BMJ Open Systematic review of preoperative physical activity and its impact on postcardiac surgical outcomes

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ABSTRACT

Objectives The objective of this systematic review was to study the impact of preoperative physical activity levels on adult cardiac surgical patients' postoperative: (1) major adverse cardiac and cerebrovascular events (MACCEs), (2) adverse events within 30 days, (3) hospital length of stay (HLOS), (4) intensive care unit length of stay (ICU LOS), (5) activities of daily living (ADLs), (6) quality of life, (7) cardiac rehabilitation attendance and (8) physical activity behaviour.

Methods A systematic search of MEDLINE, Embase, AgeLine and Cochrane library for cohort studies was conducted.

Results Eleven studies (n=5733 patients) met the inclusion criteria. Only self-reported physical activity tools were used. Few studies used multivariate analyses to compare active versus inactive patients prior to surgery. When comparing patients who were active versus inactive preoperatively, there were mixed findings for MACCE, 30 day adverse events. HLOS and ICU LOS, Of the studies that adjusted for confounding variables, five studies found a protective, independent association between physical activity and MACCE (n=1), 30-day postoperative events (n=2), HLOS (n=1) and ICU LOS (n=1), but two studies found no protective association for 30-day postoperative events (n=1) and postoperative ADLs (n=1). No studies investigated if activity status before surgery impacted quality of life or cardiac rehabilitation attendance postoperatively. Three studies found that active patients prior to surgery were more likely to be inactive postoperatively.

Conclusion Due to the mixed findings, the literature does not presently support that self-reported preoperative physical activity behaviour is associated with postoperative cardiac surgical outcomes. Future studies should objectively measure physical activity, clearly define outcomes and adjust for clinically relevant variables. Registration Trial registration number NCT02219815. PROSPERO number CRD42015023606.



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INTRODUCTION

Recent reports suggest that more than half of cardiac surgeries are being performed on older adults who are more likely to be frail

Strengths and limitations of this study

- There were mixed findings regarding the impact of physical activity on postcardiac surgical outcomes.
- Only self-reported physical activity tools were used.
- The multiple tools to measure physical activity and the variety of definitions of outcomes did not allow for a quantitative synthesis (meta-analysis).

and have multiple comorbidities. While cardiac surgery has been shown to improve the outcomes of these patients, more than 75% of major perioperative complications and deaths occur in older adults.^{2 3} Before surgery, many of these patients are deconditioned and have diminished resilience in the face of major stressors such as cardiac surgery, and it has been postulated that they could benefit from a therapeutic intervention prior to their major surgical procedure in order to reduce their operative risk. However, little information exists to evaluate the benefit of preoperative risk reduction strategies for the older cardiac surgery patient.

Adopting and sustaining a more physically active lifestyle is typically intended to be a part of an interdisciplinary rehabilitation plan that is instituted postoperatively and has been shown to reduce the risk of cardiac mortality and hospital admissions and improve health-related quality of life (OOL) in patients. Importantly, older adults who sustain a physically active lifestyle after a postoperative exercise-based rehabilitation programme can continue to improve their functional walking status.⁵ However, evidence suggests that cardiac surgery patients are highly sedentary during the preoperative period, especially in older adults.⁶ Furthermore, few randomised controlled trials exist that evaluate the therapeutic benefit of preoperative lifestyle modification in patients



undergoing cardiac surgery.^{7–9} Information regarding the link between preoperative physical activity and postoperative health outcomes in cardiac surgery patients would be valuable for healthcare providers to assist them in selecting patients who might benefit from preoperative exercise therapy.

The purpose of this systematic review was to compare the following postoperative outcomes between cardiac surgery patients defined as physically active prior to surgery and those who were defined as physically inactive preoperatively: (1) major adverse cerebrovascular and cardiovascular events (MACCEs), (2) 30-day adverse events as defined by the Society of Thoracic Surgeons (STS), ¹⁰ (3) hospital length of stay, (4) intensive care unit (ICU) length of stay, (5) health-related QOL, (6) activities of daily living (ADLs), (7) cardiac rehabilitation attendance and (8) physical activity levels postoperatively.

MATERIAL AND METHODS

The protocol for this systematic review has been described in PROSPERO: CRD42015023606. Note the following ad hoc changes to the previous protocol: ICU length of stay and postoperative physical activity as additional outcomes were explored in this systematic review.

Eligibility criteria

Eligible studies included cohort studies that examined adult (>18 years) cardiac surgery patients undergoing coronary artery bypass grafting (CABG), aortic or mitral valve repair/replacement, transcatheter aortic valve implantation or combined procedures. Studies with patients undergoing congenital cardiac surgery, heart transplantation or left ventricular assist device implantation procedures were excluded. Studies could compare physically active versus inactive patients prior to cardiac surgery on the basis of subjective (eg, questionnaire) or objective (eg, pedometer and accelerometry) assessments of physical activity.

Eligible studies had to compare at least one of the following postoperative outcomes: MACCE defined as death, stroke, myocardial infarction and the need for emergency cardiac surgery; 30-day adverse events as defined by the STS, ¹⁰ including an unexpected return to the operating room, complications due to pulmonary, cardiovascular, gastrointestinal, haematological, urological, infection, and neurological deficits, other important miscellaneous outcomes (eg, unexpected admission to ICU, or other events requiring admission to operating room requiring anaesthesia); hospital length of stay; ICU length of stay; health-related QOL with any assessment tool; ADLs using any evaluation strategy; cardiac rehabilitation attendance; and physical activity behaviour using either subjective or objective forms of assessment.

Search strategy

The search strategy was completed by a librarian and reviewed by a second librarian. The search included

keywords and controlled vocabulary. English language limits were applied. Databases used included MEDLINE, Embase, AgeLine and Cochrane Library (CDSR, CENTRAL and DARE), and articles were searched from inception to December 2016. The MEDLINE strategy was registered and published online in PROSPERO (http://www.crd.york.ac.uk/PROSPEROFILES/23606_STRATEGY_20150518.pdf) and is also available as a online supplementary file 1. The search was validated through a cross-check of references of studies selected for inclusion. In addition, conference abstracts were hand searched using the internet. Attempts were made to contact authors of conference abstracts to determine if their findings were published in a peer-reviewed journal.

Study selection

The title, abstract and full-text article screening processes were independently completed by two reviewers. A training exercise for the title and abstract phase was conducted by the independent reviewers using a random sample of 100 titles and abstracts. Discrepancies in studies for inclusion were resolved by discussion of the two reviewers. The final observed agreement was 98% with a kappa statistic of 0.47 for the title and abstract screen. One training exercise of 10 randomly selected articles was completed for the full-text screen. Discrepancies for inclusion were resolved through discussion. The observed agreement for the full-text screen was 96% with a kappa statistic of 0.83.

Data abstraction

Two reviewers independently extracted relevant data for the selected outcomes described above. Discrepancies in the data extraction procedure were resolved through discussion. Data abstraction items included study characteristics (eg, authors, year of publication, sample size and follow-up time points if relevant), patient characteristics (eg, age, sex and surgery type), physical activity tool used and the outcomes that were measured.

Risk of bias assessment

Two reviewers independently reviewed the risk of bias of each included study using the Newcastle-Ottawa Scale. Items within this tool assess the risk of bias associated with selection of participants, comparability (eg, study authors controlled for patient demographics and clinical characteristics) and outcome assessment (eg, data collection method for outcome, sufficient follow-up and adequacy of follow-up of cohorts). Each study was given a score within each category (selection: 0–4, comparability: 0–2 and outcome: 0–3) and an overall score ranging from 0 to 9. A score of 0 suggests an increased risk of bias and a higher score suggests a lower risk of bias.

Quantitative synthesis

Due to the significant heterogeneity between studies in terms of physical activity assessment tools used and outcomes assessed, meta-analyses were not performed.

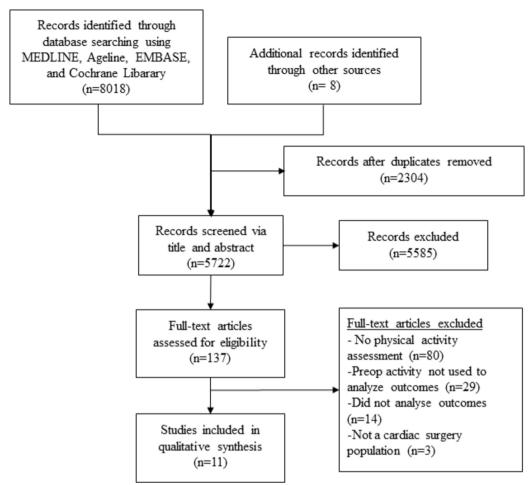


Figure 1 Study flow diagram.

RESULTS

The literature search results are shown in figure 1. After removing duplicates, 5722 articles were title and abstract screened. A total of 137 articles were then assessed in full text. Eleven studies met the eligibility criteria for the final analysis, and they included a total of 5733 patients. ¹²⁻²²

An overview of the included studies can be viewed in table 1. In the studies by Markou et al, 12 14 Nery et al 13 16 and Martini et al, 15 they evaluated CABG-only patients. Rengo et al, 17 Giaccardi et al, 18 Cacciatore et al, 19 Noyez et at^{20} and Min et at^{21} evaluated both CABG and/or valve procedures, and van Laar et al^{22} evaluated isolated aortic valve repair patients. The average age of participants in different studies ranged from 60 years (Martini and Nery et al¹⁵ 16) to 75 years (Rengo et al, Giaccardi et al, Min et al, van Laar et $al^{1/718\ 21\ 22}$). Rengo et $al, ^{17}$ Giaccardi et $al, ^{18}$ Min et al^{21} and van Laar et al^{22} excluded patients with physical impairments or with New York Heart Association heart failure class IV symptoms (severe cardiac symptoms), but in general exclusion criteria were not explicitly reported. Studies were conducted in the Netherlands (Markou et al, 12 14 Noyez et al 20 and van Laar et al 22), Brazil (Nery et al¹³ 16 and Martini et al¹⁵), Italy (Rengo et al, 17 Giaccardi et al^{18} and Cacciatore et al^{18}) and the USA (Min et al^{21}). Two studies by Nery et al^{13} and Martini et al^{15} used the same patient sample but examined different outcomes.

The sample size of studies ranged from 35 in the Min *et al*²¹ study to 3150 in the Noyez *et al*²⁰ study.

Physical activity tools

The physical activity assessments in each study were based on self-reported assessment tools. The timing of the physical activity assessments prior to surgery was not reported by Cacciatore *et al*, ¹⁹ Nery *et al*, ¹³ ¹⁶ Markou *et al* ¹² ¹⁴ or Martini *et al*. ¹⁵ Rengo *et al* ¹⁷ reported the timing of their physical activity assessment, which was within 35±6 days prior to surgery. Noyez *et al* and van Laar *et al* measured activity the day before surgery. ²⁰ ²² Min and colleagues measured physical activity 4 weeks prior to the patients' surgical procedure. ²¹ Finally, Giaccardi *et al* measured preoperative physical activity levels approximately 1 week following surgery. ¹⁸

Four studies used the Corpus Christi Heart Project questionnaire, 12 14 20 22 which asks participants about their typical physical activity behaviours over the past year during their leisure time. Participants were categorised into a sedentary group if they accumulated less than 30 min per day of light intensity activity, or into an active group if they accumulated at least one session per week of dynamic activity lasting ≥ 15 min marked by moderate intensity. Nery *et al* 13 16 and Martini *et al* 15 used a structured questionnaire confirmed by the Minnesota Leisure

Table 1 Chara	Characteristics of included studies						
First author, year	Study population	Country	Participants at follow-up	Physical activity assessment	Longest follow- up	Main findings	ı
Giaccardi, 2011 ¹⁸	All patients≥65 years undergoing CABG and/or valve procedures (total sample: 74.1±5.8 years old); 43% female	Italy	158	Harvard Alumni Questionnaire	4 weeks postoperatively	Physical activity had an independent association with postoperative atrial fibrillation within 30 days.	
Markou, 2007 ¹²	Elective CABG patients (active: 64.4±9.4, inactive: 63.8±9.0 years old); % female not reported	The Netherlands	428	The Corpus Christi Heart Project	1 year	Inactive versus active group had significantly more perioperative MIs, but not reoperations, ICU LOS, HLOS or postoperative complications at 1 year. Inactive group was more likely than active group to be physically active at 1 year.	
Nery, 2007 ¹³	All patients undergoing CABG (active: 63±11, inactive 66±14 years old); 42% female	Brazil	55	Structured Questionnaire confirmed by Minnesota Leisure Time Physical Activity Questionnaire	1 year	Inactive versus active groups had significantly longer HLOS and more postoperative events at 1 year.	
Markou, 2008 ¹⁴	Elective CABG patients (64.3±9.04 years old); 18% female	The Netherlands	568	The Corpus Christi Heart Project	1 year	Inactive versus active groups were more likely to be more physically active 1 year postoperatively.	
Martini, 2010 ¹⁵	Elective CABG patients (active: 60±10, inactive: 62±10 years old); 34% female	Brazil	185	Baecke Usual Physical Activity Questionnaire	Two years	Inactive versus active group did not have significantly different MACCE outcomes at 2 years.	
Nery, 2010 ¹⁶	Elective CABG patients (active: 60±10, inactive: 62±10 years old); 34% female	Brazil	202	Baecke Usual Physical Activity Questionnaire	Hospital discharge	Hospital discharge Inactive versus active groups had more postoperative events within 30 days and a longer HLOS.	
Rengo, 2010 ¹⁷	Acute or elective CABG patients ≥ 70 years (active: 72.3±3.2, inactive: 76.1±3.9 years old); 34% female	Italy	587	Physical Activity Scale for the Elderly	Mean 44.3±21.0 months	Physical activity had an independent and dose association with cardiac and all-cause mortality 5 years postoperatively.	0
Cacciatore, 2012 ¹⁹	All patients≥65 years undergoing CABG and/or valve procedures (72.9±4.8 years old); 48% female	ltaly	250	Physical Activity Scale for the Elderly	Hospital discharge	Physical activity was independently associated with reduced prolonged ICU LOS. Physical activity was not independently associated with postoperative ADLs.	φ
Noyez, 2013 ²⁰	Elective CABG and/or valve patients (69.7±10.1 years old);	The Netherlands	3150	The Corpus Christi Heart Project	30 days postoperatively	Physical activity was not independently associated with hospital or 30 day mortality. Inactive vs. Active group had a significantly longer ICU LOS.	
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Continued

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Table 1 Continued	tinued					
First author, year	Study population	Country	Participants at follow-up	Participants Physical activity at follow-up assessment	Longest follow- up	Main findings
Min, 2015 ²¹	Elective CABG and/or valve patients≥65 years (74.7±5.9 years old)	USA	62	The Health and Retirement Survey	4-6 months	Inactive versus active groups had significantly higher postoperative physical activity up to 6 months postoperatively.
van Laar ²²	Patients ≥75 years undergoing elective isolated aortic valve replacement (79.5±2.8 years old); 59% female	The Netherlands	115	The Corpus Christi Heart Project	2 years postoperatively	Inactive versus active groups had significantly higher mortality rates 2 years postoperatively.

ADL, activities of daily living; CABG, coronary artery bypass graft surgery; HLOS, hospital length of stay; ICU LOS, intensive care unit length of stay; MACCEs, major adverse cerebrovascular and cardiac events; MI, myocardial infarction.

Time Physical Activity Questionnaire¹³ or the Baecke Usual Physical Activity Questionnaire. 15 16 Both physical activity tools ask participants to recall their usual activities 12 months prior and determine the frequency, intensity and time of activity. Participants were categorised into an inactive group if they engaged only in light intensity (<3 metabolic equivalents) activity or into an active group if they achieved≥3 metabolic equivalents. Rengo et al¹⁷ and Cacciatore et al¹⁹ used the Physical Activity Scale for the Elderly, which is a 7-day recall of a participant's frequency, intensity, duration and type of activity. Participants receive a total score from 0 to 400. Rengo et al^{17} separated participants by inactive and active groups using the median score, whereas Cacciatore et al used the continuous measure. The Harvard Alumni Questionnaire was implemented by Giaccardi and colleagues, 18 which measures the typical weekly amount and intensity of physical activity over the past year. Participants were categorised as inactive if they participated in <1 hour per week of light activity and as active if they participated in either≥4hours of light or more than 1-2hours of moderate activity per week. In the study by Min et al,²¹ the physical activity-related questions were used from the Health and Retirement Survey, which determines a participant's frequency and intensity of activity in a typical week. These authors used the continuous score in their study.

MAJOR ADVERSE CARDIAC AND CEREBROVASCULAR EVENTS

Outcomes within the definition of MACCE were evaluated in four studies (table 2) by Nery et al, 13 Martini et al, 15 Rengo et al¹⁷ and van Laar et al.²² The follow-up periods were one (Nery et al¹³), two (Martini et al¹⁵ and van Laar et al²²) and 5 years (Rengo et al¹⁷) postoperatively. Unadjusted differences between active versus inactive patients and MACCE (defined as atrial fibrillation, hospital admission, reoperation and myocardial infarction) were found 1 year postoperatively in the Nery et al¹³ study. The Martini et al¹⁵ study found no differences (defined as mortality, rehospitalisation, cerebrovascular accident and MI) at 2 years postoperatively. The unadjusted rates of mortality within 2 years postsurgery were significantly lower in the active versus inactive group in the study by van Laar and colleagues.²² The study by Rengo and colleagues found a significant and dose-response relationship between physical activity and postoperative cardiac and all-cause mortality after controlling for preoperative demographics, medical history, medications and clinical characteristics. 17

30-day events

Five studies (Markou et al, 12 Nery et al, 16 Rengo et al, 17 Giaccardi et al^{18} and Noyez et al^{20}) evaluated postoperative events within 30 days of surgery (table 2). The postoperative events measured varied significantly between the studies. Three studies (Nery et al, 16 Giaccardi et al 18 and Noyez et $a\ell^{0}$) examined if physical activity was an

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F	Table 2 Major adverse	Major adverse and cerebrovascular events and postoperative events within 30 days	ostoperative events within	30 days	
œ	Reference	Outcome definition	Adjustment variables	Number of events per group	OR or HR and 95% CI
2	Aajor adverse cerebro	Major adverse cerebrovascular and cardiac events			
	Nery et al ¹³	1-year postoperative AF, hospital Non readmission, new CABG, PCI, MI	None	Active: 8/25 (31%); inactive: 17/30 (57%)*	W.
	Martini and Barbisan ¹⁵	2-year postoperative death, rehospitalisation, cerebrovascular accident, MI	None	Active: 9/66 (14%); inactive: 31/119 (26%)	£
	Rengo <i>et al¹⁷</i>	5-year postoperative cardiac and all-cause mortality	Demographics, medical history, medications, and clinical findings.	A.B.	Adjusted proportional hazard models: All-cause mortality: Exp(B) 0.248 (95% CI 0.141 to 0.434)* Cardiac mortality: Exp(B) 0.272 (0.133 to 0.555)*
	van Laar et al ²²	2-year mortality	None	Active: 5/65 (13%); inactive: 11/50 (22%)*	Z.
Δ.	Postoperative events within 30 days	within 30 days			
	Markou e <i>t al¹²</i>	Perioperative MI, reintervention, postoperative complications (wound, renal, neurological, pulmonary, gastrointestinal)	None	MI: active: 4/226 (2%); inactive: 11/202 (5%)* Reoperation: active: 15/226 (7%); inactive: 9/202 (5%), Wound infection: active: 3/226 (1%); inactive: 7/202 (3%), Renal: active: 3/226; inactive: 7/202	K
	Nery <i>et al</i> ¹⁶	Mortality, MI, reoperation	Age, smoking, PVD, COPD, Cleveland Risk Score.	Mortality: active: 0/66 (0%); inactive: 7/136 (5%) MI: active: 1/66 (2%); inactive: 6/136 (4%) Reoperation: active: 0/66 (0%); inactive: 1/136 (0.5%)	Multivariate OR for being active: 0.22 (95% CI 0.09 to 0.51, p=0.001)
	Rengo e <i>t al¹⁷</i>	Low-output syndromes, MI, cardiac support, stroke, bleedings, mediastinitis, pneumonia, dialysis	None	Any surgical complication: active: 53/267 (19.7%); inactive: 60/320 (18.6%)	E.
	Giaccardi e <i>t al</i> ¹⁸	Atrial fibrillation	Age, episodes of AF 1 year preop, episodes of AF in the first week, β-blockers, amiodarone, left ventricular volume, left atrial emptying fraction	Postoperative atrial fibrillation: active: 6/74 (8.1%); inactive: 27/84 (32.1%)*	Multivariate OR for being inactive: 4.04 (95% CI 1.16 to 14.14, p=0.029)

Table 2 Continued				
Reference	Outcome definition	Adjustment variables	Adjustment variables Number of events per group	OR or HR and 95% CI
Noyez et af ²⁰	Mortality, reoperation, stroke, renal insufficiency, sternal wound, ventilation	>75 years, valve surgery, Hospital mortality female, high operative risk, renal disease, obesity, NYHA IV, insulin, 20/1335 (1.5%)* vascular pathology, poor Reoperation: act LVEF, lung disease, MI, neurological event (0.9%) Renal insufficience inactive: 39/1335 (3.3%)* Ventilation>2 day mortality (0.9%) Renal insufficience inactive: 39/1335 (3.3%)* Ventilation>2 day inactive: 54/1335 (3.3%)* Ventilation>2 day mortality (3.3%)* Ventilation>2 day inactive: 54/1335	275 years, valve surgery, Hospital mortality: active: 7/1815 (0.4%); inactive: female, high operative 15/1335 (1.1%)* risk, renal disease, 30-day mortality: active: 10/1815 (0.6%); inactive: obesity, NYHA IV, insulin, 20/1335 (1.5%)* vascular pathology, poor Reoperation: active: 105/1815 (5.8%); inactive: LVEF, lung disease, MI, 68/1335 (5%) neurological event (0.9%) Renal insufficiency: active: 32/1815 (1.8%); inactive: 39/1335 (2.9%)* Sternal wound: active: 10/1815 (0.6%); inactive: 17/1335 (1.3%)* Ventilation>2 days: active: 31/1815 (1.7%); inactive: 54/1335 (4.0%)*	Hospital mortality multivariate OR for being inactive: 1.20 (95% CI 0.4 to 3.5, p=0.617) 30 day mortality multivariate OR for being inactive: 1.10 (95% CI 0.5 to 2.7, p=0.70)

AF, atrial fibrillation; BMI, body mass index; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; LVEF, left ventricular ejection fraction; MI, myocardial nfarction; NR, not reported; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PVD, peripheral vascular disease. Indicates statistical significance (p<0.05).

independent protective factor against postoperative events. Physical activity was an independent protective factor against the combined outcome of mortality, MI and reoperation in the study by Nery $et~al^{16}$ as well as postoperative atrial fibrillation in the Giaccardi and colleagues study but was not significant for in-hospital or 30-day mortality in the Noyez $et~al^{20}$ study.

Postoperative health-related QOL

No studies evaluated postoperative health-related QOL.

Hospital and ICU length of stay

Three studies by Markou $et\ al^{12}$ and Nery $et\ al^{13}$ 16 compared hospital length of stay between active and inactive cardiac surgery patients (table 3). Hospital length of stay was longer in the inactive group in two of three studies (both by Nery $et\ al$). ¹³ 16 One of the studies by Nery $et\ al^{16}$ did not report hospital length of stay summary statistics between the active and inactive groups. However, that study reported an independent association between the preoperative active and inactive group and a reduced likelihood of prolonged hospital length of stay, though 'prolonged' was not defined in the study.

Three studies compared ICU length of stay between the preoperative physical activity groups (table 3) (Markou et al, ¹² Cacciatore et al¹⁹ and Noyez et al). ²⁰ Two studies (Markou et al¹² and Noyez et al²⁰) found that the inactive group had a significantly longer ICU length of stay compared with the active group. In the study by Cacciatore and colleagues, they found in their multivariate analysis that the active group was less likely to have a prolonged ICU length of stay >3 days compared with the inactive group after controlling for age, off-pump CABG, stroke and renal failure.

Postoperative ADLs

One study by Min *et al*¹⁹ examined the impact of preoperative physical activity and postoperative ADLs at the time of hospital discharge and revealed no statistically significant (p=0.079) association between the two after adjusting for preoperative demographics and clinical variables.

Cardiac rehabilitation attendance

No studies evaluated cardiac rehabilitation attendance postoperatively.

Postoperative physical activity behaviour

The impact of preoperative physical activity on postoperative physical activity levels was examined in the two studies by Markou *et al*¹² ¹⁴ and in the other study by Min *et al*² (table 3). These studies found that the active group preoperatively was more likely to be physically inactive postoperatively. In both of the Markou *et al*¹² ¹⁴ studies, they completed a multivariate analyses and found that this association remained statistically significant after controlling for age, gender and preoperative clinical characteristics.

Table 3 Hospital leng	Hospital length of stay, ICU length of stay and postoperative activities of daily living and physical activity	tivities of daily living and physical activity	
First author, year	Adjustment variables	Length of stay/number of events per group	OR or HR and 95% CI
Hospital length of stay			
Markou, 2007 ¹²	None	Active: 6.9±8.2 days; inactive: 7.3±7.1 days	NR
Nery, 2007 ¹³	None	Active: 12±5 days, median 9 days (IQR 8-15); inactive: 15±8 days, median 12 (IQR 9-19)*	N. C.
Nery, 2010 ¹⁶	Age, sex, Cleveland Risk Score, smoking, systemic arterial hypertension, stroke, MI and PVD.	NB	HR: 0.67 (95% CI 0.49 to 0.93)*
ICU length of stay			
Markou, 2007 ¹²	None	Active: 2.2±5.3 days; inactive: 2.1±3.5 days	NR
Cacciatore, 2012 ¹⁹	For ICU length of stay >3 days: age, off-pump CABG, stroke, renal failure.	Active: 2.58±1.09 days; inactive: 3.33±1.68 days*†	For ICU length of stay >3 days Univariate OR: 0.984 (95% CI 0.977 to 0.992)* Multivariate OR: 0.992 (95% CI 0.983 to 1.000)*
Noyez, 2013 ²⁰	None	Active: 1.3±1.9 days; inactive 3.0±41.8 days* ICU >5 days: Active: 19/1815 (1.0%); Inactive: 46/1335 (3.4%)*	N. N
Postoperative ADLs			
Cacciatore, 2012 ¹⁹	Age, gender, CABG, NYHA≥3, ICU length of stay≥3days, off-pump CABG, diabetes, renal failure, stroke, PVD, COPD, Cumulative Illness Rating Scale.	NB	Beta: 0.099
Postoperative physical activity	activity		
Markou ¹²	Age≥75 years, gender, neurological disease, vascular disease, diabetes and preoperative physical activity.	Better PA post-operatively: active: 48/226 (21.2 %), inactive: 129/202 (64%)* Equal PA postoperatively: active: 112/226 (49.6%), inactive: 59/202 (29.2%)* Worse PA postoperatively: active: 66/226 (29.2%), inactive: 14/202 (6.9%)*	Decreased postoperative PA OR (inactive group as reference): 8.1 (95% CI 3.5 to 13.5)*
Markou ¹⁴	Diabetes, vascular disease, neurological disease, renal disease, MI, preoperative activity level.	Æ	For becoming physically inactive postoperatively Male OR (inactive group as reference): 7.11 (95% CI 3.6 to 13.9)* Female OR (inactive group as reference): 11.0 (95% CI 2.2 to 55)*
Min ²¹	None	NR	Each weekly preoperative activity point was associated with a loss of 0.78 points at 6 weeks, p<0.001 and 0.65 points at 6 months*
*Indicates statistical significance (20 0>0)			

^{*}Indicates statistical significance (p<0.05).

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[†]Unpublished data obtained from Cacciatore et al. 19

ADL, activities of daily living; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; MI, myocardial infarction; NR, not reported; NYHA, New York Heart Association; PA, physical activity; PVD, peripheral vascular disease.

Table 4 Newcastle-Ottawa So	cale risk of bias scores	S		
Reference	Selection	Comparability	Outcome	Total
Markou et al ¹²	3	2	3	8
Nery et al ¹³	3	0	2	5
Markou et al ¹⁴	3	2	2	7
Martini and Barbisan ¹⁵	3	0	2	5
Nery and Barbisan ¹⁶	3	2	2	7
Rengo et al ¹⁷	4	2	3	9
Giaccardi et al ¹⁸	3	2	2	7
Cacciatore et al ¹⁹	3	2	2	7
Noyez et al ²⁰	3	2	3	8
Min et al ²¹	4	2	1	7
van Laar et al ²²	3	0	3	6
Average scores±SD	3.18±0.40	1.45±0.93	2.27±0.65	6.91±1.22

Maximum scores are 4, 2 and 3 for selection, comparability and outcome, respectively. Maximum total score is 9. A lower score within each category and for a total score indicates a higher risk of bias.

Risk of bias

The risk of bias assessment via the Newcastle-Ottawa Scale can be viewed in table 4. Since some studies assessed multiple outcomes, the risk of bias assessments were based on their highest possible score (eg, some outcomes were assessed with a multivariable analysis, while others were not in the same study). All studies scored at least 3 out of 4 for the selection of study groups. There was variability across studies for the ascertainment of exposure or outcome of interest. Total risk of bias scores ranged from 5 to 9, suggesting the studies were of moderate to high quality, respectively.

DISCUSSION

The purpose of this systematic review was to determine if physical activity before cardiac surgery was associated with postoperative health outcomes. Given the different self-reported physical activity tools used that prevented comparison across studies, the inconsistent use of adjustment for potential confounders, and the varying outcomes evaluated for MACCE and 30-day postoperative events, it cannot be concluded that preoperative physical activity is associated with postoperative outcomes in adult cardiac surgery patients. This systematic review highlights important gaps within the literature on this topic. Therefore, key recommendations for examining the impact of preoperative physical activity behaviour on postsurgical outcomes of cardiac patients are provided (table 5).

The different self-reported physical activity tools used across the studies makes it difficult to compare the preoperative physical activity levels of patients prior to cardiac surgery. Even so, it is important to note that in the studies included in this systematic review, most of the studies identified a subsample of cardiac surgery patients who were more vulnerable to poor health outcomes by categorising patients as active or inactive prior to surgery using their

self-reported physical activity measures. However, the way the physical activity tools measured physical activity (eg, over the past year or in the past week; see the Methods section) could have influenced the outcomes of the study. There seems to be no universally accepted tool to measure self-reported physical activity levels, ²³ and it is unclear if any of the physical activity tools identified by this review have been validated in the cardiac surgery patient. One advantage of using self-reported physical activity measures in studies is their ease of administration compared with other objectively measured physical activity tools. Furthermore, self-reported physical activity tools appear to provide some value when assessing the independent association between activity levels and poor outcomes. In fact, most physical activity guideline recommendations for health benefits, including those in North America, are based on self-reported measures.²⁴ ²⁵ Another strength of using a subjective physical activity tool in the preoperative cardiac surgery patient is that it would capture a patient's physical activity behaviour before they are placed on a waiting list, when they might refrain from being physically active in fear of making their condition worse. However, cardiac surgery patients and other patient populations tend to misreport their physical activity levels compared with objectively measured physical activity. 626 Nevertheless, this systematic review found no studies that evaluated objectively measured physical activity before cardiac surgery and its link to postoperative health outcomes. Evidence suggests there is a stronger association between objective measures of physical activity and various cardiovascular and metabolic biomarkers as compared with subjective measures of physical activity.^{27 28} While it is unclear which objective measures of physical activity are most appropriate in the complex cardiac surgical patients, future studies should use a physical activity tools such as accelerometers or pedometers.

Guidelines for physical activity measurement and outcome assessment in cardiac surgery patients: limitations and opportunities for future research

Drawbacks

Opportunity

Physical activity

- 1. Heterogeneity in tools used across studies
- 2. Only subjective measures were used
- 3. Time of preoperative physical activity assessment was unclear in most studies
- ▶ Use of objectively measured tools (eg, pedometers and accelerometers) accompanied by a questionnaire that can produce data that can be compared across studies, such as step counts, intensity and duration of physical activity.
- ► Capture physical activity behaviour as soon as a patient is placed on a wait list, or in non-elective cases, as soon as possible prior to surgery.
- ▶ Physical activity should be assessed ideally over a 7-day period.
- ▶ Physical activity should be assessed by intensity and duration per week and in steps per day.

Outcomes

4. Heterogeneity in MACCE and postoperative events within 30 days definitions

- ▶ MACCE should be evaluated as a long-term outcome and defined as death, stroke, myocardial infarction and the need for redo cardiac surgery. Each outcome should be evaluated individually.
- ▶ 30-day postoperative events should be evaluated using the STS checklist 10: along with reasons, evaluate unexpected return to the operating room, complications due to pulmonary, cardiovascular, gastrointestinal, haematological, urological, infection, neurological and other important miscellaneous outcomes (eg, unexpected admission to ICU, or other events requiring admission to operating room requiring anaesthesia.
- ▶ Rehospitalisation for any cause after cardiac surgery should also be added to
- were assessed
- 5. No patient-oriented outcomes
 Capture postoperative health-related quality of life, mental health, pain and cardiac symptoms using validated tools within the first 30 days and at least 1 year postoperatively.

Statistical procedures

- 6. Shortage of studies addressing confounders
- ▶ Use multivariate analysis, including logistic or linear regression, or analysis of variance statistical procedures. Ensure that a power analysis is conducted prior to conducting the study.

ICU, intensive care unit; MACCE, major adverse cerebrovascular and cardiac events; STS, Society of Thoracic Surgeons.

There were inconsistent findings across studies assessing the same outcomes, and many studies did not adjust for clinically relevant variables that could influence the health outcomes of cardiac surgery patients. It is possible that most of the included studies were not statistically powered to detect changes between inactive and active groups. The study by Rengo et al¹⁷ had the largest sample size of the four studies that assessed MACCE outcomes, which found a significant protective association between preoperative physical activity and cardiac and all-cause mortality 5 years postoperatively after controlling for clinically relevant variables (table 2). In contrast, the largest study examined in this systematic review by Noyez and colleagues²⁰ found no association between preoperative activity and hospital and 30-day mortality after controlling for covariates (table 2). It is difficult to determine if patient-level factors influence outcomes (eg, elective or acute patients, surgery type, older vs younger, females vs males) as the samples were somewhat heterogeneous. Even so, some of the results of this systematic review are promising. Specifically, of the studies that controlled for confounding variables, five studies found a protective, independent association between higher preoperative physical activity

levels when assessing clinical outcomes, including MACCE, ¹⁷30-day postoperative events, ¹⁶ ¹⁸hospital length of stay 16 and ICU length of stay, 19 whereas only two studies found no protective association for 30-day postoperative events²⁰ and postoperative ADLs.¹⁹ Yet, more studies are needed to elucidate the impact of preoperative physical activity on postcardiac surgical outcomes that control for clinically relevant variables. Clinical variables included in the cardiac surgical risk models (eg, EuroSCORE and STS score) could attenuate or mitigate the relationship between preoperative physical activity behaviour and postoperative outcomes. Collectively, future studies are needed to determine if preoperative physical activity is a protective factor for health outcomes after cardiac surgery that control for clinically relevant variables known to impact cardiac surgery outcomes.

An unanticipated finding was that patients who were active before surgery had a higher likelihood of being physically inactive postoperatively, after controlling for comorbidities. 12 14 21 Healthcare providers may have advised patients with more severe symptomology prior to surgery to refrain from physical activity. Also, the relief of cardiac symptoms after surgery among inactive patients could have led them to become more active postoperatively. However, these possibilities were not explored in the included studies.

While outside the scope of this systematic review, future studies should investigate if changes to physical activity levels prior to cardiac surgery impact long-term patient health outcomes. Cardiac rehabilitation programmes are intended to support cardiac patients in becoming more physically active postoperatively, and it has been shown that patients who attend such programmes reduce their risk for cardiac-related mortality and hospitalisation rates.²⁹ Evidence suggests that among those referred to cardiac rehabilitation after cardiac surgery, only 40% attend.⁶ However, the literature is less clear on whether patients who attend cardiac rehabilitation are more physically active compared with those who do not attend. It is possible that patients who adopt and sustain a more physically active lifestyle on their own after cardiac surgery could yield similar health benefits compared with those who attend an exercise-based rehabilitation programme, but this hypothesis requires further investigation.

Previous randomised controlled trials comparing an exercise programme to standard care prior to elective cardiac surgery (ie, 'Prehab') demonstrate reductions in hospital length of stay and improvements in walking ability postoperatively.⁷⁻⁹ However, there were mixed findings from this systematic review when comparing preoperative physical activity behaviour and hospital stay. 12 16 These divergent findings suggest either that a medically supervised and individualised physical activity programme is needed to derive the health benefits of physical activity prior to cardiac surgery, or that patients are misreporting their physical activity behaviours. Future cohort studies in this area should address the drawbacks of the included studies in this systematic review included in table 5, while randomised trials should focus on whether preoperative exercise therapy programmes are feasible and efficacious in clinical practice.

The findings of this systematic review suggest that the literature would benefit from standardisation of the definition of measures such as MACCE and postoperative events within 30 days. The heterogeneity in reporting of outcomes can lead to considerably different conclusions across studies. Attempts should also be made to ensure other clinically important outcomes are captured, such as the addition of 30 day events. Only one study in this review compared physically active versus inactive patients preoperatively and reported on the individual postoperative events within 30 days. Collectively, uniform outcome reporting and appropriate outcome definitions are recommended when examining the outcomes of cardiac surgery.

Patient-oriented outcomes should also be captured to ensure that cardiac surgery is improving other outcomes that patients value. No studies in this review determined if there was a link between preoperative physical activity behaviour and postoperative health-related QOL, and only one study evaluated postoperative ADLs.¹⁹ QOL

postoperatively tends to improve in some older patients, while others tend to decline. Importantly, the preoperatively physical activity and overall functional status of cardiac surgery patients could play a role in the postoperative trajectory of these outcomes such as QOL. Other patient-oriented outcomes, including postoperative pain and cardiac symptoms, could also be investigated.

If physical activity is to be assessed in the preoperative period, the extent of missing data may also be a concern, especially with objective physical activity measures. The possibility of missing data from individual studies included in this systematic review was outside the objectives of the present study but is a salient point that should be considered for future investigations. It is also important to understand patient-level factors associated with missing data. The use of statistical techniques that address missing data, such as multiple imputation, is one approach to address missing physical activity data. Importantly, it has been shown that multiple imputation leads to precise estimates of predicting 30-day mortality risk in cardiac surgery patients when important clinical variables are missing, as compared with estimating risk with a complete case analysis.32

Limitations

One limitation to consider is that the patients included across the studies evaluated in this systematic review may have been different, as the recruitment criteria were not always clearly stated. A small sample of studies explicitly stated that they excluded those with physical limitations and healthcare providers may have advised higher risk patients to not participate in physical activity. There is also a limitation associated with the methodology of this systematic review: only studies written in English were included, raising the possibility that some studies were missed.

CONCLUSION

Due to the mixed findings in this systematic review, it cannot be concluded that self-reported physical activity behaviour before cardiac surgery is associated with health outcomes after surgery. The mixed findings could be due to the heterogeneity in physical activity tools used, definitions of outcomes and the few studies adjusting for other potentially confounding variables. These findings highlight the need for more research in this area.

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