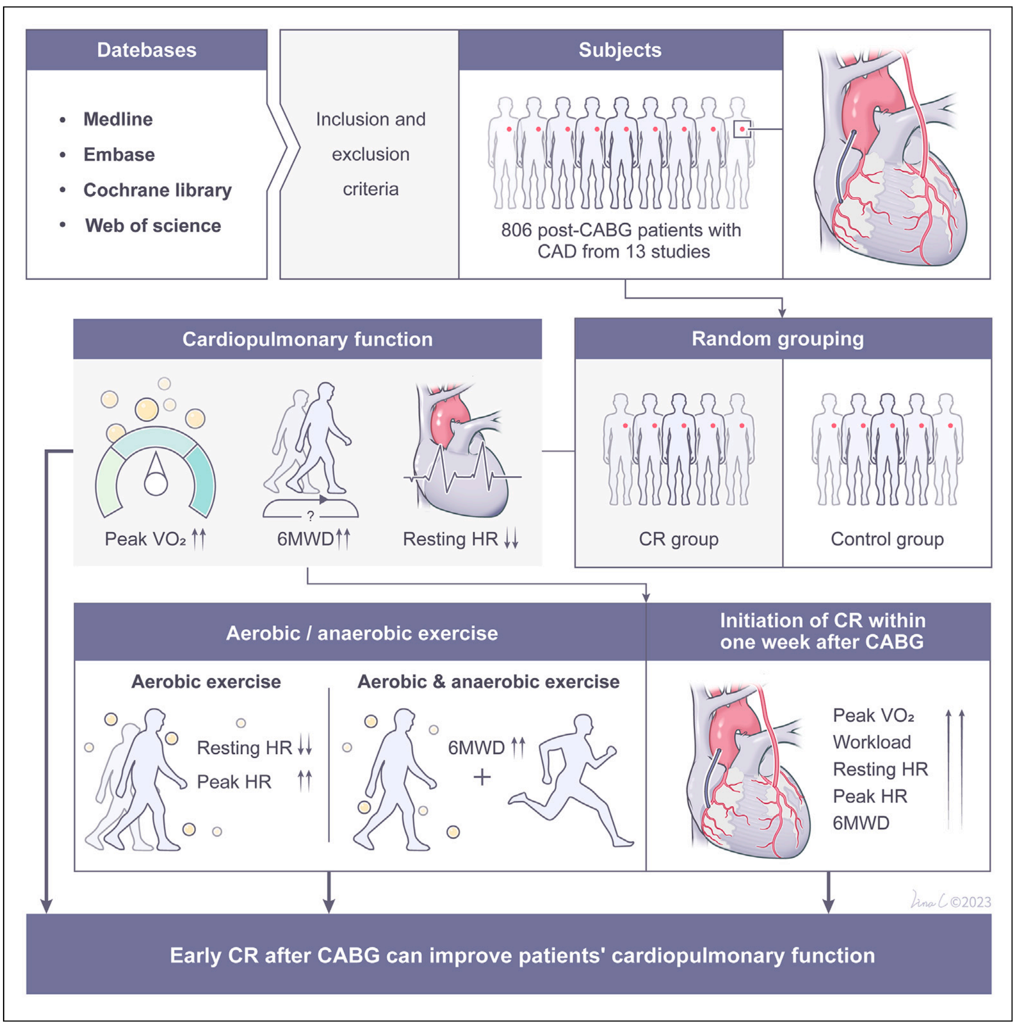
iScience



Article

# The effect of cardiac rehabilitation on cardiopulmonary function after coronary artery bypass grafting: A systematic review and meta-analysis




Jiapeng Miao, Huayun Yang, Ruizheng Shi, Chengming Wang

xyshiruizheng@csu.edu.cn (R.S.)
46595842@qq.com (C.W.)

## Highlights

We are the first to conduct a meta-analysis of the effects of CR after CABG surgery

CR after CABG could improve patients' cardiopulmonary function

The benefit of CR was affected by the modality, duration and start time of the exercise

Miao et al., iScience *26*, 107861
December 15, 2023 © 2023 The Author(s).
https://doi.org/10.1016/j.isci.2023.107861

iScience

CellPress
OPEN ACCESS

Article

# The effect of cardiac rehabilitation on cardiopulmonary function after coronary artery bypass grafting: A systematic review and meta-analysis

Jiapeng Miao,[1,4] Huayun Yang,[2,4] Ruizheng Shi,[3,*] and Chengming Wang[1,5,*]

## SUMMARY

**We carried out a meta-analysis on the effect of cardiac rehabilitation (CR) on cardiopulmonary function after coronary artery bypass grafting (CABG). Four databases were searched for studies comparing CR with control. A random-effects model was used to pool mean difference (MD). The meta-analysis showed an increase in peak oxygen consumption (peak $VO_2$) (MD = 1.93 mL/kg/min, p = 0.0006), and 6-min walk distance (6MWD) (MD = 59.21 m, p < 0.00001), and a decrease in resting heart rate (resting HR) (MD = 5.68 bpm, p < 0.0001) in the CR group. The subgroup analysis revealed aerobic exercise could further improve resting HR and peak HR, and physical/combination with aerobic exercise could further increase 6MWD. The improvement of peak $VO_2$, workload, resting HR, peak HR, and 6MWD regarding CR performed within one week after CABG is greater than that one week after CABG. CR after CABG can improve the cardiopulmonary function, which is reflected by the improvement of peak $VO_2$, 6MWD, and resting HR.**

## INTRODUCTION

Atherosclerosis causing stenosis or obstruction of the coronary arteries is known as coronary atherosclerotic disease (CAD). CAD is a major health problem worldwide and is one of the leading causes of death. Revascularization of the obstructed blood vessels can restore blood perfusion to the heart and protect the viable myocardium, thereby improving the long-term prognosis of patients. Revascularization mainly includes coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI), with CABG mostly used to treat lesions in multiple coronary arteries or the left main artery, or combined mechanical complications.[1]

Cardiac autonomic nervous system dysfunction can be present in patients with CAD, and autonomic imbalance can lead to life-threatening arrhythmias and sudden cardiac death.[2] Sympathetic nerve activation may occur after CABG due to myocardial damage or surgical stimulation, which negatively impacts patient rehabilitation after CABG.[3] It is now believed that postoperative cardiac rehabilitation (CR) may reduce the risk of mortality by modulating functions of the autonomic nervous system.[4,5]

Declined respiratory muscle strength and pulmonary function can also be present after CABG.[6] Therefore, CR, the primary intervention of which is aerobic exercise, is often used after CABG.[7] In recent years, CR has been used to improve cardiopulmonary function, and Hamazaki N et al. found that postoperative CR significantly improved the respiratory muscle strength and function of patients.[8] Overall, CR can improve cardiac function, reduce complications and cardiovascular mortality, and thereby improve the quality of life.[9]

Recent studies evaluated the effects of CR on the physical performance and psychological status after revascularization (including PCI and CABG) for CAD, which showed that CR after revascularization could alleviate anxiety and depressive symptoms, improve physical performance, and reduce the recurrence of myocardial infarction and cardiac mortality.[10–12] However, to the best of our knowledge, there has been no meta-analysis exploring the effect of CR on the cardiopulmonary function after CABG. Therefore, this systematic review and meta-analysis aimed to analyze the effect of CR on the cardiopulmonary function of patients with CAD after CABG and to assess whether CR could improve the postoperative cardiopulmonary function in patients. However, different durations and modalities of CR may have different effects. The modalities of CR include aerobic exercise, anaerobic physical exercise, and their combination. Therefore, we aimed to conduct a subgroup analysis of different durations (>1000 min vs. <1000 min) and modalities (aerobic exercise vs. physical exercise/combined aerobic exercise) of CR.

[1]Department of Cardiovascular Medicine, Zhuzhou Central Hospital, Xiangya hospital Zhuzhou, Central South University, 116 Changjiang South Road, Zhuzhou 412000, China
[2]Department of Cardiovascular Medicine, Guilin People's Hospital, 12 Wenming Road, Guilin 541002, China
[3]Department of Cardiovascular Medicine, Xiangya Hospital, Central South University, 87 Xiangya Road, Changsha 410008, China
[4]These authors contributed equally
[5]Lead contact
*Correspondence: xyshiruizheng@csu.edu.cn (R.S.), 46595842@qq.com (C.W.)
https://doi.org/10.1016/j.isci.2023.107861

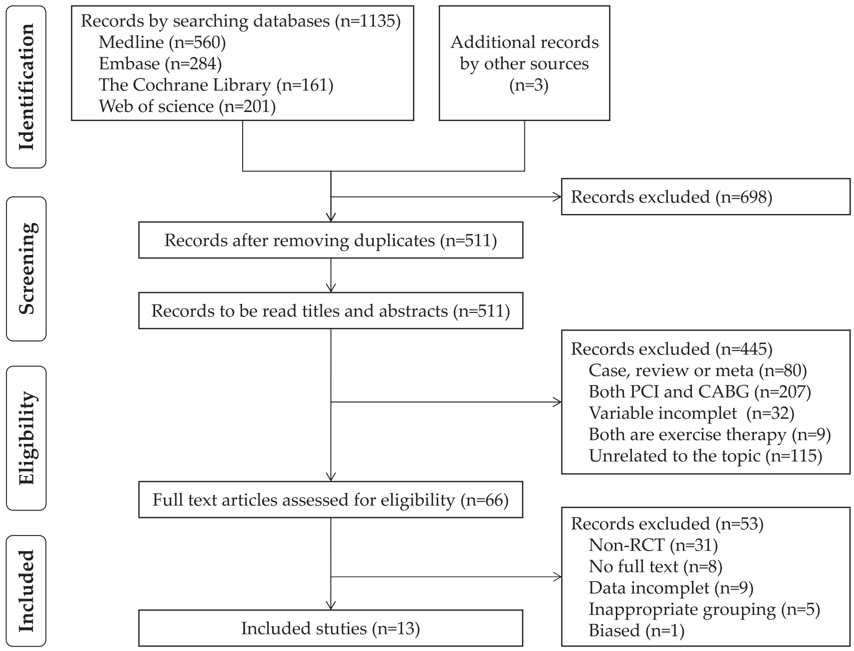



**Figure 1. PRISMA flow chart of study selection**

Abbreviations: PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis; RCT, randomized controlled trials.

## RESULTS

### Characteristics of included studies

The literature screening process is shown in Figure 1. A total of 1,209 relevant articles were retrieved, among which 698 duplicates were removed, 445 articles were excluded by reading the title and abstract during the first screening, and 53 articles were further excluded by reading the full text during the second screening; thus, 13 RCTs were included in the subsequent meta-analysis.[5,13–25] The RCTs involved a total of 806 subjects, with 403 in the CR group and 403 in the control group. The baseline characteristics of the included studies are presented in Table 1.

### Risk of bias assessment

The risk of bias was assessed for all RCTs (Figure 2). Nine RCTs were considered low risk and the other four RCTs were unable to assess the risk of bias due to the presence of four "unclear risk of bias" or "high risk."

### Cardiac rehabilitation and cardiopulmonary exercise testing

A total of 594 subjects in 7 studies were assessed for the effect of CR on peak $VO_2$, and the random-effects model analysis showed that patients who underwent CR had significantly greater improvement than controls (MD = 1.93 mL/kg/min, 95% CI: 0.83 to 3.04, $p = 0.0006$; $I^2 = 77.0\%$) (Figures 3A and 4A). A total of 316 subjects in 5 studies were assessed for the effect of CR on resting HR, and the random-effects model analysis showed that patients who underwent CR had significantly lower resting HR than controls (MD = 5.68 bpm, 95% CI: 3.05 to 8.32, $p < 0.0001$; $I^2 = 60.0\%$) (Figures 3C and 4C). A total of 239 subjects in 3 studies and 343 subjects in 5 studies were assessed for the effect of CR on the workload and peak HR, respectively, but the random-effects model analysis revealed no statistical difference in workload (MD = 9.94 W, 95% CI: −3.49 to 23.37, $p = 0.15$; $I^2 = 74.0\%$) (Figures 3B and 4B) or peak HR (MD = 2.66 bpm, 95% CI: −2.45 to 7.77, $p = 0.31$; $I^2 = 72.0\%$) between the two groups (Figures 3D and 4D).

### Cardiac rehabilitation and 6-min walk test

A total of 472 subjects in 6 studies were assessed for the effect of CR on the 6MWD, and the random-effects model analysis revealed that patients who underwent CR had significantly greater improvement than controls (MD = 59.21 m, 95% CI: 34.25 to 84.16, $p < 0.00001$; $I^2 = 94.0\%$) (Figures 3E and 4E).

**Table 1. Characteristics of the included studies**

| Authors | Year | N Exp/Con | Modalities | Time to start CR after surgery | Site of CR | Experiment | Control | Variables |
|---|---|---|---|---|---|---|---|---|
| Adachi H et al.[14] | 2001 | 23/34 | Aerobic exercise | After 2 weeks | Hospital | Aerobic exercise using a bicycle or treadmill for 30 min, twice a week for 2 weeks. | Stayed sedentary. | Peak $VO_2$<br>Peak HR |
| Tsai SW et al.[15] | 2005 | 15/15 | Aerobic exercise | Within a week | Home | 30-40 min of aerobic exercise training (60–85% of peak HR) three times a week for 12 weeks. | No further advice about specific exercise programs. | Resting HR |
| Wu SK et al.[16] | 2006 | 18/18 | Aerobic exercise | Upon discharge or within 1 week of discharge | Home | Warm up and relax for 10 min followed by 30–60 min of aerobic exercise (60–85% of peak HR), three times a week for 12 weeks. | Normal levels of daily physical activity. | Workload<br>Peak $VO_2$<br>Resting HR<br>Peak HR |
| Bilinska M et al.[17] | 2010 | 59/59 | Aerobic exercise | 3 months | Rehabilitation center | Interval training for 60 min (4 min of exercise with a 2-min break, 70–80% of peak HR), three times a week for 6 weeks. | Habitual activities. | Peak $VO_2$<br>6MWD<br>Resting HR<br>Peak HR |
| Savci S et al.[18] | 2011 | 22/21 | Physical exercise | The second day | Hospital | Upper and lower limb exercise and chest physiotherapy, plus inspiratory muscle training for 30 min, twice a day for 10 days. | Usual care. | FVC<br>$FEV_1$ |
| Busch JC et al.[19] | 2012 | 84/89 | Physical exercise | Within 4 weeks | Rehabilitation center | Usual training plus resistance and balance training for 3 weeks, plus another 30 sessions of exercise, with an average duration of 10.8 min for each session. | Usual training (240 min per week). | 6MWD<br>Workload<br>Peak $VO_2$ |
| Ghashghaei FE et al.[20] | 2012 | 15/17 | Aerobic plus physical exercise | 2 months | Rehabilitation center | 60 min of interval cycling (4 min of exercise with a 2-min break, 70–80% of peak HR), 3 times a week for 6 weeks. | Walk for 15–30 min, 2 or 3 times a week for 8 weeks. | 6MWD<br>Resting HR<br>Peak HR |

(*Continued on next page*)

**Table 1. *Continued***

| Authors | Year | N Exp/Con | Modalities | Time to start CR after surgery | Site of CR | Experiment | Control | Variables |
|---|---|---|---|---|---|---|---|---|
| Bilińska M et al.[21] | 2013 | 50/50 | Aerobic exercise | 3 months | Not mentioned. | 60 min of cycling, 3 times a week for 6 weeks, with intervals. Exercise for 4 min with a 2-min break, with HR gradually increased to 70–80% of the peak HR. | Habitual activities. | Peak $VO_2$<br>Resting HR<br>Peak HR |
| Ximenes NN et al.[22] | 2015 | 17/17 | Physical exercise | The first day | Hospital | Diaphragmatic breathing exercises, progressive ambulation, and resistance exercises for 30 min, once or twice a day, from before surgery to discharge. | Conventional physical therapy (diaphragmatic breathing exercises and progressive ambulation). | FVC<br>$FEV_1$ |
| Højskov IE et al.[23] | 2016 | 15/15 | Aerobic plus physical exercise | The first day | Hospital | Physical therapy: deep breathing exercises (7–10 breaths, 10 sets), incentive spirometry with positive expiratory airway pressure (3–5 min, twice daily), and neck and shoulder exercises (repeated 10 times, twice daily). Aerobic training: Stationary cycling for 10 min, with warming up in the first 5 min and cooling down in the last 5 min, twice daily for 1 week; exercise was then continued for 4 weeks. | Usual care. | 6MWD<br>Workload<br>Peak $VO_2$ |
| Borges DL et al.[5] | 2016 | 15/19 | Aerobic exercise | The first day | Hospital | Aerobic exercise for 5 min, once to twice a day, for 2 weeks. | Conventional physiotherapy. | FVC<br>$FEV_1$ |

(*Continued on next page*)

**Table 1. *Continued***

| Authors | Year | N<br>Exp/Con | Modalities | Time to start CR after surgery | Site of CR | Experiment | Control | Variables |
|---|---|---|---|---|---|---|---|---|
| Zanini M et al.[24] | 2019 | 30/9 | Physical exercise | The first day | Hospital | Intervention group 1 received upper and lower limb activity training, progressive early walking, IMT, and conventional CPT. Group 2 received active upper and lower limb exercise training, progressive early ambulation, and conventional CPT. Group 3 was treated with IMT plus conventional CPT. The above three groups were combined into one CR group as previously described. | Conventional CPT. | 6MWD<br>FVC<br>$FEV_1$ |
| Shan R et al.[25] | 2022 | 40/40 | Aerobic plus physical exercise | The first day | Hospital | In ICU: abdominal breathing exercises for 5–10 min, twice daily; lip retraction breathing training, abdominal breathing training, sputum expulsion training, back patting, and deep breathing for 10–15 min, 2 to 3 times/d,/time.<br>In postoperative ward: treadmill training or walking on the ground for 10–20 min/d. | Usual care. | Peak VO2<br>6MWD |

HR, heart rate; $VO_2$, oxygen consumption; 6MWD, 6-min walk distance; IMT, inspiratory muscle training; CPT, chest physical therapy; FVC, forced vital capacity; $FEV_1$, forced expiratory volume in 1 s; Exp, experiment; Con, control; N, number.

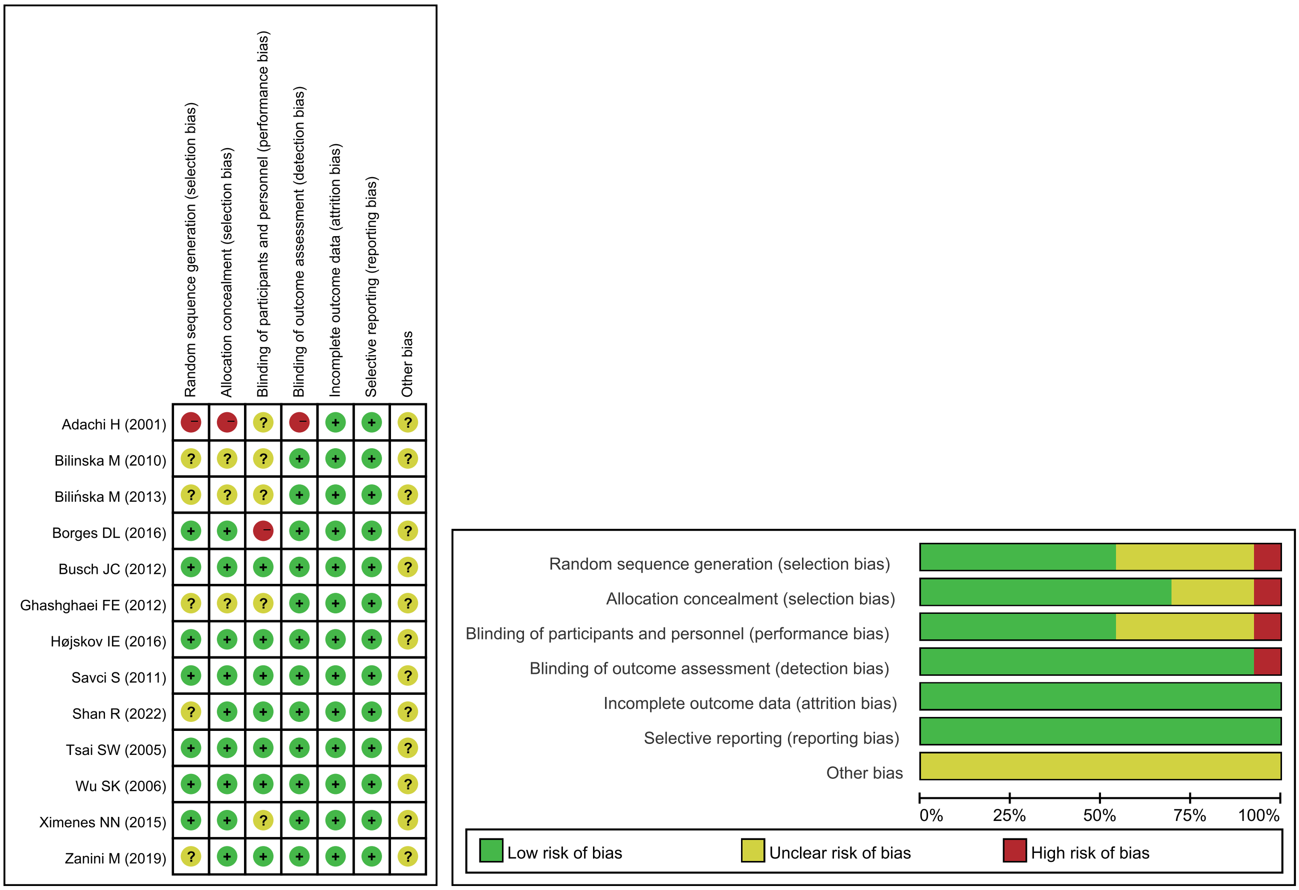



**Figure 2. Assessment of risk of bias**

## Cardiac rehabilitation and pulmonary function

A total of 150 subjects in 4 studies were assessed for the effect of CR on FVC and $FEV_1$, but the random-effects model analysis showed no statistical difference in FVC (MD = 0.19%, 95% CI: −6.11 to 6.48, p = 0.95; $I^2$ = 63.0%) (Figure 3F) or $FEV_1$ (MD = 1.23%, 95% CI: −4.59 to 7.05, p = 0.08; $I^2$ = 56.0%) between the two groups (Figure 3G).

## Subgroup analysis

Subgroup analysis of CR modalities revealed a statistical difference in the improvement in peak $VO_2$ in patients who received aerobic exercise training compared to the other subgroup (Figure 3A). There was no heterogeneity between the two subgroups after the subgroup analysis, and no decrease in heterogeneity was found for either subgroup (Figure 3A). The resting HR was significantly lower in patients who received CR than in controls for both subgroups, with significantly decreased heterogeneity in the aerobic subgroup (Figure 3C). No statistical difference in peak HR was found between the two subgroups, and the heterogeneity was significantly lower in the aerobic subgroup (Figure 3D). With regard to 6MWD, patients who received CR showed significantly greater improvement than controls for both subgroups (Figure 3E). Subgroup analysis on the time to start CR after CABG showed that peak $VO_2$, workload, and peak HR could be improved only when CR was performed within one week after CABG (Figures 4A, 4B, and 4D). However, both resting HR and 6MWD were improved regardless of when CR was initiated after CABG (Figures 4C and 4E). Subgroup analysis of CR duration showed that the subgroup with an exercise duration greater than 1000 min exhibited improvements in peak $VO_2$ (MD = 1.47, 95% CI: 0.02 to 2.92, p = 0.02; $I^2$ = 70.0%) and 6-MWD (MD = 64.99, 95% CI: 38.22 to 91.76, <0.00001; $I^2$ = 89.0%), while different exercise duration had no different effect on peak HR (Figure S1).

The resting HR was significantly lower in patients in the aerobic subgroup than in the other subgroup (heterogeneity was present between the two subgroups, $I^2$ = 72.8%) (Figure 3C), and the peak HR was significantly higher in patients in the aerobic subgroup than in the other subgroup ($I^2$ = 75.6%) (Figure 3D). For the 6MWD, patients in the physical or combined aerobic subgroup had significantly greater improvement than the other subgroup ($I^2$ = 80.9%) (Figure 3E).

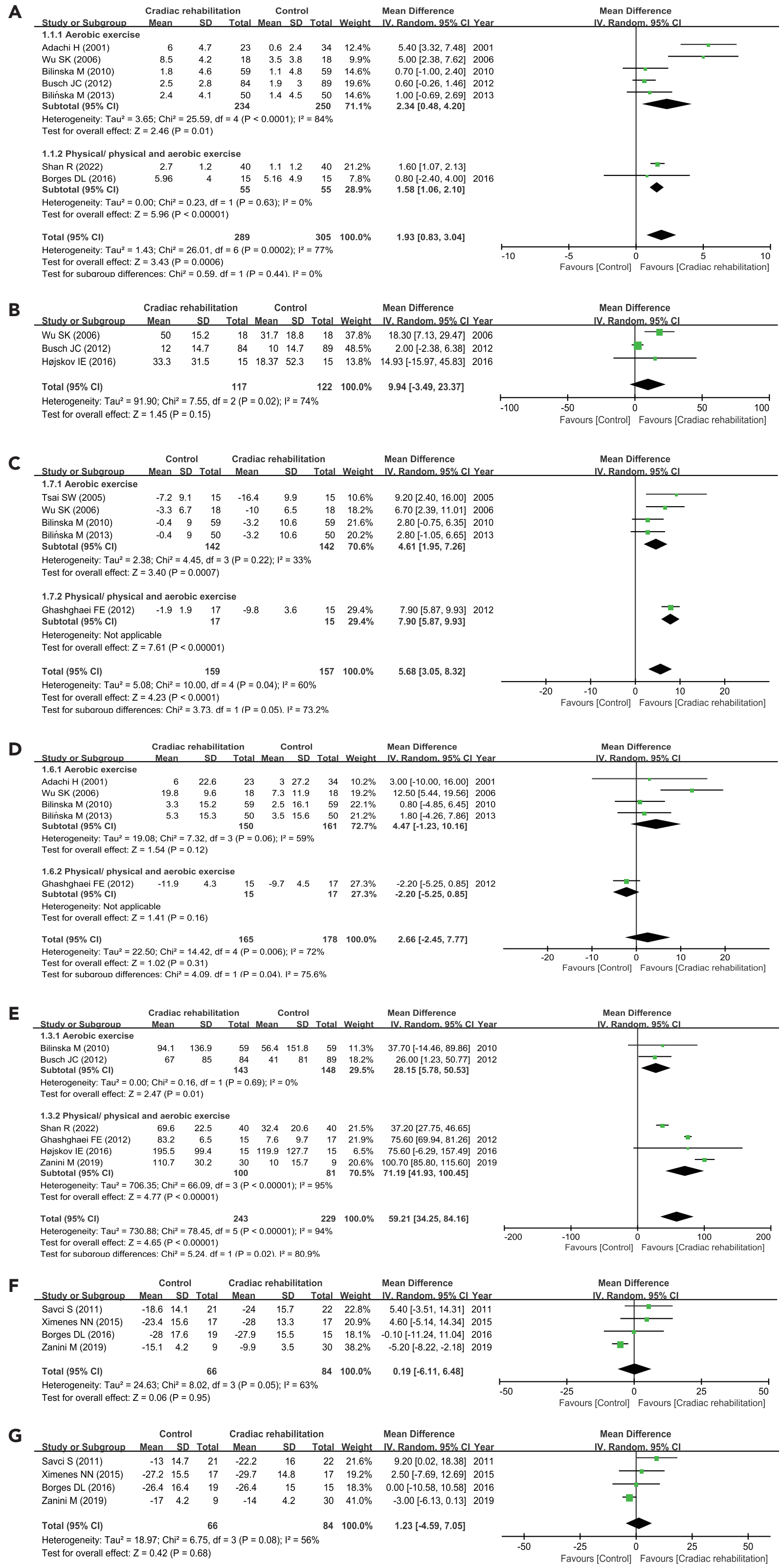

A
Cradiac rehabilitation Control Mean Difference Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year IV, Random, 95% CI
1.1.1 Aerobic exercise
Adachi H (2001) 6 4.7 23 0.6 2.4 34 12.4% 5.40 [3.32, 7.48] 2001
Wu SK (2006) 8.5 4.2 18 3.5 3.8 18 9.9% 5.00 [2.38, 7.62] 2006
Bilinska M (2010) 1.8 4.6 59 1.1 4.8 59 14.6% 0.70 [-1.00, 2.40] 2010
Busch JC (2012) 2.5 2.8 84 1.9 3 89 19.6% 0.60 [-0.26, 1.46] 2012
Bilińska M (2013) 2.4 4.1 50 1.4 4.5 50 14.6% 1.00 [-0.69, 2.69] 2013
Subtotal (95% CI) 234 250 71.1% 2.34 [0.48, 4.20]
Heterogeneity: Tau² = 3.65; Chi² = 25.59, df = 4 (P < 0.0001); I² = 84%
Test for overall effect: Z = 2.46 (P = 0.01)
1.1.2 Physical/ physical and aerobic exercise
Shan R (2022) 2.7 1.2 40 1.1 1.2 40 21.2% 1.60 [1.07, 2.13]
Borges DL (2016) 5.96 4 15 5.16 4.9 15 7.8% 0.80 [-2.40, 4.00] 2016
Subtotal (95% CI) 55 55 28.9% 1.58 [1.06, 2.10]
Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 1 (P = 0.63); I² = 0%
Test for overall effect: Z = 5.96 (P < 0.00001)
Total (95% CI) 289 305 100.0% 1.93 [0.83, 3.04]
Heterogeneity: Tau² = 1.43; Chi² = 26.01, df = 6 (P = 0.0002); I² = 77%
Test for overall effect: Z = 3.43 (P = 0.0006)
Test for subgroup differences: Chi² = 0.59, df = 1 (P = 0.44), I² = 0%
-10 -5 0 5 10
Favours [Control] Favours [Cradiac rehabilitation]
B
Cradiac rehabilitation Control Mean Difference Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year IV, Random, 95% CI
Wu SK (2006) 50 15.2 18 31.7 18.8 18 37.8% 18.30 [7.13, 29.47] 2006
Busch JC (2012) 12 14.7 84 10 14.7 89 48.5% 2.00 [-2.38, 6.38] 2012
Højskov IE (2016) 33.3 31.5 15 18.37 52.3 15 13.8% 14.93 [-15.97, 45.83] 2016
Total (95% CI) 117 122 100.0% 9.94 [-3.49, 23.37]
Heterogeneity: Tau² = 91.90; Chi² = 7.55, df = 2 (P = 0.02); I² = 74%
Test for overall effect: Z = 1.45 (P = 0.15)
-100 -50 0 50 100
Favours [Control] Favours [Cradiac rehabilitation]
C
Control Cradiac rehabilitation Mean Difference Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year IV, Random, 95% CI
1.7.1 Aerobic exercise
Tsai SW (2005) -7.2 9.1 15 -16.4 9.9 15 10.6% 9.20 [2.40, 16.00] 2005
Wu SK (2006) -3.3 6.7 18 -10 6.5 18 18.2% 6.70 [2.39, 11.01] 2006
Bilinska M (2010) -0.4 9 59 -3.2 10.6 59 21.6% 2.80 [-0.75, 6.35] 2010
Bilińska M (2013) -0.4 9 50 -3.2 10.6 50 20.2% 2.80 [-1.05, 6.65] 2013
Subtotal (95% CI) 142 142 70.6% 4.61 [1.95, 7.26]
Heterogeneity: Tau² = 2.38; Chi² = 4.45, df = 3 (P = 0.22); I² = 33%
Test for overall effect: Z = 3.40 (P = 0.0007)
1.7.2 Physical/ physical and aerobic exercise
Ghashghaei FE (2012) -1.9 1.9 17 -9.8 3.6 15 29.4% 7.90 [5.87, 9.93] 2012
Subtotal (95% CI) 17 15 29.4% 7.90 [5.87, 9.93]
Heterogeneity: Not applicable
Test for overall effect: Z = 7.61 (P < 0.00001)
Total (95% CI) 159 157 100.0% 5.68 [3.05, 8.32]
Heterogeneity: Tau² = 5.08; Chi² = 10.00, df = 4 (P = 0.04); I² = 60%
Test for overall effect: Z = 4.23 (P < 0.0001)
Test for subgroup differences: Chi² = 3.73, df = 1 (P = 0.05), I² = 73.2%
-20 -10 0 10 20
Favours [Control] Favours [Cradiac rehabilitation]
D
Cradiac rehabilitation Control Mean Difference Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year IV, Random, 95% CI
1.6.1 Aerobic exercise
Adachi H (2001) 6 22.6 23 3 27.2 34 10.2% 3.00 [-10.00, 16.00] 2001
Wu SK (2006) 19.8 9.6 18 7.3 11.9 18 19.2% 12.50 [5.44, 19.56] 2006
Bilinska M (2010) 3.3 15.2 59 2.5 16.1 59 22.1% 0.80 [-4.85, 6.45] 2010
Bilińska M (2013) 5.3 15.3 50 3.5 15.6 50 21.2% 1.80 [-4.26, 7.86] 2013
Subtotal (95% CI) 150 161 72.7% 4.47 [-1.23, 10.16]
Heterogeneity: Tau² = 19.08; Chi² = 7.32, df = 3 (P = 0.06); I² = 59%
Test for overall effect: Z = 1.54 (P = 0.12)
1.6.2 Physical/ physical and aerobic exercise
Ghashghaei FE (2012) -11.9 4.3 15 -9.7 4.5 17 27.3% -2.20 [-5.25, 0.85] 2012
Subtotal (95% CI) 15 17 27.3% -2.20 [-5.25, 0.85]
Heterogeneity: Not applicable
Test for overall effect: Z = 1.41 (P = 0.16)
Total (95% CI) 165 178 100.0% 2.66 [-2.45, 7.77]
Heterogeneity: Tau² = 22.50; Chi² = 14.42, df = 4 (P = 0.006); I² = 72%
Test for overall effect: Z = 1.02 (P = 0.31)
Test for subgroup differences: Chi² = 4.09, df = 1 (P = 0.04), I² = 75.6%
-20 -10 0 10 20
Favours [Control] Favours [Cradiac rehabilitation]
E
Cradiac rehabilitation Control Mean Difference Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year IV, Random, 95% CI
1.3.1 Aerobic exercise
Bilinska M (2010) 94.1 136.9 59 56.4 151.8 59 11.3% 37.70 [-14.46, 89.86] 2010
Busch JC (2012) 67 85 84 41 81 89 18.2% 26.00 [1.23, 50.77] 2012
Subtotal (95% CI) 143 148 29.5% 28.15 [5.78, 50.53]
Heterogeneity: Tau² = 0.00; Chi² = 0.16, df = 1 (P = 0.69); I² = 0%
Test for overall effect: Z = 2.47 (P = 0.01)
1.3.2 Physical/ physical and aerobic exercise
Shan R (2022) 69.6 22.5 40 32.4 20.6 40 21.5% 37.20 [27.75, 46.65]
Ghashghaei FE (2012) 83.2 6.5 15 7.6 9.7 17 21.9% 75.60 [69.94, 81.26] 2012
Højskov IE (2016) 195.5 99.4 15 119.9 127.7 15 6.5% 75.60 [-6.29, 157.49] 2016
Zanini M (2019) 110.7 30.2 30 10 15.7 9 20.6% 100.70 [85.80, 115.60] 2019
Subtotal (95% CI) 100 81 70.5% 71.19 [41.93, 100.45]
Heterogeneity: Tau² = 706.35; Chi² = 66.09, df = 3 (P < 0.00001); I² = 95%
Test for overall effect: Z = 4.77 (P < 0.00001)
Total (95% CI) 243 229 100.0% 59.21 [34.25, 84.16]
Heterogeneity: Tau² = 730.88; Chi² = 78.45, df = 5 (P < 0.00001); I² = 94%
Test for overall effect: Z = 4.65 (P < 0.00001)
Test for subgroup differences: Chi² = 5.24, df = 1 (P = 0.02), I² = 80.9%
-200 -100 0 100 200
Favours [Control] Favours [Cradiac rehabilitation]
F
Control Cradiac rehabilitation Mean Difference Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year IV, Random, 95% CI
Savci S (2011) -18.6 14.1 21 -24 15.7 22 22.8% 5.40 [-3.51, 14.31] 2011
Ximenes NN (2015) -23.4 15.6 17 -28 13.3 17 20.9% 4.60 [-5.14, 14.34] 2015
Borges DL (2016) -28 17.6 19 -27.9 15.5 15 18.1% -0.10 [-11.24, 11.04] 2016
Zanini M (2019) -15.1 4.2 9 -9.9 3.5 30 38.2% -5.20 [-8.22, -2.18] 2019
Total (95% CI) 66 84 100.0% 0.19 [-6.11, 6.48]
Heterogeneity: Tau² = 24.63; Chi² = 8.02, df = 3 (P = 0.05); I² = 63%
Test for overall effect: Z = 0.06 (P = 0.95)
-50 -25 0 25 50
Favours [Control] Favours [Cradiac rehabilitation]
G
Control Cradiac rehabilitation Mean Difference Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI Year IV, Random, 95% CI
Savci S (2011) -13 14.7 21 -22.2 16 22 21.6% 9.20 [0.02, 18.38] 2011
Ximenes NN (2015) -27.2 15.5 17 -29.7 14.8 17 19.2% 2.50 [-7.69, 12.69] 2015
Borges DL (2016) -26.4 16.4 19 -26.4 15 15 18.3% 0.00 [-10.58, 10.58] 2016
Zanini M (2019) -17 4.2 9 -14 4.2 30 41.0% -3.00 [-6.13, 0.13] 2019
Total (95% CI) 66 84 100.0% 1.23 [-4.59, 7.05]
Heterogeneity: Tau² = 18.97; Chi² = 6.75, df = 3 (P = 0.08); I² = 56%
Test for overall effect: Z = 0.42 (P = 0.68)
-50 -25 0 25 50
Favours [Control] Favours [Cradiac rehabilitation]

**Figure 3. Forest plots for overall and subgroup analyses of exercise modalities after cardiac rehabilitation**
(A) peak oxygen consumption.
(B) workload.
(C) resting heart rate.
(D) peak heart rate.
(E) 6-min walk distance.
(F) forced vital capacity.
(G) forced expiratory volume in 1 s. Abbreviation: SD, standard deviation; IV, inverse variance; CI, confidence interval; Random, random-effects model.

### Publication bias

Egger's test showed $p > 0.05$ for peak $VO_2$, resting HR, peak HR, and 6MWD, suggesting no publication bias for these variables (Table 2; Figure 5).

### Sensitivity analysis

For the variables of peak $VO_2$, resting HR, peak HR, and 6MWD, the direction of values for the recombined effect in the leave-one-out analysis was unchanged and none of the 95% CIs contained null values, indicating that the result was stable (Figure 6).

## DISCUSSION

This meta-analysis involving 806 subjects from 13 RCTs to assess the effect of CR on cardiopulmonary function in patients with CAD after CABG showed that the cardiopulmonary function of patients who received CR was significantly better than that of the controls, as reflected by a significant increase in peak $VO_2$ and 6MWD and a significant decrease in resting HR in these patients. Furthermore, patients who received CR for over 1000 min or within one week after CABG had greater improvement in cardiopulmonary function.

Our findings are partially consistent with a prior meta-analysis showing that CR could improve the physical performance after revascularization.[12] That study, involving CAD patients who received CABG and/or PCI, demonstrated the benefits of CR after revascularization. However, the CABG and PCI are fundamentally different in terms of surgical procedure, with CABG associated with more surgical trauma and general anesthesia, as well as a greater effect on cardiopulmonary function, compared to PCI. In the present study, we only selected patients after CABG as study subjects and conducted subgroup analysis by exercise modality and duration to clarify the source of heterogeneity. CABG can cause a variety of complications due to physiological changes associated with extracorporeal circulation, mechanical injuries from intraoperative sternotomy, cardiac surgical procedures, phrenic nerve injuries, and effects of general anesthesia, which can significantly impact the postoperative mortality, medical costs, and length of hospital stay of patients.[26]

Literature indicates that cardiac output is positively correlated with $VO_2$[27–29]; thus, changes in peak $VO_2$ can be used for the indirect estimation of changes in cardiac function. Carbone et al. found that a CR endpoint, peak $VO_2$, was an independent predictor of long-term survival in patients with CAD; according to their findings, peak $VO_2$ was negatively correlated with the risk of death (HR = 0.84) and the mortality risk was significantly higher below the cut-off value of 17.6 mL/kg/min (HR = 2.39).[30] Our results suggest a longer CR duration can lead to greater improvement in cardiopulmonary function. Similarly, it has been suggested that the number of CR sessions is an independent predictor of improvement in peak $VO_2$, specifically, each additional CR session could increases peak $VO_2$ by 4%.[31] This suggests that CR is an ongoing process requiring long-term adherence of patients. De Schutter et al. found that each 1 mL/kg/min of increment in peak $VO_2$ was associated with an approximately 10% decrease in all-cause mortality,[32] and Vanhees et al. found that a 1% increase in peak $VO_2$ was associated with a 2% decrease in cardiovascular mortality.[33] Unlike the above studies, the present study used the change in peak $VO_2$ as an indicator, and the results suggested that the improvement in peak $VO_2$ was significantly greater in patients who underwent CABG with CR than in controls, which reflected improved cardiac function, decreased all-cause and cardiovascular mortality in the CR group.

Patients with cardiovascular diseases (CVDs) can exhibit autonomic dysfunction characterized by increased sympathetic excitability and vagal inhibition, leading to cardiovascular events.[34,35] Exercise modulates the autonomic nervous system, indicating the necessity of CR programs in this patient population.[36] Guiraud et al. found that in patients with chronic heart failure, a single session of high-intensity interval exercise improved autonomic function significantly reduce heart rate within 24 h after training (beats per minute, $71.1 \pm 2.7$ vs. $68 \pm 3.2$) and reduce arrhythmic events (premature ventricular beats, beats/24h, $1671 \pm 1604$ vs. $531 \pm 338$).[37] Badrov et al. also found that 6 months of CR in patients with CAD reduced resting blood pressure, frequency of sympathetic bursts of activity, and improved the sensitivity of sympathetic stress reflexes in patients with CAD.[38] Consistent with the above, our supplemental results showed that patients with CR greater than 1000 min had better improvements in peak $VO_2$ and 6MWD than patients with CR less than 1000 min, but no improvement in peak HR. Higher HR is associated with an elevated risk of cardiac death in patients with CAD, and may reduce the odds of poor prognosis in patients undergoing CABG.[39,40] Taken together, these results suggest that resting HR decreased significantly in patients with CAD undergoing CR after CABG, thus might reduce the incidence of adverse cardiovascular events in these patients.

It has been recognized that CR can bring important benefits for patients with CAD, including reduced risk of myocardial infarction, all-cause mortality, and all-cause hospitalization rates.[41] CR has also been recommended to patients with CAD by a variety of guidelines, but the participation in CR is still low.[42–44] A study in Japan reported that only 32% of patients with CAD participated in CR after discharge, with the percentage being higher among patients undergoing CABG than those undergoing PCI (80% vs. 28%).[45] CR

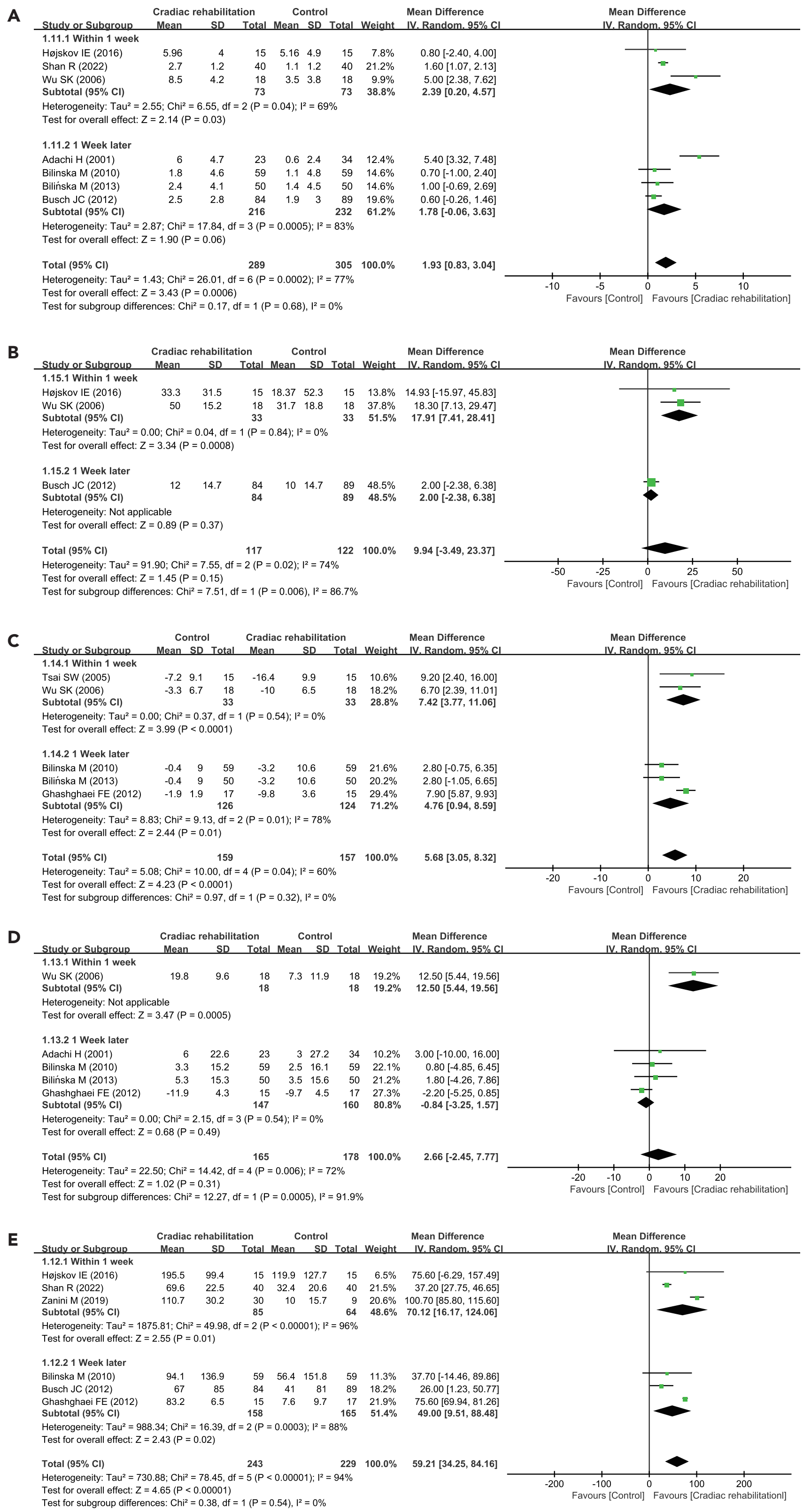

A
Cradiac rehabilitation
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.11.1 Within 1 week
Højskov IE (2016) 5.96 4 15 5.16 4.9 15 7.8% 0.80 [-2.40, 4.00]
Shan R (2022) 2.7 1.2 40 1.1 1.2 40 21.2% 1.60 [1.07, 2.13]
Wu SK (2006) 8.5 4.2 18 3.5 3.8 18 9.9% 5.00 [2.38, 7.62]
Subtotal (95% CI) 73 73 38.8% 2.39 [0.20, 4.57]
Heterogeneity: Tau² = 2.55; Chi² = 6.55, df = 2 (P = 0.04); I² = 69%
Test for overall effect: Z = 2.14 (P = 0.03)
1.11.2 1 Week later
Adachi H (2001) 6 4.7 23 0.6 2.4 34 12.4% 5.40 [3.32, 7.48]
Bilinska M (2010) 1.8 4.6 59 1.1 4.8 59 14.6% 0.70 [-1.00, 2.40]
Bilińska M (2013) 2.4 4.1 50 1.4 4.5 50 14.6% 1.00 [-0.69, 2.69]
Busch JC (2012) 2.5 2.8 84 1.9 3 89 19.6% 0.60 [-0.26, 1.46]
Subtotal (95% CI) 216 232 61.2% 1.78 [-0.06, 3.63]
Heterogeneity: Tau² = 2.87; Chi² = 17.84, df = 3 (P = 0.0005); I² = 83%
Test for overall effect: Z = 1.90 (P = 0.06)
Total (95% CI) 289 305 100.0% 1.93 [0.83, 3.04]
Heterogeneity: Tau² = 1.43; Chi² = 26.01, df = 6 (P = 0.0002); I² = 77%
Test for overall effect: Z = 3.43 (P = 0.0006)
Test for subgroup differences: Chi² = 0.17, df = 1 (P = 0.68), I² = 0%
-10 -5 0 5 10
Favours [Control] Favours [Cradiac rehabilitation]
B
Cradiac rehabilitation
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.15.1 Within 1 week
Højskov IE (2016) 33.3 31.5 15 18.37 52.3 15 13.8% 14.93 [-15.97, 45.83]
Wu SK (2006) 50 15.2 18 31.7 18.8 18 37.8% 18.30 [7.13, 29.47]
Subtotal (95% CI) 33 33 51.5% 17.91 [7.41, 28.41]
Heterogeneity: Tau² = 0.00; Chi² = 0.04, df = 1 (P = 0.84); I² = 0%
Test for overall effect: Z = 3.34 (P = 0.0008)
1.15.2 1 Week later
Busch JC (2012) 12 14.7 84 10 14.7 89 48.5% 2.00 [-2.38, 6.38]
Subtotal (95% CI) 84 89 48.5% 2.00 [-2.38, 6.38]
Heterogeneity: Not applicable
Test for overall effect: Z = 0.89 (P = 0.37)
Total (95% CI) 117 122 100.0% 9.94 [-3.49, 23.37]
Heterogeneity: Tau² = 91.90; Chi² = 7.55, df = 2 (P = 0.02); I² = 74%
Test for overall effect: Z = 1.45 (P = 0.15)
Test for subgroup differences: Chi² = 7.51, df = 1 (P = 0.006), I² = 86.7%
-50 -25 0 25 50
Favours [Control] Favours [Cradiac rehabilitation]
C
Control
Cradiac rehabilitation
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.14.1 Within 1 week
Tsai SW (2005) -7.2 9.1 15 -16.4 9.9 15 10.6% 9.20 [2.40, 16.00]
Wu SK (2006) -3.3 6.7 18 -10 6.5 18 18.2% 6.70 [2.39, 11.01]
Subtotal (95% CI) 33 33 28.8% 7.42 [3.77, 11.06]
Heterogeneity: Tau² = 0.00; Chi² = 0.37, df = 1 (P = 0.54); I² = 0%
Test for overall effect: Z = 3.99 (P < 0.0001)
1.14.2 1 Week later
Bilinska M (2010) -0.4 9 59 -3.2 10.6 59 21.6% 2.80 [-0.75, 6.35]
Bilińska M (2013) -0.4 9 50 -3.2 10.6 50 20.2% 2.80 [-1.05, 6.65]
Ghashghaei FE (2012) -1.9 1.9 17 -9.8 3.6 15 29.4% 7.90 [5.87, 9.93]
Subtotal (95% CI) 126 124 71.2% 4.76 [0.94, 8.59]
Heterogeneity: Tau² = 8.83; Chi² = 9.13, df = 2 (P = 0.01); I² = 78%
Test for overall effect: Z = 2.44 (P = 0.01)
Total (95% CI) 159 157 100.0% 5.68 [3.05, 8.32]
Heterogeneity: Tau² = 5.08; Chi² = 10.00, df = 4 (P = 0.04); I² = 60%
Test for overall effect: Z = 4.23 (P < 0.0001)
Test for subgroup differences: Chi² = 0.97, df = 1 (P = 0.32), I² = 0%
-20 -10 0 10 20
Favours [Control] Favours [Cradiac rehabilitation]
D
Cradiac rehabilitation
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.13.1 Within 1 week
Wu SK (2006) 19.8 9.6 18 7.3 11.9 18 19.2% 12.50 [5.44, 19.56]
Subtotal (95% CI) 18 18 19.2% 12.50 [5.44, 19.56]
Heterogeneity: Not applicable
Test for overall effect: Z = 3.47 (P = 0.0005)
1.13.2 1 Week later
Adachi H (2001) 6 22.6 23 3 27.2 34 10.2% 3.00 [-10.00, 16.00]
Bilinska M (2010) 3.3 15.2 59 2.5 16.1 59 22.1% 0.80 [-4.85, 6.45]
Bilińska M (2013) 5.3 15.3 50 3.5 15.6 50 21.2% 1.80 [-4.26, 7.86]
Ghashghaei FE (2012) -11.9 4.3 15 -9.7 4.5 17 27.3% -2.20 [-5.25, 0.85]
Subtotal (95% CI) 147 160 80.8% -0.84 [-3.25, 1.57]
Heterogeneity: Tau² = 0.00; Chi² = 2.15, df = 3 (P = 0.54); I² = 0%
Test for overall effect: Z = 0.68 (P = 0.49)
Total (95% CI) 165 178 100.0% 2.66 [-2.45, 7.77]
Heterogeneity: Tau² = 22.50; Chi² = 14.42, df = 4 (P = 0.006); I² = 72%
Test for overall effect: Z = 1.02 (P = 0.31)
Test for subgroup differences: Chi² = 12.27, df = 1 (P = 0.0005), I² = 91.9%
-20 -10 0 10 20
Favours [Control] Favours [Cradiac rehabilitation]
E
Cradiac rehabilitation
Control
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
1.12.1 Within 1 week
Højskov IE (2016) 195.5 99.4 15 119.9 127.7 15 6.5% 75.60 [-6.29, 157.49]
Shan R (2022) 69.6 22.5 40 32.4 20.6 40 21.5% 37.20 [27.75, 46.65]
Zanini M (2019) 110.7 30.2 30 10 15.7 9 20.6% 100.70 [85.80, 115.60]
Subtotal (95% CI) 85 64 48.6% 70.12 [16.17, 124.06]
Heterogeneity: Tau² = 1875.81; Chi² = 49.98, df = 2 (P < 0.00001); I² = 96%
Test for overall effect: Z = 2.55 (P = 0.01)
1.12.2 1 Week later
Bilinska M (2010) 94.1 136.9 59 56.4 151.8 59 11.3% 37.70 [-14.46, 89.86]
Busch JC (2012) 67 85 84 41 81 89 18.2% 26.00 [1.23, 50.77]
Ghashghaei FE (2012) 83.2 6.5 15 7.6 9.7 17 21.9% 75.60 [69.94, 81.26]
Subtotal (95% CI) 158 165 51.4% 49.00 [9.51, 88.48]
Heterogeneity: Tau² = 988.34; Chi² = 16.39, df = 2 (P = 0.0003); I² = 88%
Test for overall effect: Z = 2.43 (P = 0.02)
Total (95% CI) 243 229 100.0% 59.21 [34.25, 84.16]
Heterogeneity: Tau² = 730.88; Chi² = 78.45, df = 5 (P < 0.00001); I² = 94%
Test for overall effect: Z = 4.65 (P < 0.00001)
Test for subgroup differences: Chi² = 0.38, df = 1 (P = 0.54), I² = 0%
-200 -100 0 100 200
Favours [Control] Favours [Cradiac rehabilitation]

**Figure 4. Forest plots for overall and subgroup analyses of the start time of exercise after cardiac rehabilitation**
(A) peak oxygen consumption.
(B) workload.
(C) resting heart rate.
(D) peak heart rate.
(E) 6-min walk distance. Abbreviation: SD, standard deviation; IV, inverse variance; CI, confidence interval; Random, random-effects model.

participation was also particularly low in low/middle-income countries (LMICs).[46] The low participation rate can be attributed to three aspects:[47] 1) patient-related factors such as older age, low socioeconomic status, and lack of awareness,[48] 2) physicians having inadequate knowledge of CR and their failure to recommend CR to patients,[49] and 3) limited availability of CR, financial difficulty of patients, and lack of medical insurance.[7] All of the above factors indicated the need for relevant measures to improve CR participation among patients with CAD.

Autonomic dysfunction is known to adversely affect the outcome of patients with CVDs. Postoperative CR can regulate the cardiovascular system and improve cardiopulmonary function by regulating autonomic nervous function. Therefore, patients should be encouraged to participate in long-term CR after CABG for their best recovery.

Aerobic exercise is one of the interventions recommended in a variety of international guidelines. However, the intensity of exercise, duration, and frequency of training in the recommendations vary greatly. Exercise intensity is one of the most controversial issues for patients with coronary heart disease. Studies have shown that high-intensity exercise generally leads to a more pronounced improvement in cardiopulmonary function[50] but may be associated with an increased risk of cardiac events.[51] Therefore, CR must be personalized in terms of intensity, frequency, and duration. Some guidelines recommend that most adults engage in moderate-to-intensity cardiopulmonary exercise training for $\geq$150 min/wk, vigorous-intensity cardiopulmonary exercise training for $\geq$75 min/wk, or a combination of moderate- and vigorous-intensity exercise to achieve a total energy expenditure of $\geq$500–1000 MET·min/wk. Adults should also engage in resistance exercises for major muscle groups as well as neuromotor exercise involving balance, agility, and coordination for 2–3 days/wk.[51] Taken together, it is speculated that appropriate extension of CR can increase patients' improvement in cardiopulmonary function. In addition, the combination of physical exercise and aerobic exercise can also improve cardiopulmonary function, which should also be recommended to patients with low tolerance to aerobic exercise.

As there was significant heterogeneity among studies, we conducted the subgroup analysis of exercise modality and duration, which, however, showed no significant reduction in heterogeneity between groups. It is difficult to avoid heterogeneity due to the difference in exercise modalities as well as the duration and frequency of exercise adopted in the studies. In addition, the total exercise duration was more comparable between groups, as compared with other meta-analyses[10] that indicated the frequency of exercise only. The benefits from different exercise modalities may vary greatly, which might have also affected the results of our subgroup analysis.

The leave-one-out sensitivity analysis of the 6MWD suggested that Busch's study had a greater impact on the stability. Compared with other studies, patients in the control group of Busch's study could complete up to 240 min of general exercise per week, which was significantly longer than the control group in other studies; this might have resulted in a greater improvement in 6MWD in the control group. Furthermore, the inclusion criteria in Busch's study specified that the patients' 6MWD was 100–350 m at enrollment, which might have excluded those CAD patients with very poor or very good cardiac function; this might also have affected our result.

In conclusion, the present meta-analysis showed that CR with aerobic exercises after CABG could positively affect patients' cardiopulmonary function, which was reflected by improvements in peak $VO_2$, resting HR, and 6MWD. However, the use of physical exercise or combined aerobic exercise helped improve resting HR and 6MWD. Patients who had received over 1000 min of CR after CABG exhibited greatly improved cardiopulmonary function, which was reflected by improvement in peak $VO_2$ and 6MWD. In addition, CR within one week after CABG can better improve cardiopulmonary function, which was reflected by improvement in peak $VO_2$, workload, resting HR, peak HR, and 6MWD. Therefore, personalized and long-term CR should be recommended to patients with CAD who have undergone CABG to improve their cardiopulmonary function, and patient education should also be provided to improve their adherence to this helpful intervention.

## Limitations of the study

The present study still has some limitations. First, because there is no standard CR protocol, the aerobic and physical exercises for the experimental groups varied in modality, duration, and frequency; the interventions for the control groups also varied across studies, which

**Table 2. Egger's test for publication bias**

| Variables | t value | *p* value | 95% CI |
|---|---|---|---|
| Peak $VO_2$ | 0.82 | 0.450 | −2.52 - 4.88 |
| Resting HR | 0.63 | 0.576 | −5.24 - 7.80 |
| Peak HR | 1.57 | 0.214 | −2.78 - 8.19 |
| 6MWD | −0.46 | 0.668 | −9.06–6.47 |

$VO_2$, oxygen consumption; HR, heart rate; 6MWD, 6-min walk distance; CI, confidence interval.

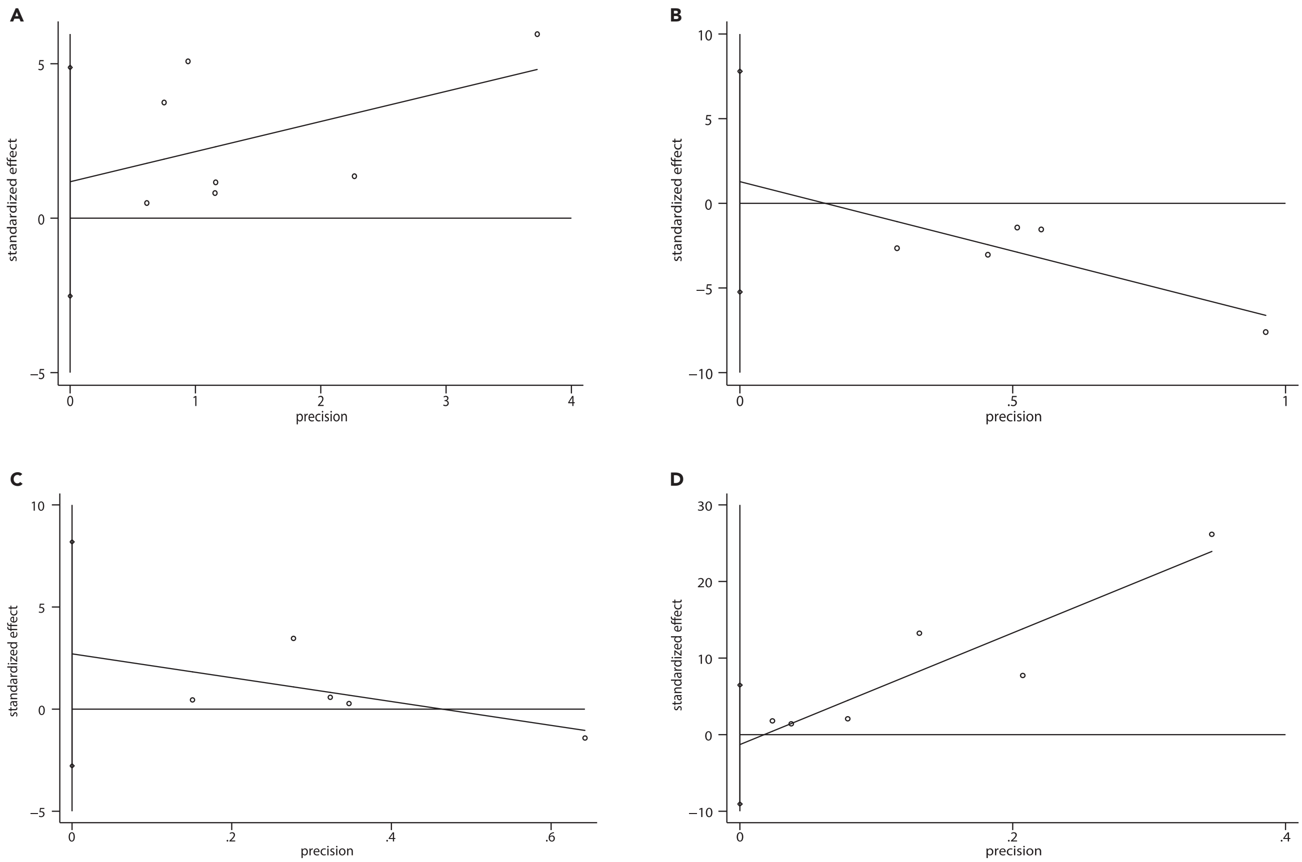



**Figure 5. Results on publication bias**

(A) peak oxygen consumption.

(B) resting heart rate.

(C) peak heart rate.

(D) 6-min walk distance.

inevitably led to heterogeneity. Second, only 13 studies were included in the present review and analysis, and most of them were single-center, small-scale studies; thus, the sample size of the present study was small, and the findings may need to be validated by multi-center, large-scale clinical trials. In addition, our meta-analysis was only able to obtain secondary data from other studies, thus, our findings might be less accurate than primary studies. Finally, although 13 studies were included in this study, not all of them were involved in the analysis of each outcome, which might also have affected test performance and increased heterogeneity.

## STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

- KEY RESOURCES TABLE
- RESOURCE AVAILABILITY
  - Lead contact
  - Materials availability
  - Data and code availability
- EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS
  - Experimental model
  - Study participant details
- METHOD DETAILS
  - Subjects
  - Intervention
  - Outcomes

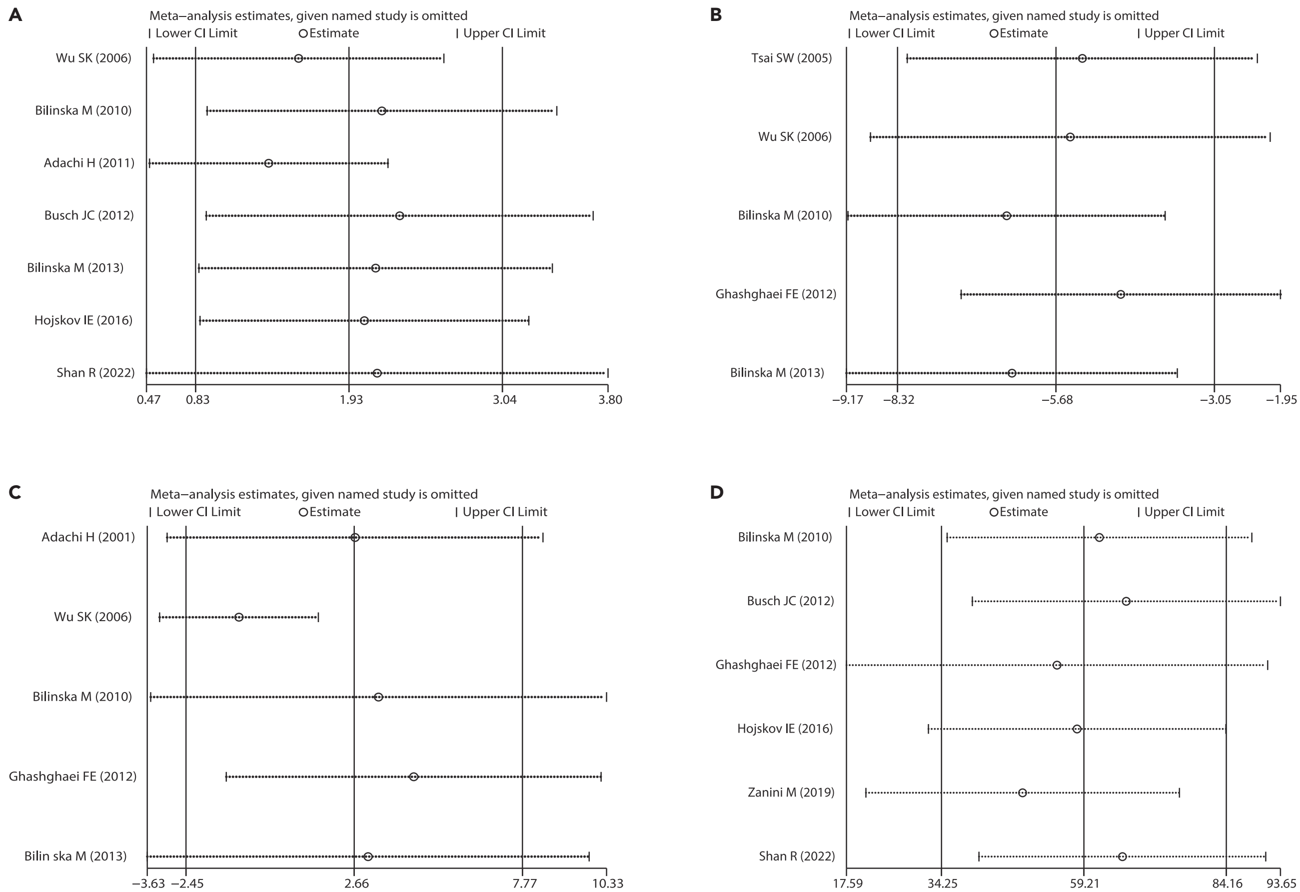



**Figure 6. Sensitivity analysis**

(A) peak oxygen consumption.

(B) resting heart rate.

(C) peak heart rate.

(D) 6-min walk distance. Abbreviation: CI, confidence interval. The dashed line corresponding to each study indicates the results of the leave-one-out analysis with the exclusion of this study, which are presented with estimates and 95%CIs. Three vertical solid lines indicate the estimates and 95%CIs for all studies.

  - Literature search
  - Screening and data extraction
  - Assessment of risk of bias
- QUANTIFICATION AND STATISTICAL ANALYSIS

## SUPPLEMENTAL INFORMATION

Supplemental information can be found online at https://doi.org/10.1016/j.isci.2023.107861.

## ACKNOWLEDGMENTS

The study was conducted using RCT studies. We would like to thank all participants. This study was funded by the National Natural Science Foundation of China (Grant No. 82170292).

## AUTHOR CONTRIBUTIONS

Conceptualization, J.M. and C.W.; methodology, H.Y.; software, J.M.; validation, J.M., C.W., and H.Y.; formal analysis, J.M. and H.Y.; investigation, J.M. and H.Y.; resources, J.M.; data curation, J.M. and C.W.; writing—original draft preparation, J.M.; writing—review and editing, J.M., C.W. and H.Y.; visualization, J.M.; supervision, R.S. and C.W.; project administration, R.S. and C.W.; funding acquisition, R.S. All authors have read and agreed to the published version of the article.

## DECLARATION OF INTERESTS

The authors have no conflict of interest to disclose.

## INCLUSION AND DIVERSITY

We support inclusive, diverse, and equitable conduct of research.

Received: June 7, 2023
Revised: July 15, 2023
Accepted: September 6, 2023
Published: September 9, 2023

## REFERENCES

1. Lawton, J.S., Tamis-Holland, J.E., Bangalore, S., Bates, E.R., Beckie, T.M., Bischoff, J.M., Bittl, J.A., Cohen, M.G., DiMaio, J.M., Don, C.W., et al. (2022). 2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation *145*, e18–e114. https://doi.org/10.1161/CIR.0000000000001038.
2. Lido, P., Romanello, D., Tesauro, M., Bei, A., Perrone, M.A., Palazzetti, D., Noce, A., Di Lullo, L., Calò, L., and Cice, G. (2022). Verapamil: prevention and treatment of cardio-renal syndromes in diabetic hypertensive patients? Eur. Rev. Med. Pharmacol. Sci. *26*, 1524–1534. https://doi.org/10.26355/eurrev_202203_28217.
3. Kushwaha, P., Moiz, J.A., and Mujaddadi, A. (2022). Exercise training and cardiac autonomic function following coronary artery bypass grafting: a systematic review and meta-analysis. Egypt. Heart J. *74*, 67. https://doi.org/10.1186/s43044-022-00306-5.
4. Mungovan, S.F., Singh, P., Gass, G.C., Smart, N.A., and Hirschhorn, A.D. (2017). Effect of physical activity in the first five days after cardiac surgery. J. Rehabil. Med. *49*, 71–77. https://doi.org/10.2340/16501977-2165.
5. Borges, D.L., Silva, M.G., Silva, L.N., Fortes, J.V., Costa, E.T., Assunção, R.P., Lima, C.M., da Silva Nina, V.J., Bernardo-Filho, M., and Caputo, D.S. (2016). Effects of Aerobic Exercise Applied Early After Coronary Artery Bypass Grafting on Pulmonary Function, Respiratory Muscle Strength, and Functional Capacity: A Randomized Controlled Trial. J. Phys. Activ. Health *13*, 946–951. https://doi.org/10.1123/jpah.2015-0614.
6. Altree, T., Bussell, L., Nguyen, P., and Johnston, S. (2019). Adverse cardiac outcomes after pulmonary function testing with recent myocardial infarction. Respir. Med. *155*, 49–50. https://doi.org/10.1016/j.rmed.2019.07.003.
7. Ades, P.A., Khadanga, S., Savage, P.D., and Gaalema, D.E. (2022). Enhancing participation in cardiac rehabilitation: Focus on underserved populations. Prog. Cardiovasc. Dis. *70*, 102–110. https://doi.org/10.1016/j.pcad.2022.01.003.
8. Hamazaki, N., Kamiya, K., Yamamoto, S., Nozaki, K., Ichikawa, T., Matsuzawa, R., Tanaka, S., Nakamura, T., Yamashita, M., Maekawa, E., et al. (2020). Changes in Respiratory Muscle Strength Following Cardiac Rehabilitation for Prognosis in Patients with Heart Failure. J. Clin. Med. *9*, 952. https://doi.org/10.3390/jcm9040952.
9. Taylor, R.S., Dalal, H.M., and McDonagh, S.T.J. (2022). The role of cardiac rehabilitation in improving cardiovascular outcomes. Nat. Rev. Cardiol. *19*, 180–194. https://doi.org/10.1038/s41569-021-00611-7.
10. Wang, L., Sun, Y., Zhan, J., Wu, Z., Zhang, P., Wen, X., Ge, S., Han, X., and Lu, L. (2021). Effects of Exercise Therapy on Anxiety and Depression in Patients With Coronary Heart Disease: A Meta-Analysis of a Randomized Controlled Study. Front. Cardiovasc. Med. *8*, 730155. https://doi.org/10.3389/fcvm.2021.730155.
11. Ji, H., Fang, L., Yuan, L., and Zhang, Q. (2019). Effects of Exercise-Based Cardiac Rehabilitation in Patients with Acute Coronary Syndrome: A Meta-Analysis. Med. Sci. Mon. Int. Med. J. Exp. Clin. Res. *25*, 5015–5027. https://doi.org/10.12659/MSM.917362.
12. Campos, H.O., Rodrigues, Q.T., Drummond, L.R., Lima, P.M.A., Monteiro, M.D.C., Wanner, S.P., and Coimbra, C.C. (2022). Exercise-based cardiac rehabilitation after myocardial revascularization: a systematic review and meta-analysis. Rev. Cardiovasc. Med. *23*, 74. https://doi.org/10.31083/j.rcm2302074.
13. Froelicher, V., Jensen, D., and Sullivan, M. (1985). A randomized trial of the effects of exercise training after coronary artery bypass surgery. Arch. Intern. Med. *145*, 689–692.
14. Adachi, H., Itoh, H., Sakurai, S., Takahashi, T., Toyama, T., Naito, S., Hoshizaki, H., Oshima, S., Taniguchi, K., Kato, M., et al. (2001). Short-term physical training improves ventilatory response to exercise after coronary arterial bypass surgery. Jpn. Circ. J. *65*, 419–423. https://doi.org/10.1253/jcj.65.419.
15. Tsai, S.W., Lin, Y.W., and Wu, S.K. (2005). The effect of cardiac rehabilitation on recovery of heart rate over one minute after exercise in patients with coronary artery bypass graft surgery. Clin. Rehabil. *19*, 843–849. https://doi.org/10.1191/0269215505cr915oa.
16. Wu, S.K., Lin, Y.W., Chen, C.L., and Tsai, S.W. (2006). Cardiac rehabilitation vs. home exercise after coronary artery bypass graft surgery: a comparison of heart rate recovery. Am. J. Phys. Med. Rehabil. *85*, 711–717. https://doi.org/10.1097/01.phm.0000228597.64057.66.
17. Bilinska, M., Kosydar-Piechna, M., Gasiorowska, A., Mikulski, T., Piotrowski, W., Nazar, K., and Piotrowicz, R. (2010). Influence of dynamic training on hemodynamic, neurohormonal responses to static exercise and on inflammatory markers in patients after coronary artery bypass grafting. Circ. J. *74*, 2598–2604. https://doi.org/10.1253/circj.cj-10-0104.
18. Savci, S., Degirmenci, B., Saglam, M., Arikan, H., Inal-Ince, D., Turan, H.N., and Demircin, M. (2011). Short-term effects of inspiratory muscle training in coronary artery bypass graft surgery: a randomized controlled trial. Scand. Cardiovasc. J. *45*, 286–293. https://doi.org/10.3109/14017431.2011.595820.
19. Busch, J.C., Lillou, D., Wittig, G., Bartsch, P., Willemsen, D., Oldridge, N., and Bjarnason-Wehrens, B. (2012). Resistance and balance training improves functional capacity in very old participants attending cardiac rehabilitation after coronary bypass surgery. J. Am. Geriatr. Soc. *60*, 2270–2276. https://doi.org/10.1111/jgs.12030.
20. Ghashghaei, F.E., Sadeghi, M., Marandi, S.M., and Ghashghaei, S.E. (2012). Exercise-based cardiac rehabilitation improves hemodynamic responses after coronary artery bypass graft surgery. ARYA Atheroscler. *7*, 151–156.
21. Bilińska, M., Kosydar-Piechna, M., Mikulski, T., Piotrowicz, E., Gąsiorowska, A., Piotrowski, W., Nazar, K., and Piotrowicz, R. (2013). Influence of aerobic training on neurohormonal and hemodynamic responses to head-up tilt test and on autonomic nervous activity at rest and after exercise in patients after bypass surgery. Cardiol. J. *20*, 17–24. https://doi.org/10.5603/CJ.2013.0004.
22. Ximenes, N.N.P.S., Borges, D.L., Lima, R.O., Barbosa e Silva, M.G., Silva, L.N.d., Costa, M.d.A.G., Baldez, T.E.P., and Nina, V.J.d.S. (2015). Effects of Resistance Exercise Applied Early After Coronary Artery Bypass Grafting: a Randomized Controlled Trial. Braz. J. Cardiovasc. Surg. *30*, 620–625. https://doi.org/10.5935/1678-9741.20150077.
23. Højskov, I.E., Moons, P., Hansen, N.V., Greve, H., Olsen, D.B., Cour, S.L., Glud, C., Winkel, P., Lindschou, J., Egerod, I., et al. (2016). Early physical training and psycho-educational intervention for patients undergoing coronary artery bypass grafting. The SheppHeart randomized 2 x 2 factorial clinical pilot trial. Eur. J. Cardiovasc. Nurs. *15*, 425–437. https://doi.org/10.1177/1474515115594524.
24. Zanini, M., Nery, R.M., de Lima, J.B., Buhler, R.P., da Silveira, A.D., and Stein, R. (2019). Effects of Different Rehabilitation Protocols in Inpatient Cardiac Rehabilitation After Coronary Artery Bypass Graft Surgery: A RANDOMIZED CLINICAL TRIAL. J. Cardiopulm. Rehabil. Prev. *39*, E19–E25. https://doi.org/10.1097/HCR.0000000000000431.
25. Shan, R., Zhang, L., Zhu, Y., Ben, L., Xin, Y., Wang, F., and Yan, L. (2022). Effect of Early Exercise Rehabilitation on Cardiopulmonary

Function and Quality of Life in Patients after Coronary Artery Bypass Grafting. Contrast Media Mol. Imaging *2022*, 4590037. https://doi.org/10.1155/2022/4590037.

26. Montrief, T., Koyfman, A., and Long, B. (2018). Coronary artery bypass graft surgery complications: A review for emergency clinicians. Am. J. Emerg. Med. *36*, 2289–2297. https://doi.org/10.1016/j.ajem.2018.09.014.
27. Skattebo, Ø., Calbet, J.A.L., Rud, B., Capelli, C., and Hallén, J. (2020). Contribution of oxygen extraction fraction to maximal oxygen uptake in healthy young men. Acta Physiol. *230*, e13486. https://doi.org/10.1111/apha.13486.
28. Agostoni, P.G., Wasserman, K., Perego, G.B., Guazzi, M., Cattadori, G., Palermo, P., Lauri, G., and Marenzi, G. (2000). Non-invasive measurement of stroke volume during exercise in heart failure patients. Clin. Sci. *98*, 545–551.
29. Del Torto, A., Corrieri, N., Vignati, C., Gentile, P., Cattadori, G., Paolillo, S., and Agostoni, P. (2017). Contribution of central and peripheral factors at peak exercise in heart failure patients with progressive severity of exercise limitation. Int. J. Cardiol. *248*, 252–256. https://doi.org/10.1016/j.ijcard.2017.07.071.
30. Carbone, S., Kim, Y., Kachur, S., Billingsley, H., Kenyon, J., De Schutter, A., Milani, R.V., and Lavie, C.J. (2022). Peak oxygen consumption achieved at the end of cardiac rehabilitation predicts long-term survival in patients with coronary heart disease. Eur. Heart J. Qual. Care Clin. Outcomes *8*, 361–367. https://doi.org/10.1093/ehjqcco/qcab032.
31. Little, K.A., Smith, J.R., Medina-Inojosa, J.R., Chacin Suarez, A.S., Taylor, J.L., Hammer, S.M., Fischer, K.M., Bonikowske, A.R., Squires, R.W., Thomas, R.J., and Olson, T.P. (2022). Predictors of Changes in Peak Oxygen Uptake After Outpatient Cardiac Rehabilitation: Importance of Cardiac Rehabilitation Attendance. Mayo Clin. Proc. Innov. Qual. Outcomes *6*, 428–435. https://doi.org/10.1016/j.mayocpiqo.2022.07.002.
32. De Schutter, A., Kachur, S., Lavie, C.J., Menezes, A., Shum, K.K., Bangalore, S., Arena, R., and Milani, R.V. (2018). Cardiac rehabilitation fitness changes and subsequent survival. Eur. Heart J. Qual. Care Clin. Outcomes *4*, 173–179. https://doi.org/10.1093/ehjqcco/qcy018.
33. Vanhees, L., Fagard, R., Thijs, L., and Amery, A. (1995). Prognostic value of training-induced change in peak exercise capacity in patients with myocardial infarcts and patients with coronary bypass surgery. Am. J. Cardiol. *76*, 1014–1019. https://doi.org/10.1016/s0002-9149(99)80287-2.
34. Besnier, F., Labrunée, M., Pathak, A., Pavy-Le Traon, A., Galès, C., Sénard, J.M., and Guiraud, T. (2017). Exercise training-induced modification in autonomic nervous system: An update for cardiac patients. Ann. Phys. Rehabil. Med. *60*, 27–35. https://doi.org/10.1016/j.rehab.2016.07.002.
35. Qiu, S., Cai, X., Sun, Z., Li, L., Zuegel, M., Steinacker, J.M., and Schumann, U. (2017). Heart Rate Recovery and Risk of Cardiovascular Events and All-Cause Mortality: A Meta-Analysis of Prospective Cohort Studies. J. Am. Heart Assoc. *6*, e005505. https://doi.org/10.1161/JAHA.117.005505.
36. Hsu, C.Y., Hsieh, P.L., Hsiao, S.F., and Chien, M.Y. (2015). Effects of Exercise Training on Autonomic Function in Chronic Heart Failure: Systematic Review. BioMed Res. Int. *2015*, 591708. https://doi.org/10.1155/2015/591708.
37. Guiraud, T., Labrunee, M., Gaucher-Cazalis, K., Despas, F., Meyer, P., Bosquet, L., Gales, C., Vaccaro, A., Bousquet, M., Galinier, M., et al. (2013). High-intensity interval exercise improves vagal tone and decreases arrhythmias in chronic heart failure. Med. Sci. Sports Exerc. *45*, 1861–1867. https://doi.org/10.1249/MSS.0b013e3182967559.
38. Badrov, M.B., Wood, K.N., Lalande, S., Sawicki, C.P., Borrell, L.J., Barron, C.C., Vording, J.L., Fleischhauer, A., Suskin, N., McGowan, C.L., and Shoemaker, J.K. (2019). Effects of 6 Months of Exercise-Based Cardiac Rehabilitation on Autonomic Function and Neuro-Cardiovascular Stress Reactivity in Coronary Artery Disease Patients. J. Am. Heart Assoc. *8*, e012257. https://doi.org/10.1161/JAHA.119.012257.
39. Michael, S., Jay, O., Halaki, M., Graham, K., and Davis, G.M. (2016). Submaximal exercise intensity modulates acute post-exercise heart rate variability. Eur. J. Appl. Physiol. *116*, 697–706. https://doi.org/10.1007/s00421-016-3327-9.
40. Gambassi, B.B., Almeida, F.d.J.F., Almeida, A.E.A.F., Ribeiro, D.A.F., Gomes, R.S.A., Chaves, L.F.C., Sousa, T.M.d.S., and Nina, V.J.d.S. (2019). Acute Response to Aerobic Exercise on Autonomic Cardiac Control of Patients in Phase III of a Cardiovascular Rehabilitation Program Following Coronary Artery Bypass Grafting. Braz. J. Cardiovasc. Surg. *34*, 305–310. https://doi.org/10.21470/1678-9741-2019-0030.
41. Dibben, G., Faulkner, J., Oldridge, N., Rees, K., Thompson, D.R., Zwisler, A.D., and Taylor, R.S. (2021). Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database Syst. Rev. *11*, CD001800. https://doi.org/10.1002/14651858.CD001800.pub4.
42. Thomas, R.J., Balady, G., Banka, G., Beckie, T.M., Chiu, J., Gokak, S., Ho, P.M., Keteyian, S.J., King, M., Lui, K., et al. (2018). ACC/AHA Clinical Performance and Quality Measures for Cardiac Rehabilitation: A Report of the American College of Cardiology/American Heart Association Task Force on Performance Measures. J. Am. Coll. Cardiol. *71*, 1814–1837. https://doi.org/10.1016/j.jacc.2018.01.004.
43. Mehra, V.M., Gaalema, D.E., Pakosh, M., and Grace, S.L. (2020). Systematic review of cardiac rehabilitation guidelines: Quality and scope. Eur. J. Prev. Cardiol. *27*, 912–928. https://doi.org/10.1177/2047487319878958.
44. Visseren, F.L.J., Mach, F., Smulders, Y.M., Carballo, D., Koskinas, K.C., Bäck, M., Benetos, A., Biffi, A., Boavida, J.M., Capodanno, D., et al. (2022). 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur. J. Prev. Cardiol. *29*, 5–115. https://doi.org/10.1093/eurjpc/zwab154.
45. Ohtera, S., Kato, G., Ueshima, H., Mori, Y., Nakatani, Y., Ozasa, N., Nakayama, T., and Kuroda, T. (2021). A nationwide survey on participation in cardiac rehabilitation among patients with coronary heart disease using health claims data in Japan. Sci. Rep. *11*, 20096. https://doi.org/10.1038/s41598-021-99516-1.
46. Ragupathi, L., Stribling, J., Yakunina, Y., Fuster, V., McLaughlin, M.A., and Vedanthan, R. (2017). Availability, Use, and Barriers to Cardiac Rehabilitation in LMIC. Glob. Heart *12*, 323–334.e10. https://doi.org/10.1016/j.gheart.2016.09.004.
47. Turk-Adawi, K., Sarrafzadegan, N., and Grace, S.L. (2014). Global availability of cardiac rehabilitation. Nat. Rev. Cardiol. *11*, 586–596. https://doi.org/10.1038/nrcardio.2014.98.
48. Bohplian, S., and Bronas, U.G. (2022). Motivational Strategies and Concepts to Increase Participation and Adherence in Cardiac Rehabilitation: AN INTEGRATIVE REVIEW. J. Cardiopulm. Rehabil. Prev. *42*, 75–83. https://doi.org/10.1097/HCR.0000000000000639.
49. Chacin-Suarez, A., Grace, S.L., Anchique-Santos, C., Supervia, M., Turk-Adawi, K., Britto, R.R., Scantlebury, D.C., Araya-Ramirez, F., Gonzalez, G., Benaim, B., et al. (2021). Cardiac rehabilitation availability and characteristics in Latin America and the Caribbean: A Global Comparison. Am. Heart J. *240*, 16–27. https://doi.org/10.1016/j.ahj.2021.05.010.
50. Franklin, B.A., Thompson, P.D., Al-Zaiti, S.S., Albert, C.M., Hivert, M.F., Levine, B.D., Lobelo, F., Madan, K., Sharrief, A.Z., and Eijsvogels, T.M.H.; American Heart Association Physical Activity Committee of the Council on Lifestyle and Cardiometabolic Health; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; and Stroke Council (2020). Exercise-Related Acute Cardiovascular Events and Potential Deleterious Adaptations Following Long-Term Exercise Training: Placing the Risks Into Perspective-An Update: A Scientific Statement From the American Heart Association. Circulation *141*, e705–e736. https://doi.org/10.1161/CIR.0000000000000749.
51. Garber, C.E., Blissmer, B., Deschenes, M.R., Franklin, B.A., Lamonte, M.J., Lee, I.M., Nieman, D.C., and Swain, D.P.; American College of Sports Medicine (2011). American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med. Sci. Sports Exerc. *43*, 1334–1359. https://doi.org/10.1249/MSS.0b013e318213fefb.
52. Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.3. www.training.cochrane.org/handbook (accessed on 21 August 2023).

## STAR★METHODS

### KEY RESOURCES TABLE

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---|---|---|
| Deposited data | | |
| International prospective register of systematic reviews | https://www.crd.york.ac.uk/PROSPERO/ | PROSPERO |
| Medline | https://www.medline.eu/ | N/A |
| Embase | https://www.embase.com/ | N/A |
| Cochrane Library | https://www.cochranelibrary.com/ | N/A |
| Web of Science | https://www.webofscience.com/ | N/A |
| Software and algorithms | | |
| EndNote | https://support.clarivate.com/Endnote/s/article/Download-EndNote?language=en_US | Version 20.0.0.14672 |
| RevMan | https://training.cochrane.org/online-learning/core-software/revman | version 5.4.1 |
| STATA | https://www.stata.com/order/new/edu/profplus/student-pricing/ | version 12.0 |

## RESOURCE AVAILABILITY

### Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Chengming Wang (46595842@qq.com).

### Materials availability

The study did not generate any new materials.

### Data and code availability

- All data reported in this paper will be shared by the lead contact upon request.
- This study did not report original code.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

## EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

### Experimental model

Our study does not use experimental models typical in the life sciences.

### Study participant details

A total of 806 participants were included in this study, including 403 in the CR group and 403 in the control group. They were all diagnosed with CAD and underwent CABG surgery. The specific CR procedures of patients participating in CR in each study are different, which has been shown in Table 1. Ethical approval is not required for this study because the original RCTs had previously received authorization from the ethics and institutional review board.

## METHOD DETAILS

### Subjects

Subjects of randomized controlled trials (RCTs) who were 1) 18 years of age or older, 2) diagnosed with CAD and treated with CABG, and 3) randomized into the CR or the control group were included in the present study. Studies were excluded if they 1) had unavailable or incomplete data on outcomes, 2) had subjects grouped by other indicators, and 3) were not RCTs (e.g., reviews, meta-analyses, case reports). The present review was prospectively registered in the PROSPERO systematic review registry (ID: CRD42021249396).

### Intervention

All the subjects included in the present study received CR after CABG, with CR including any combination of aerobic, strength or balance training, and inspiratory muscle training. There were no restrictions on the duration, frequency or method of CR.

### Outcomes

The outcomes were the cardiopulmonary function assessed using cardiopulmonary exercise testing (CPET), 6-minute walk test (6MWT), and pulmonary function test, with CPET measures including peak oxygen consumption (peak $VO_2$), resting heart rate (resting HR), peak heart rate (peak HR), workload, and pulmonary function test measures such as forced vital capacity (FVC) and forced expiratory volume in 1 second ($FEV_1$). The outcomes were measured before and after CR for further analysis.

### Literature search

The Medline, Embase, the Cochrane Library, and the Web of Science were searched from September 1, 1982 to August 31, 2022. The study design and implementation were based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement and the PROSPERO registration. Search terms were identified and freely combined to allow for a comprehensive search of relevant literature. Articles retrieved from the above four electronic databases were further screened for potential eligible studies. Relevant meta-analyses and reviews were also searched to ensure that all relevant studies were included.

The specific keywords were as follows:

#1 Coronary disease OR coronary heart disease OR coronary artery disease OR coronary atherosclerotic disease OR CAD OR CHD.
#2 Coronary artery bypass grafting OR coronary artery bypass surgery OR CABG.
#3 Exercise training OR cardiac rehabilitation OR exercise rehabilitation training.
#1 AND #2 AND #3.

### Screening and data extraction

All retrieved articles were imported into EndNote 20. After eliminating duplicate articles, screening was performed by two investigators (J.M. and C.W.) independently according to the inclusion and exclusion criteria; this was followed by cross-checking, and any disagreement was resolved through discussion between the two investigators or seeking third-party opinions. The extracted data included 1) basic information of the included studies, such as the title, first author, time of publication, and study type; 2) baseline characteristics of the study subjects, such as the number of subjects in each group and exercise modality; 3) mean and standard deviation (SD) of each indicator; and 4) key elements of quality assessment.

### Assessment of risk of bias

The Cochrane Collaboration Risk of Bias Tool was used to assess the quality of the included RCTs (Supplementary Materials Table S1). Two investigators independently judged each item as "high risk" or "low risk" or "unclear". Differences in their judgments were resolved through discussion between the two investigators or seeking third-party advice.

## QUANTIFICATION AND STATISTICAL ANALYSIS

RevMan version 5.4.1 and STATA version 12.0 were used for statistical analysis and generation of graphs. The results were presented using the mean difference (MD) with 95% confidence intervals (CIs) and illustrated using the forest map. Data were analyzed through comparison of measures before and after CR, with the differences of original values before and after CR calculated using the formula before analysis.[52] If a study contained multiple CR groups, the groups were combined into a whole CR group for comparison using the formula in the Cochrane

Handbook.[52] The heterogeneity was determined using the $I^2$ statistic and $P$ value of the chi-square test. $I^2 \leq 50\%$ or $P > 0.1$ in the chi-square test indicated low heterogeneity, and a fixed-effects model was used; otherwise, a random-effects model was used. If the pooled results showed significant heterogeneity, subgroup analysis should be performed to identify the source of heterogeneity. We conducted subgroup analysis of different exercise modalities and durations. For variables involved in five or more studies, publication bias was analyzed using Egger's test, with $P < 0.05$ indicating the presence of publication bias. Leave-one-out sensitivity analysis was performed to test the robustness of the results.