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Inspiratory Muscle Strength After Threshold Inspiratory Muscle Training Versus Incentive Spirometry in Patients Undergoing Coronary Artery Bypass Grafting: A Randomized Controlled Trial

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ABSTRACT: Respiratory dysfunction after coronary artery bypass grafting (CABG) may reduce inspiratory muscle strength and affect health-related quality of life. This single-center, assessor-blinded randomized controlled trial compared threshold inspiratory muscle training (IMT) with incentive spirometry (IS) in 30 adults undergoing elective CABG. Participants were randomized 1:1 to IMT or IS. IMT was performed for five preoperative days and IS for two days; both interventions were resumed after extubation and continued until discharge. Preoperative Strength Index (S-Index) was analyzed using ANCOVA adjusted for baseline values, while SF-12 Physical and Mental Component Summary scores were assessed at baseline, discharge, and 30 days. After baseline adjustment, preoperative S-Index was significantly higher with IMT than IS (85.85 vs 75.48 cmH₂O; adjusted mean difference 10.37 cmH₂O, 95% CI 2.52–18.22; $p=0.012$; partial $\eta^2=0.214$). PCS-12 and MCS-12 changed significantly over time (both $p<0.001$), but time-by-group interactions were not significant ($p=0.621$ and $p=0.174$, respectively). Hospital stay (9.60 vs 11.93 days; $p=0.004$) and ICU stay [median 2.0 vs 4.0 days; $p=0.027$] were shorter with IMT, although these were exploratory outcomes. Threshold IMT produced greater short-term preoperative improvement in dynamic inspiratory muscle strength than IS, while health-related quality-of-life trajectories did not differ between groups.

1. INTRODUCTION

Coronary artery bypass grafting (CABG) can be followed by substantial respiratory and functional deterioration during the early postoperative period. Patients who develop postoperative complications show greater reductions in inspiratory muscle strength, peripheral muscle strength, pulmonary function, and functional performance at hospital discharge, with some impairments persisting for up to six months [1]. Early diaphragmatic dysfunction was detected in 40.7% of patients after cardiac surgery and was associated with greater requirements for noninvasive ventilation and advanced oxygen support after weaning from mechanical ventilation [2].

The preoperative period therefore provides an opportunity to increase respiratory reserve before exposure to surgical stress. Inspiratory muscle training (IMT) applies a progressive inspiratory load to improve inspiratory muscle performance. A systematic review of eight randomized trials involving adults undergoing elective open cardiac surgery found that preoperative respiratory muscle training reduced postoperative pulmonary complications and pneumonia, increased maximal inspiratory pressure, and shortened hospital stay by approximately 1.7 days [3]. A CABG-specific meta-analysis similarly found that perioperative IMT reduced the risks of pneumonia and atelectasis and improved inspiratory muscle strength, although the included protocols varied in timing, intensity, and duration [4].

Incentive spirometry (IS) provides visual feedback during slow, sustained inspiration and is frequently incorporated into perioperative respiratory care. In patients undergoing CABG, postoperative IS combined with deep-breathing exercises produced a smaller decline in maximal inspiratory pressure on postoperative day four than deep-breathing exercises alone, but did not reduce pulmonary complications or hospital stay [5]. Another randomized trial reported that two days of preoperative IS, when added to a multimodal program of deep breathing, directed coughing, postoperative respiratory therapy, and early mobilization, was associated with less atelectasis, shorter mechanical ventilation and hospitalization, and better postoperative oxygenation [6]. Because this intervention combined several respiratory and mobilization components, its findings cannot establish the isolated effect of IS. Moreover, a recent meta-analysis found that IS was not superior to standard respiratory care for preventing pulmonary complications or improving major clinical outcomes after cardiac surgery [7].

Thus, IMT has shown relatively consistent effects on inspiratory muscle strength, whereas evidence for IS remains mixed. Existing trials have generally compared either intervention with usual care or other respiratory exercises rather than directly comparing threshold IMT with IS in patients undergoing CABG. Importantly, the immediate preoperative period represents a clinically relevant window in which inspiratory muscle performance may be optimized before exposure to surgical stress. However, direct evidence comparing the short-term preoperative effects of threshold IMT and IS on dynamic inspiratory muscle performance remains limited. The Strength Index (S-Index) provides a dynamic assessment of inspiratory muscle performance and correlates strongly with maximal inspiratory pressure, although the two measurements represent different muscle contractions and should not be considered interchangeable [8]. Beyond physiological preparedness, postoperative recovery also includes physical and mental dimensions that may be captured by patient-reported health-related quality of life. The Indonesian SF-12 has demonstrated acceptable reliability and construct validity for assessing the physical and mental components of health-related quality of life in middle-aged and older adults [9].

Therefore, this randomized controlled trial compared threshold IMT with IS in patients undergoing elective CABG. The primary objective was to compare preoperative dynamic inspiratory muscle strength between groups after adjustment for baseline S-Index. We also evaluated changes in the physical and mental components of health-related quality of life from baseline through early postoperative recovery using the SF-12. Intensive care unit and hospital length of stay were explored as additional clinical outcomes. We hypothesized that threshold IMT would result in higher preoperative S-Index than IS after adjustment for baseline S-Index.

2. MATERIALS AND METHODS

2.1 Study design and participants

This single-center, assessor-blinded, parallel-group randomized controlled trial compared threshold inspiratory muscle training (IMT) with incentive spirometry (IS) in adults undergoing elective coronary artery bypass grafting (CABG) at Dr. Wahidin Sudirohusodo Central General Hospital, Makassar, Indonesia, from March to December 2025.

Patients were eligible if at least five days remained before surgery and their Montreal Cognitive Assessment–Indonesian version score was >23 . Exclusion criteria included cerebrovascular or neuromuscular disease, cardiovascular instability, aneurysm, previous cardiac or pulmonary surgery, unresolved pneumothorax, tympanic membrane perforation, increased intracranial pressure, or an intracranial space-occupying lesion. Written informed consent was obtained before baseline assessment.

Participants were randomized 1:1 using a computer-generated permuted block sequence with a block size of four. Allocation was concealed using sequentially numbered, opaque, sealed envelopes. Participants and rehabilitation personnel were unblinded, whereas outcome assessment was performed by an independent blinded assessor. No formal a priori sample-size calculation was performed because of the limited number of elective CABG procedures. Thirty participants were randomized, with 15 allocated to each group, and were analyzed according to assigned group.

2.2 Interventions

Both groups received standard perioperative rehabilitation, including diaphragmatic breathing, effective coughing, ankle-pumping, shoulder and chest flexibility exercises, upper-limb mobility, and progressive postoperative mobilization.

The IMT group trained with a threshold device for five consecutive preoperative days at an initial resistance of 30% of baseline S-Index. Participants performed three sets of 10 slow maximal inspirations twice daily, with 30–60-second rest intervals between sets. Resistance was increased or decreased by 2 cmH₂O according to modified Borg scores of ≤ 5 or ≥ 9 , respectively. Out-of-hospital sessions were monitored by telephone and training diary. After extubation, IMT was resumed when participants were conscious and hemodynamically stable, using 30% of the most recent S-Index, with 30 inspirations performed twice daily until discharge.

The IS group used a flow-oriented incentive spirometer during the final two preoperative days. Participants performed 10 slow deep inspirations four times daily while upright or with approximately 45° trunk elevation, sustaining each inspiration for approximately three seconds. IS was resumed after extubation when participants were conscious and clinically stable and continued until discharge. Adherence and symptoms were recorded in daily diaries.

2.3 Outcomes

The main physiological outcome was preoperative inspiratory muscle strength measured using the S-Index with a POWERbreathe K5 device (POWERbreathe International Ltd., Warwickshire, UK). From residual volume, participants performed three rapid maximal inspirations separated by 30-second rest intervals, and the highest value was recorded in cmH₂O. For this analysis, baseline and immediately preoperative S-Index measurements were used.

Health-related quality of life was assessed using the Indonesian 12-item Short Form Health Survey [9]. Physical Component Summary (PCS-12) and Mental Component Summary (MCS-12) scores were measured at baseline, hospital discharge, and 30 days after surgery; higher scores indicate better health-related quality of life. Intensive care unit and hospital length of stay were obtained from medical records as exploratory clinical outcomes.

2.4 Statistical analysis

Analyses were performed using IBM SPSS Statistics version 30.0. Categorical data are presented as n (%), and continuous data as mean $\pm$ standard deviation or median (interquartile range), as appropriate. Normality and homogeneity of variance were assessed using the Shapiro–Wilk and Levene tests. Baseline characteristics were summarized descriptively.

Preoperative S-Index was compared between groups using analysis of covariance (ANCOVA), with preoperative S-Index as the dependent variable, intervention group as the fixed factor, and baseline S-Index as the covariate. Homogeneity of regression slopes was assessed using the baseline S-Index-by-group interaction. Adjusted means, adjusted between-group differences with 95% confidence intervals, p values, and partial η^2 were reported.

PCS-12 was analyzed using mixed repeated-measures ANOVA, with time as the within-subject factor and group as the between-subject factor; Greenhouse–Geisser correction was applied when required. MCS-12 was analyzed using generalized estimating equations with a normal distribution, identity link, exchangeable working correlation, and robust covariance. For both SF-12 outcomes, the time-by-group interaction represented the comparative treatment effect. ICU and hospital length of stay were compared using independent-samples t tests or Mann–Whitney U tests, as appropriate. All tests were two-sided, with $p < 0.05$ considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Participant flow and baseline characteristics

Of 34 patients assessed for eligibility, 30 were randomized to IMT ($n=15$) or IS ($n=15$), and all were included in the analysis (Figure 1). Baseline characteristics are shown in Table 1. Participants were predominantly male (93.3% in each group), with similar mean ages (54.00 ± 9.18 vs 54.93 ± 9.16 years).

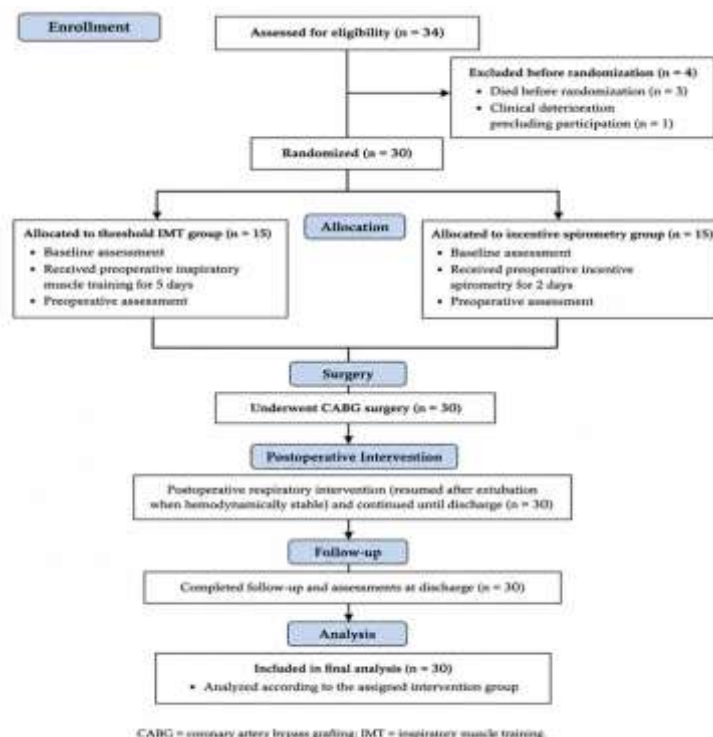


Figure 1. CONSORT flow diagram of participant screening, randomization, intervention, follow-up, and analysis.

Table 1. Baseline characteristics of the study participants

Characteristic	Threshold IMT (n=15)	Incentive spirometry (n=15)
Age, years	54.00 ± 9.18	54.93 ± 9.16
Male sex	14 (93.3)	14 (93.3)
Female sex	1 (6.7)	1 (6.7)
Body mass index, kg/m ²	27.14 ± 4.26	25.30 ± 3.55
Underweight	0 (0.0)	0 (0.0)
Normal weight	2 (13.3)	4 (26.7)
Overweight	4 (26.7)	5 (33.3)
Obesity	9 (60.0)	6 (40.0)
Hypertension	8 (53.3)	13 (86.7)
Diabetes mellitus	5 (33.3)	7 (46.7)
Smoking history	9 (60.0)	11 (73.3)

Note: Data are presented as mean ± standard deviation or n (%), as appropriate. IMT, inspiratory muscle training.

3.2 Preoperative inspiratory muscle strength

S-Index increased from baseline to preoperative assessment in both groups, from 63.27±25.83 to 84.73±23.71 cmH₂O with IMT and from 65.80±28.44 to 76.60±28.33 cmH₂O with IS (Table 2; Figure 2A). Homogeneity of regression slopes was satisfied (interaction p=0.254). After baseline adjustment, preoperative S-Index was significantly higher with IMT than IS

(adjusted means 85.85 vs 75.48 cmH₂O; adjusted mean difference 10.37 cmH₂O, 95% CI 2.52–18.22; F(1,27)=7.352; p=0.012; partial η^2 =0.214).

Table 2. Preoperative inspiratory muscle strength and descriptive health-related quality-of-life outcomes

Outcome and assessment	Threshold IMT (n=15)	Incentive spirometry (n=15)	Adjusted between-group difference (95% CI)	p value
S-Index, cmH ₂ O				
Baseline	63.27 ± 25.83	65.80 ± 28.44	—	—
Preoperative	84.73 ± 23.71	76.60 ± 28.33	—	—
Adjusted preoperative mean (95% CI)	85.85 (80.31–91.40)	75.48 (69.93–81.03)	10.37 (2.52–18.22)	0.012 ^{a*}
PCS-12				
Baseline	42.47 ± 16.46	37.19 ± 22.30	—	—
Hospital discharge	17.34 ± 10.40	15.69 ± 8.84	—	—
30 days after surgery	49.70 ± 18.73	50.75 ± 17.45	—	—
MCS-12				
Baseline	67.63 ± 23.99	67.14 ± 18.51	—	—
Hospital discharge	70.00 (54.10–77.50)	47.50 (43.40–80.00)	—	—
30 days after surgery	86.60 (70.00–90.00)	76.60 (64.10–93.30)	—	—

Note: Data are presented as mean ± standard deviation or median (Q1–Q3), as appropriate. Adjusted preoperative S-Index values are estimated marginal means with 95% confidence intervals. ^aAnalysis of covariance (ANCOVA), with preoperative S-Index as the dependent variable, intervention group as the fixed factor, and baseline S-Index as the covariate. The group effect was F(1,27)=7.352, partial η^2 =0.214. *p<0.05. CI, confidence interval; IMT, inspiratory muscle training; PCS-12, Physical Component Summary; MCS-12, Mental Component Summary.

3.3 Physical health-related quality of life

PCS-12 declined at discharge and recovered by 30 days in both groups (Table 2; Figure 2B). There was a significant effect of time (F=56.932, p<0.001; partial η^2 =0.670), but no group effect (p=0.678) or time-by-group interaction (p=0.621; partial η^2 =0.017) (Table 3). Interval changes did not differ significantly between groups (Table 4).

Table 3. Longitudinal effects of time, intervention group, and their interaction on health-related quality of life

Outcome and effect	Test statistic	df	p value	Effect size
PCS-12				
Time	F=56.932	2, 56	<0.001 ^{a*}	Partial η^2 =0.670
Group	F=0.176	1, 28	0.678 ^a	Partial η^2 =0.006
Time × group	F=0.480	2, 56	0.621 ^a	Partial η^2 =0.017
MCS-12				
Time	Wald χ^2 =141.127	2	<0.001 ^{b*}	—
Group	Wald χ^2 =0.187	1	0.665 ^b	—
Time × group	Wald χ^2 =3.495	2	0.174 ^b	—

Note: ^aMixed repeated-measures analysis of variance (ANOVA). ^bGeneralized estimating equations (GEE) with a normal distribution, identity link, exchangeable working-correlation structure, and robust covariance estimation. The time-by-group interaction represents the comparative treatment effect for each SF-12 component. Partial η^2 is reported for the repeated-measures ANOVA model; GEE effects are reported using Wald χ^2 statistics. * $p < 0.05$. PCS-12, Physical Component Summary; MCS-12, Mental Component Summary.

3.4 Mental health-related quality of life

MCS-12 also changed significantly over time (Wald $\chi^2 = 141.127$, $df = 2$; $p < 0.001$), with no significant group effect ($p = 0.665$) or time-by-group interaction ($p = 0.174$) (Tables 2–3; Figure 2C). No interval-specific between-group differences were observed (Table 4).

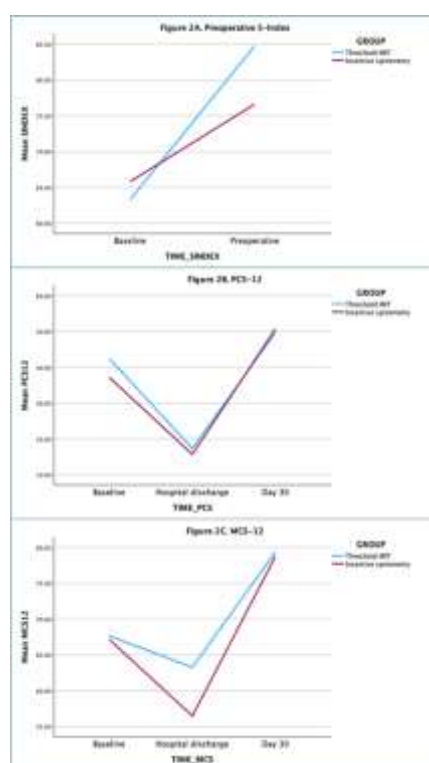


Figure 2. Inspiratory muscle strength and health-related quality-of-life trajectories. (A) Strength Index at baseline and preoperative assessment. (B) Physical Component Summary and (C) Mental Component Summary at baseline, hospital discharge, and 30 days after surgery.

3.5 Exploratory clinical outcomes

Hospital length of stay was shorter with IMT than IS (9.60 ± 2.17 vs 11.93 ± 1.87 days; $p = 0.004$), as was ICU stay [2.00 (Q1–Q3, 2.00 – 4.00) vs 4.00 (3.00– 4.00) days; $p = 0.027$] (Table 4). These findings were exploratory, and total hospital stay included preoperative hospitalization of differing duration between groups.

Table 4. Exploratory changes in health-related quality of life and clinical outcomes

Outcome	Threshold IMT (n=15)	Incentive spirometry (n=15)	p value
PCS-12 change			
Discharge – baseline	-25.13 ± 20.29	-21.51 ± 19.04	0.618 ^a
Day 30 – discharge	32.36 ± 19.12	35.06 ± 15.57	0.675 ^a
Day 30 – baseline	7.23 ± 13.51	13.55 ± 17.88	0.284 ^a

MCS-12 change			
Discharge – baseline	–4.10 (–16.70 to 0.00)	–10.00 (–19.10 to 1.60)	0.678 ^b
Day 30 – discharge	16.11 ± 7.02	22.29 ± 11.26	0.084 ^a
Day 30 – baseline	6.60 (3.40–22.50)	11.60 (0.00–22.50)	0.803 ^b
Clinical outcomes			
Total hospital length of stay, days	9.60 ± 2.17	11.93 ± 1.87	0.004 ^{a*}
Intensive care unit length of stay, days	2.00 (2.00–4.00)	4.00 (3.00–4.00)	0.027 ^{b*}

Note: Data are presented as mean ± standard deviation or median (Q1–Q3), as appropriate. ^aIndependent-samples t test.

^bMann–Whitney U test. * $p < 0.05$. Length-of-stay outcomes were exploratory. Total hospital length of stay included the preoperative hospitalization period. IMT, inspiratory muscle training; PCS-12, Physical Component Summary; MCS-12, Mental Component Summary.

3.6 Discussion

The principal finding of this randomized trial was that threshold inspiratory muscle training (IMT) produced a greater preoperative improvement in dynamic inspiratory muscle strength than incentive spirometry (IS). After adjustment for baseline S-Index, the preoperative S-Index was significantly higher in the IMT group, with an adjusted between-group difference of 10.37 cmH₂O (95% CI 2.52–18.22; $p = 0.012$; partial $\eta^2 = 0.214$). In contrast, although the physical and mental components of health-related quality of life changed significantly during postoperative recovery, their trajectories did not differ significantly between interventions. These findings indicate that the clearest differential response to the intervention protocols occurred in inspiratory muscle performance during the short preoperative period. The clinical interpretation of the 10.37-cmH₂O difference nevertheless requires caution. Available S-Index research has primarily addressed concurrent validity, prediction equations, and diagnostic reference values, whereas clinically important difference estimates for inspiratory muscle function have been developed using other measures and populations rather than S-Index in patients undergoing CABG [8,10,11]. Accordingly, the observed difference should be interpreted as a significant physiological treatment effect rather than as an established threshold of clinical benefit.

The greater preoperative improvement in S-Index with threshold IMT is physiologically plausible because pressure-threshold loading imposes a defined inspiratory resistance and requires active pressure generation during each breath. Threshold-loaded IMT combined with visual biofeedback has previously been shown to favor preservation and recovery of dynamic inspiratory strength during CABG hospitalization compared with placebo loading [12]. Longer-term inspiratory resistance training has also been shown to alter diaphragm and accessory inspiratory-muscle behavior [13]. Given that the preoperative IMT exposure in the present study lasted only five days, however, the observed improvement is more cautiously interpreted as an early functional or task-specific response, potentially involving improved inspiratory-muscle recruitment, coordination, familiarization with maximal inspiratory maneuvers, and tolerance to loading. Structural muscle remodeling cannot be inferred from such a short intervention period.

Importantly, IS was an active respiratory intervention rather than a sham comparator. In patients undergoing CABG, postoperative IS combined with deep-breathing exercises resulted in a smaller decline in maximal inspiratory pressure than deep-breathing exercises alone [5]. More recently, adding IS to pulmonary rehabilitation after CABG improved postoperative oxygenation indices, including PaO₂, SaO₂, and SpO₂ [14]. Thus, both groups received interventions capable of stimulating respiratory performance in addition to the same standard perioperative rehabilitation. The significant baseline-adjusted difference therefore demonstrates a differential preoperative response under the two intervention protocols tested. However, the protocols differed not only in training modality but also in preoperative exposure, with five days of threshold IMT compared with two days of IS. The observed difference therefore cannot be attributed exclusively to pressure-threshold loading because differences in intervention dose and duration may also have contributed. This distinction is important when interpreting the apparent advantage of IMT and should be addressed in future trials using duration- and contact-matched comparators. This is

consistent with a larger cardiac-surgery trial in which combined exercise and IMT prehabilitation improved maximal inspiratory pressure without improving the primary functional outcome or quality of life [15].

The clinical rationale for improving inspiratory muscle performance before CABG is to increase respiratory reserve before exposure to anesthesia, sternotomy, mechanical ventilation, and the physiological stress of surgery. Systematic review evidence indicates that preoperative respiratory muscle training in cardiac surgery can improve inspiratory muscle strength, reduce postoperative pulmonary complications and pneumonia, and shorten hospitalization [3], while a CABG-specific meta-analysis similarly reported reductions in pneumonia and atelectasis together with improved inspiratory muscle strength [4]. Postoperative pulmonary complications remain common after cardiac surgery and are associated with longer ICU and hospital stays [16]. Early diaphragm dysfunction is another relevant mechanism; ultrasonographic dysfunction has been identified in a substantial proportion of patients after cardiac surgery and is associated with greater requirements for noninvasive ventilation and oxygen support [2]. CABG-specific observational data likewise show greater reductions in inspiratory muscle strength, pulmonary function, peripheral muscle strength, and functional performance among patients who develop postoperative complications [1]. These findings provide biological and clinical justification for targeting inspiratory muscle function before surgery. However, the present study was not designed or powered to establish whether the observed preoperative increase in S-Index prevented postoperative pulmonary complications. The improvement in inspiratory strength should therefore not be interpreted as direct evidence of complication prevention.

The HRQoL trajectories were compatible with the broader pattern of early recovery after CABG. Physical health declined substantially at hospital discharge and subsequently recovered by 30 days, whereas mental health scores increased during later recovery. However, neither PCS-12 nor MCS-12 showed a significant time-by-group interaction, indicating no evidence that the trajectories of physical or mental HRQoL differed between IMT and IS. HRQoL after CABG is multidimensional and is unlikely to be determined by respiratory muscle performance alone. Hartog et al. found that improvements in weight-normalized grip strength were associated with the physical, but not the mental, component of postoperative HRQoL [17]. Post-discharge IMT has also been associated with improvements in inspiratory strength, functional capacity, and quality-of-life measures after CABG [18]. Recovery remains heterogeneous, however: patients who respond functionally to prehabilitation may demonstrate more favorable postoperative physical recovery [19], whereas a five-week randomized cardiac prehabilitation program did not improve early quality-of-recovery scores despite reducing disability at 90 days [20]. The observed MCS-12 changes should therefore be interpreted primarily as part of broader postoperative recovery rather than as a modality-specific respiratory-training effect. Furthermore, because both IMT and IS were resumed after extubation and continued until hospital discharge, postoperative HRQoL reflects the broader perioperative intervention pathway rather than the isolated effect of preoperative training.

The shorter ICU and total hospital stays observed in the IMT group are clinically interesting but remain hypothesis-generating. A small randomized CABG trial reported fewer pulmonary complications and shorter hospitalization following IMT despite no significant benefit in maximal inspiratory pressure or 6-minute walking distance [18]. A meta-analysis of exercise-based cardiac prehabilitation similarly reported an approximately one-day reduction in hospital stay, although heterogeneity across studies was substantial [21]. In the present study, ICU stay was shorter in the IMT group, but this exploratory finding cannot establish that the difference resulted from the greater preoperative S-Index response. Both interventions also continued postoperatively, meaning that ICU and other postoperative outcomes cannot be attributed solely to the preoperative phase. Total hospital length of stay warrants even greater caution because it incorporated the preoperative hospitalization period, during which the intervention protocols differed in duration. Larger trials specifically powered for postoperative complications, ICU utilization, and postoperative length of stay are required to determine whether greater preoperative inspiratory muscle performance translates into clinically meaningful postoperative benefits.

Strengths include randomized allocation, an active comparator, blinded outcome assessment, and baseline-adjusted analysis of preoperative inspiratory muscle strength. Limitations include the small single-center sample, absence of an a priori power calculation, unequal preoperative intervention duration, 30-day follow-up, and use of precomputed SF-12 component scores. Unequal exposure limits attribution of the S-Index difference solely to training modality, while continuation of both interventions postoperatively limits attribution of postoperative outcomes specifically to preoperative conditioning. The study was also not powered for ICU stay, hospital length of stay, or postoperative complications. Overall, threshold IMT produced

greater preoperative inspiratory strength gains than IS, but larger exposure-matched multicenter trials are needed to determine whether this physiological benefit translates into clinically meaningful postoperative outcomes.

4. CONCLUSION

Threshold IMT produced greater preoperative improvement in dynamic inspiratory muscle strength than incentive spirometry in patients undergoing elective CABG. Physical and mental health-related quality of life changed during postoperative recovery without significant between-group differences. Shorter ICU and hospital stays in the IMT group were exploratory. Larger multicenter trials are needed to determine whether preoperative inspiratory gains translate into meaningful postoperative benefits.

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AUTHOR CONTRIBUTIONS

Muhammad Fikri Hadju: Conceptualization, methodology, investigation, data collection, data curation, formal analysis, project administration, visualization, writing—original draft, writing—review and editing.

Melda Warliani: Conceptualization, methodology, supervision, validation, interpretation of findings, writing—review and editing

Sylvia Evelyn Aritonang: Conceptualization, methodology, supervision, validation, interpretation of findings, writing—review and editing

Andi Alfian Zainuddin: Methodology, statistical analysis, validation, interpretation of findings, writing—review and editing.

Yose Waluyo: Supervision, validation, interpretation of findings, writing—review and editing.

Jayarasti Kusumanegara: Clinical methodology, supervision, validation, interpretation of findings, writing—review and editing.

All authors approved the final manuscript and agreed to be accountable for their respective contributions.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

FUNDING

This research received no external funding.

ETHICS STATEMENT

The protocol was approved by the Research Ethics Committee of Hasanuddin University, Hasanuddin University Hospital, and Dr. Wahidin Sudirohusodo Central General Hospital (no. 90/UN4.6.4.5.31/PP36/2025; protocol UH25010019; February 10, 2025). All participants provided written informed consent, and the study was conducted in accordance with the Declaration of Helsinki.

DATA AVAILABILITY STATEMENT

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and institutional restrictions.

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