were single-center studies and one study presents a subanalysis of an ongoing multicenter study.[11] Sample size varied from 17 to 246 participants. In three studies, patients' mean age was older than 65 yrs[6,9,11] and in the other three, it was 65 yrs or younger.[7,8,10] Four studies included patients before CABG surgery,[6–8,10] and two studies included patients before CABG and/or valve surgery (aortic valve repair/replacement[9] and mitral valve repair/replacement[11]). Five studies[7–11] integrated multimodal preoperative intervention (e.g., exercise and/or education and/or psychological support). In one study,[6] the intervention included an aerobic exercise training on cycle ergometer only.[6] Herdy et al.[8] published the only study including respiratory exercise training in the multimodal preoperative intervention.

TABLE 2. Characteristics of the included studies

Article, Year	Sample Size	Mean Age, yr	Sex, Male %	Surgery Type	Country	PreOP Intervention	Duration of PreOP Treatment	Control	Main Outcomes
Arthur et al.[7] (2000)	246	IG: 61.8 ± 8.4 CG: 63.8 ± 7.8	IG: 87.8% CG: 82.9%	CABG	Canada	Multimodal	8 wks	UC + EDU	ICU, LOS, QoL, PEP, ISEL, SSTAI, HSUQ
Herdy et al.[8] (2008)	56	IG: 61 ± 10 CG: 58 ± 9	IG: 69% CG: 74%	CABG	Brazil	Multimodal	Minimum 5 d	UC	LOS, PC, EET
Rosenfeldt et al.[9] (2011)	117	IG: 62.5 CG: 68	IG: 78% CG: 70%	CABG/valve	Australia	Multimodal	Approximately 10 wks	UC	QoL, LOS, PC
Sawatzky et al.[10] (2014)	17	IG: 64 ± 7 CG: 63 ± 9	IG: 75% CG: 86%	CABG	Canada	Multimodal	Minimum 4 wks	UC + PAM	6MWT, 5MGST, AA, QoL, PHQ-9, CAQ, ESEI
Stammers[11] (2016)	26	IG: 72.8 ± 7.1 CG: 70.3 ± 5.4	IG: 78.6% CG: 75%	CABG/valve	Canada	Multimodal	4–8 wks	UC + PAM	FFI, AA, 6MWT, SPPB, GSD, oPHA
Steinmetz et al.[6] (2020)	203	IG: 66.1 ± 9 CG: 67.9 ± 7.9	IG: 88.6% CG: 88.3%	CABG	Germany	Unimodal	2 wks	UC	6MWT, TUG, QoL

5MGST, 5-meter gait speed; AA, actical accelerometer; CAQ, Cardiac Anxiety Questionnaire; CG, control group; EDU, education; EET, endotracheal extubation time; ESEI, Exercise Self-Efficacy Index; FFI, Functional Frailty Index; GSD, grip strength dynamometer; HSUQ, Health Services Utilization Questionnaire; ISEL, Interpersonal Support Evaluation List; oPHA, other physical activity assessments; PAM, preassessment meeting; PC, postoperative complications; PEP, peak exercise performance; PHQ-9, Patient Health Questionnaire 9; preOP, preoperative; QoL, quality of life; SSTAI, Spielberger State-Trait Anxiety Inventory; UC, usual care.

However, patients did not perform an inspiratory muscle training as outlined in the study eligibility criteria.[8]

All participants of the intervention groups participated in a supervised exercise training. The preoperative interventions duration ranged from 5 days up to 8 wks and the frequency of exercise training varied from two up to seven sessions per week with a single session duration between 35 and 90 mins.

In five studies, the exercise intensity of the aerobic endurance training was calculated based on the results of a cardiopulmonary exercise test. The intensity used varied from 40%–70%[7] up to 70%–85% of maximal oxygen consumption (in milliliters per kilogram per minute).[6,10] One study did not specify exercise intensity used,[8] and one study used heart rate reserve calculation (40%–85%) to control exercise intensity.[11] The only study not using a cardiopulmonary exercise test[9] set the exercise intensity by 60% of the expected maximum heart rate (220 minus age). Furthermore, the exercise modalities and methods used varied within the integrated studies (interval or continuous aerobic exercise mode with or without light resistance exercise and/or stretching and more).

Rosenfeldt et al.[9] advised the intervention group to perform regular exercise training at home (30 mins/d) in addition to the supervised exercise program.[9]

The follow-up period was highly variable and ranged from 0–6 wks to 3–12 months postoperatively (Table 2).

Risk of Bias

All included studies are at high risk for performance bias because the type of intervention did not allow for blinding of patients and clinical staff. Herdy et al.[8] lacks critical information in their publication and was therefore rated with two unclear risks of selection bias.[8] Only in two[8,11] of the six included studies the detection bias is evaluated with a low risk of bias. Arthur et al.,[7] Rosenfeldt et al.,[9] and Steinmetz et al.[6] showed an unclear risk of detection bias, and Sawatzky et al.[10] even showed a high risk in blinding of outcome assessment. These classifications are results of missing information in the respective publications,[9] and only medical staff who collected primary end point data were blinded.[7] In the study from Steinmetz et al.,[6] all involved staff—except study nurses and surgeons—were unblinded to the intervention.[6] The study from Sawatzky et al.[10] was rated with a high risk of detection bias because the person who conducted all tests was not blinded.[10] A summary of the risk of bias is provided in Figure 2. We did not assess publication bias by funnel plot, because less than 10 studies were included in the meta-analysis.[20]

Outcomes

Table 3 summarizes all results of the review and meta-analysis.

Primary End Point

Functional Capacity

Functional capacity was assessed using 6MWD, TUG time, 5-meter gait speed, and SPPB. No meta-analysis was conducted with respect to the TUG test,[6] 5-meter gait speed test,[10] and SPPB,[11] as results were only available in individual studies (Table 3).

The 6MWD was assessed in four of the included studies.[6,8,10,11]

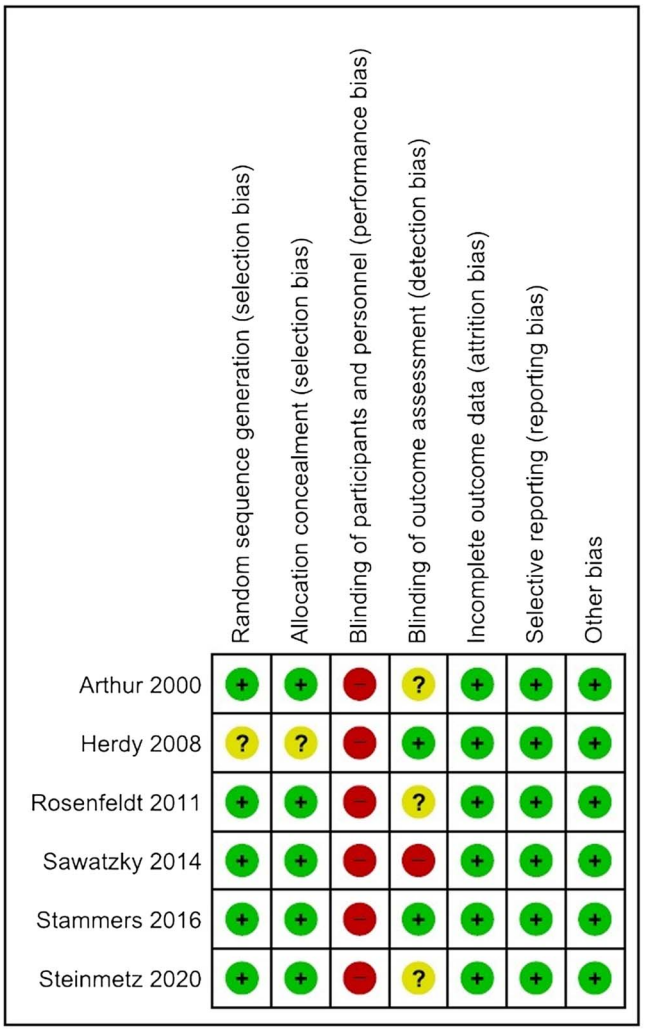

FIGURE 2. Risk of bias for all included studies.

In this meta-analysis, patients in the EBPrehab group show a significant improvement in 6MWD after intervention, compared with a control group (Fig. 3.1, Table 3). Two studies[6,8] used the 6MWD at baseline and hospital discharge, and our meta-analysis found a significant improvement in 6MWD in the EBPrehab group, when compared with controls (Fig. 3.2, Table 3). However, the meta-analysis fails to identify a positive influence of EBPrehab on the development of 6MWD in the postoperative follow-up period (Fig. 3.3, Table 3).

Selected Secondary End Points

Postoperative Surgical Parameter

Participants who received EBPrehab spent significantly less time in hospital, compared with the inactive control group (Table 3). Results of a subgroup analysis underlined that in particular, patients younger than or equal to 65 yrs had shorter hospital stays than participants older than 65 yrs (Table 3). ICU length of stay was not significantly impacted by EBPrehab (Table 3).

Postoperative Complications

Results of this meta-analysis provide no evidence for a decreased incidence of postoperative AF due to EBPrehab (Table 3). Nevertheless, a subgroup analysis of patients younger than or equal to 65 yrs showed a significantly reduced risk of postoperative AF. This effect was not seen in patients older than 65 yrs (Table 3, Fig. 4).

DISCUSSION

Our systematic review and meta-analysis finds that in patients awaiting cardiac surgery, EBPrehab has a significant impact on functional capacity (6MWD) directly after intervention and a sustained effect after surgery. Participation in EBPrehab was also associated with a significantly shorter hospital stay. In addition, we identified a significant association between EBPrehab participation and reduced risk of postoperative AF in patients 65 yrs or younger.

Because of the high heterogeneity of the included studies, we caution for a careful interpretation of the results.

Pooling and analyzing the data posed challenges due to the large differences between the EBPrehab programs, different outcome parameters used, and different measurement times. A pooling of data in between of two measurement time points in SPPB and quality of life was not conducted because of missing values (SDmeans).

We could not estimate a meaningful correlation coefficient because required data were not included in the original publications and unavailable to us. We abstained from estimating a correlation coefficient by "reasoned argument" because interpretation would have been difficult.[21]

Because of the lack of available data, other tests of functional capacity—neither SPPB or 5-meter-gait speed test—nor quality of life or exercise capacity could not be included in this meta-analysis.

This is the first meta-analysis focusing on the quality of preoperative exercise modalities and on the effect of EBPrehab on functional capacity as well as postoperative complications.

Measuring the 6MWD by 6MWT is one of the most common clinical tests to assess patients' functional capacity.[22] The 6MWT may be used before surgery to identify patients with a high likelihood of developing postoperative complications, such as postoperative cognitive dysfunction (univariate analysis: odds ratio [OR] for each increase of 50 m in the 6MWD was 0.803; 95% confidence interval [CI], 0.699 to 0.923, $P = 0.002$; multivariable analysis: OR for each increase of 50 m in the 6MWD was 0.807; 95% CI, 0.690 to 0.943, $P = 0.007$; optimal cutoff level of the preoperative 6MWD: 405 m).[23]

A meta-analysis from Marmelo et al.[5] failed to detect a significant effect of prehabilitation on 6MWD after surgery (standardized mean difference, 0.89; 95% CI, −0.06 to 1.84, two studies, 58 participants, $I^2 = 53\%$, $P = 0.07$). The authors attributed the missing effect to the paucity of available data.[5] Yau et al.[14] were unable to pool postoperative 6MWT data because of different measurement time points. The same authors[14] also found no significant effect of EBPrehab on 6MWD immediately before surgery (mean difference [MD], 81.9 m; 95% CI, −23.3 to 187.1 m; two studies, 41 participants, $I^2 = 92\%$), explaining this with different durations of prehabilitation programs.[14] Including the data of a recently published study[6] allowed us to pool results from different perioperative measurements (baseline to postintervention: MD, 75.4 m; 95% CI, 13.7 to 137.1 m; three studies, 244 participants, $I^2 = 78\%$, $P = 0.02$; postsurgery: MD, 30.5 m; 95% CI, 8.5 to 52.6 m; two studies, 259 participants,

TABLE 3. Overview of the results

	Trial(s), Sample Size	Results
Primary end points		
Functional capacity 6MWD	4 studies,[6,8,10,11] n = 302	After intervention (3 studies, n = 246[6,10,11]): MD, 75.36 m; 95% CI, 13.65 to 137.07 m, I^2 = 78%, P = 0.02; hospital discharge (2 studies, n = 259[6,8]): MD, 30.54 m; 95% CI, 8.45 to 52.63 m, I^2 = 0%, P = 0.007; follow-up (2 studies, n = 220)[6,10]: MD, 77.16 m; 95% CI, −10.96 to 165.29 m, I^2 = 80%, P = 0.09
TUG time	1 study,[6] n = 203	Overall: preop minus baseline: MD, −0.33 secs; 95% CI, −0.52 to −0.14 secs; postop minus baseline: MD, 2.10 secs; 95% CI, 1.68 to 2.51 secs
5-meter gait speed time	1 study,[10] n = 17	Overall: preop minus baseline: MD, −1.6 secs; 95% CI, −0.5 to −2.7 secs; postop minus baseline: MD, −1.2 secs; 95% CI, −2.6 to 0.3 secs
SPPB	1 study,[11] n = 26	No pooling/calculation because of missing raw data!
Secondary end points		
Exercise capacity VO_2peak	1 study,[6] n = 203	Overall: preop minus baseline: MD, 32.34 ml/min; 95% CI, 2.65 to 62.04 ml/min; postop minus baseline: MD, −320.33 ml/min; 95% CI, −375.05 to −265.61 ml/min
Peak work load	1 study,[6] n = 203	Overall: preop minus baseline: MD, 2.22 w; 95% CI, −0.29 to 4.73 w; postop minus baseline: MD, −10.44 w; 95% CI, −14.56 to −6.32 w
Quality of life QoL (SF-36[7,9]; MacNEW[6])	3 studies,[6,7,9] $n_{SF\text{-}36}$ = 363; n_{MacNew} = 203	SF-36: no pooling/calculation because of missing raw data; MacNEW: overall: preop minus baseline: MD, 0.15; 95% CI, 0.00 to 0.31; postop minus baseline: MD, −0.51; 95% CI, −0.73 to −0.28
Postoperative surgical parameter LOS	6 studies,[6–11] n = 621; ≤65[7,8,10]: n = 291; >65[6,9,11]: n = 330	MD, −1.00 d; 95% CI, −1.78 to −0.23 d, I^2 = 92%, P = 0.01; ≤65: MD, −1.67 d; 95% CI, −3.33 to 0.00, I^2 = 87%, P = 0.05; >65: MD, −0.53 d; 95% CI, −1.77 to 0.71 d, I^2 = 66%, P = 0.40
ICU	4 studies,[7,8,10,11] n = 317	MD, −265.73 mins; 95% CI, −553.21 to 21.74 mins, I^2 = 49%, P = 0.07
Endotracheal extubation	1 study,[8] n = 56	MD, −286 mins; 95% CI, −572.1 to 0.1, P = 0.05
Postoperative complications AF	5 studies,[6,8–11] n = 401; ≤65 yrs[7,8,10]: n = 291; >65 yrs[6,9,11]: n = 330	RR, 0.82; 95% CI, 0.52, to 1.29, I^2 = 33%, P = 0.39; ≤65 yrs: RR 0.34; 95% CI, 0.14 to 0.83, I^2 = 0%, P = 0.02; >65 yrs: RR 1.04; 95% CI, 0.72 to 1.49, I^2 = 0%, P = 0.85
Postoperative pneumonia	2 studies,[8,11] n = 82	RR, 0.12; 95% CI, 0.02 to 1.00, I^2 = 0%, P = 0.05
Postoperative atelectasis	2 studies,[8,10] n = 71	RR, 0.20; 95% CI, 0.06 to 0.73, I^2 = 0%, P = 0.01
Pleura effusion	2 studies,[6,8] n = 259	RR, 0.72; 95% CI, 0.28 to 1.88, I^2 = 70%, P = 0.07
Postoperative stroke	2 studies,[6,11] n = 229	RR, 0.35; 95% CI, 0.04 to 3.27, I^2 = 0%, P = 0.36
Perioperative mortality	4 studies,[6–8,11] n = 531	Peto OR, 0.54; 95% CI, 0.14 to 2.06, I^2 = 59%, P = 0.36
Cost effectiveness	1 study,[7] n = 246	Participation in EBPrehab group: one day less hospital stay, P = 0.002; net cost saving: $133 per patient per day

n, number of participants; preop, preoperative; postop, postoperative; QoL, quality of life; SF-36, Short-Form 36; w, watt.

I^2 = 0%, P = 0.007; follow-up: MD, 77.2 m; 95% CI, −11.0 to 165.3 m; two studies, 218 participants, I^2 = 80%, P = 0.09) and confirmed the positive effects of EBPrehab on perioperative 6MWD demonstrated by previous meta-analysis.[5,14] Nevertheless, these results have to be interpreted with caution because of the heterogeneity of the studies included, especially regarding EBPrehab programs details provided. More high-quality randomized controlled trials (RCTs) with comparable EBPrehab programs, outcome parameters, and follow-up intervals are needed to confirm clear evidence of the effectiveness of such programs on perioperative and postoperative functional capacity.

In patients undergoing cardiac surgery AF is the most common postoperative arrhythmia with an incidence of 20%–40%.[24–26] Advanced age is a known risk factor for developing postoperative AF (POAF).[27,28] A recently published systematic review and meta-analysis[26] including 32 studies with 155,575 patients undergoing cardiac surgery found that 23.7% of the patients developed POAF. In the same publication,[26] a meta-analysis of 10 studies (n = 44,367 patients) demonstrated increased 1-yr mortality in patients with POAF (OR, 2.60; 95% CI, 2 to 3.38, P < 0.01). Aggregate adjusted hazard of death (16 studies, n = 84,295 patients) was also increased in patients with POAF (hazard ratio, 1.25; 95% CI, 1.2 to 1.3, P < 0.01).[26] Identifying interventions to prevent POAF would therefore be of great clinical value. In our meta-analysis, we found evidence that EBPrehab may be such a promising intervention to reduce POAF in younger patients (age ≤65 yrs). Our overall cohort results on POAF (risk ratio [RR], 0.82; 95% CI, 0.52 to 1.29; five studies; 401 participants, I^2 = 33%, P = 0.39) confirm those reported in the meta-analysis from Yau et al.[14] as they documented a risk ratio of 0.75; 95% CI, 0.38 to 1.46, I^2 = 50%, in four studies, including 214 participants.[14] These findings do not allow a generalization and have to

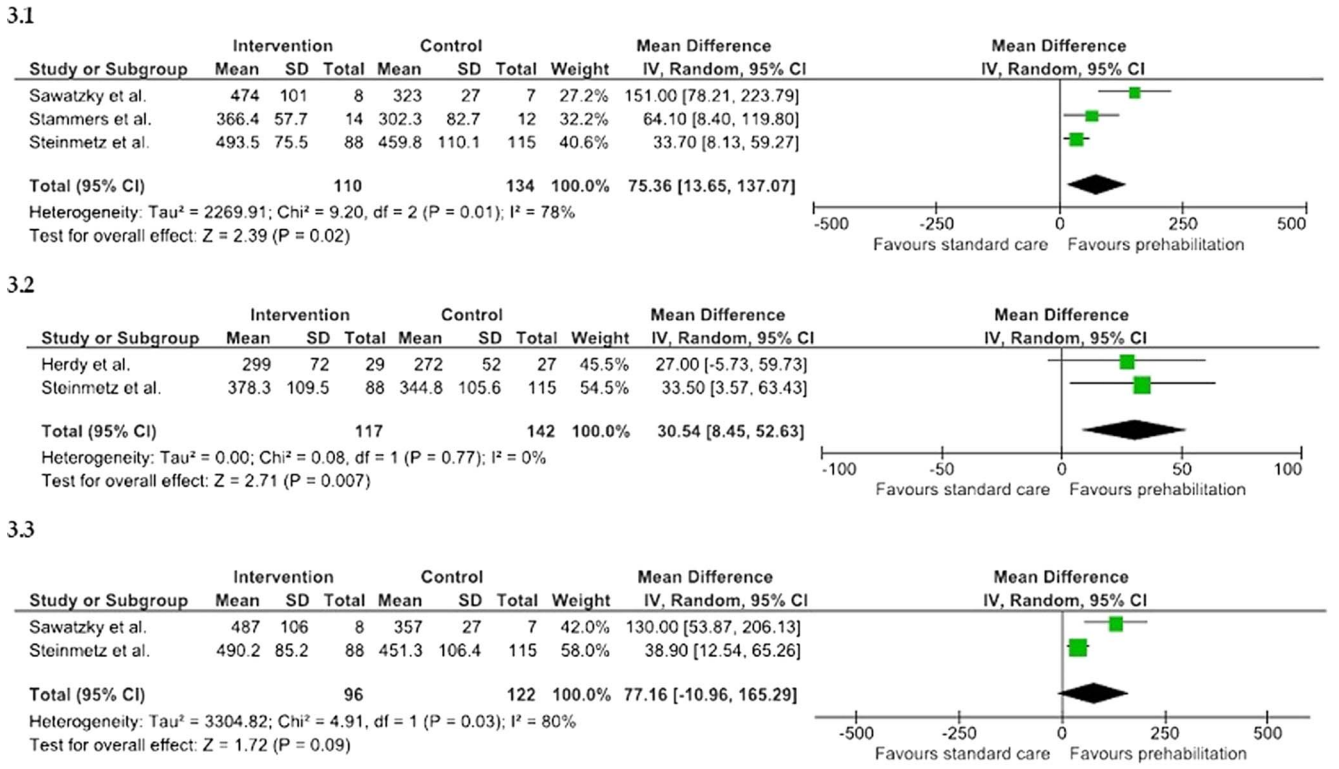

FIGURE 3. 1, Forest plot of the effect of prehabilitation versus standard care on 6MWD after intervention. 2, Forest plot of the effect of prehabilitation versus standard care on 6MWD after surgery. 3, Forest plot of the effect of prehabilitation versus standard care on 6MWD follow-up.

be interpreted with caution. Further RCTs need to substantiate these interesting results.

Poor physical health status before cardiac surgery is associated with longer hospital stay, prolonged postoperative ventilation, and a higher incidence of perioperative morbidity and mortality.[29,30]

The effect of EBPrehab on LOS is in line with the results of Yau et al.[14] Both meta-analyses confirm a reduction in LOS of 1 day after participation in EBPrehab compared with a control group (MD, −1.00 day; 95% CI, −1.78 to −0.23 day, six studies, 621 participants, I^2 = 92%, P = 0.01; Yau et al.[14]: MD, −0.66 day; 95% CI, −1.29 to −0.03 day, I^2 = 45%; four studies, 567 participants, P = 0.04). The meta-analysis from Hulzebos et al.[12] included EBPrehab as well as different kinds of respiratory muscle training. These results revealed a significant decreased LOS after prehabilitation compared with controls (MD, −3.21 days; 95% CI, −5.73 to −0.69 day).[12]

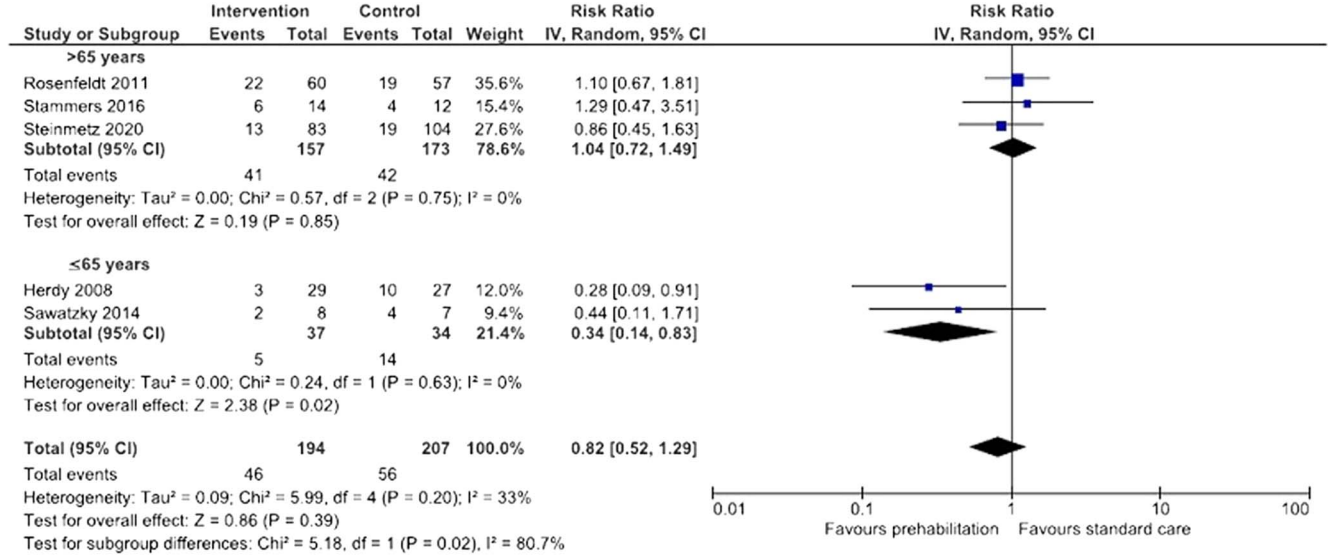

FIGURE 4. Forest plot of the effect of prehabilitation versus standard care on postoperative AF with subgroup analysis by age dichotomized at 65 yrs.

Results of our meta-analysis do not provide any information on whether EBPrehab is able to reduce mortality after cardiac surgery. Available data on preoperative mortality during waiting period before cardiac surgery is scarce. The effect of EBPrehab on perioperative mortality in our meta-analysis confirm the results from Yau et al.[14] Both meta-analyses find no significant effect on perioperative mortality but favor EBPrehab (Peto OR, 0.54; 95% CI, 0.14 to 2.06, $I^2 = 59\%$, four studies, 531 participants, $P = 0.36$; Yau et al.[14]: Peto OR, 1.30; 95% CI, 0.28 to 5.95, $I^2 = 0\%$; four studies, 532 participants, $P = 0.40$). More RCTs are needed to evaluate the effect of EBPrehab on perioperative mortality.

Limitations

We caution to keep the limitations of systematic reviews and meta-analysis in mind when interpreting the results. The main limitations of our study were that only six articles were included in the analysis and that the comparisons between the studies were compromised by considerable heterogeneity in methods used by the various authors. Some studies did not outline the detailed description of EBPrehab. Furthermore, the calculation of the individual exercise intensity was not standardized. A subgroup analysis between patients received EBPrehab or comprehensive prehabilitation was not possible because only in one study participants of the intervention group performed a pure EBPrehab.[6] In addition, all included studies show a high risk of performance bias. Blinding of patients and clinical staff was not possible because of the type of intervention.

CONCLUSIONS

In this meta-analysis, we were able to demonstrate significant improvements in postinterventional as well as postsurgical functional capacity measured using the 6MWD due to EBPrehab. In addition, we identified a significant reduction in the LOS in EBPrehab participants compared with controls. The impact of an EBPrehab program on AF or perioperative mortality remains unclear. A subgroup analysis showed a significant decrease in the risk of POAF in patients 65 yrs or younger, but not in patients older than 65 yrs. High-quality studies are needed to evaluate the impact of EBPrehab on postoperative recovery and quality of life.

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