

Timing of Cardiac Rehabilitation After Primary Percutaneous Coronary Intervention for Myocardial Infarction: A Randomized Clinical Trial

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Abstract

Background: Cardiac rehabilitation (CR) is a cornerstone of post-acute care for patients experiencing cardiovascular events or interventions. It aims to improve cardiorespiratory capacity, enhance quality of life, and maximize physical function, facilitating a return to daily activities. However, the optimal timing for initiating CR following acute coronary events or procedures remains uncertain.

Methods: In this randomized clinical trial, 40 patients diagnosed with acute myocardial infarction and treated with primary percutaneous coronary intervention (PCI) were randomly assigned to two groups. Group A commenced cardiac rehabilitation one month after PCI, while Group B initiated rehabilitation two months post-PCI. Both groups completed a supervised 12-session rehabilitation program under the guidance of a physical medicine specialist. Functional outcomes were assessed before and after rehabilitation using the SF-36 quality of life questionnaire and echocardiographic parameters. Data were analyzed using SPSS version 25. Within-group changes were evaluated with paired t-tests, and between-group comparisons of change scores were conducted using independent samples t-tests. A P -value < 0.05 was considered statistically significant.

Results: Post-rehabilitation, the mean SF-36 score was 65.85 ± 6.67 in Group A and 67.05 ± 5.96 in Group B ($P=0.192$). The mean change in Left Ventricular Ejection Fraction (LVEF) was 2.25% in Group A and 0.15% in Group B ($P=0.305$). After rehabilitation, grade 1–2 diastolic dysfunction remained present in 85% of patients in both groups, while 15% of patients in each group showed no evidence of diastolic dysfunction ($P=0.506$). No significant differences were found between groups in heart rate (HR) Max (107.45 ± 15.04 vs. 115.20 ± 13.12 ; $P=0.091$), HR Recovery (22.50 ± 7.05 vs. 23.10 ± 7.78 ; $P=0.800$), or MET change (6.60 ± 1.83 vs. 6.20 ± 2.39 ; $P=0.556$).

Conclusion: Initiating cardiac rehabilitation one month as opposed to two months after primary PCI did not yield significant differences in quality of life or cardiac functional parameters. These findings indicate that there may be flexibility in the timing of CR initiation without compromising short-term functional outcomes.

Keywords: Cardiac rehabilitation, myocardial infarction, PCI, timing, functional recovery, quality of life

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Introduction

Cardiovascular diseases (CVDs) are the leading cause of mortality worldwide, accounting for approximately 31% of global deaths (1, 2). Among the most common clinical manifestations of CVD is acute coronary syn-

drome (ACS), which is typically caused by the rupture of atherosclerotic plaques, leading to partial or complete obstruction of coronary blood flow. ACS may present as chest pain (angina), exertional dyspnea, or, in some cases,

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↑What is “already known” in this topic:

Early cardiac rehabilitation (CR) following myocardial infarction enhances functional capacity, quality of life, and cardiac outcomes. Most guidelines recommend initiating rehabilitation within 2–4 weeks post-PCI; however, real-world evidence regarding the effects of delayed initiation remains limited.

→What this article adds:

This randomized trial demonstrates that initiating CR one month versus two months post-PCI yields comparable short-term improvements in functional capacity, LVEF, diastolic function, exercise performance, and quality of life. This finding provides practical guidance for centers where moderate delays in CR initiation may occur.

remain clinically silent (3-5). Based on the extent of ischemia and the affected coronary artery, myocardial infarction (MI) is classified into ST-elevation MI (STEMI) and non-ST-elevation MI (NSTEMI) (6, 7).

Patients with coronary artery disease (CAD) often experience a variety of complications, including an imbalance in myocardial oxygen supply and demand, limited exercise tolerance, increased psychological distress (e.g., anxiety and depression), diminished quality of life, and social dysfunction. CAD is also a significant contributor to early workforce disability and imposes a considerable burden on healthcare systems through both direct and indirect costs, such as decreased productivity and elevated insurance expenditures (3, 8-10).

Cardiac rehabilitation (CR) is an evidence-based, multidisciplinary intervention aimed at optimizing secondary prevention and enhancing clinical outcomes in patients recovering from cardiac events or procedures (11, 12). CR programs typically encompass supervised exercise training, lifestyle and risk factor modification, psychosocial support, and education, delivered by a team that includes cardiologists, physiatrists, nurses, physical therapists, psychologists, and nutritionists. CR has been demonstrated to improve cardiorespiratory fitness, enhance control of cardiovascular risk factors (e.g., diabetes, hypertension, obesity, and sleep apnea), and significantly elevate quality of life (6, 11-13).

Despite its well-documented benefits, participation in CR programs remains suboptimal. Fewer than 25% of eligible patients enroll in CR, and among those who do, dropout rates are considerable—ranging from 30% to 40% within six months and reaching up to 50% within one year (14, 15). One underexplored factor that may influence CR outcomes is the timing of program initiation. Some studies suggest that delayed CR (i.e., >30 days after the index event) may independently predict reduced exercise recovery. However, the literature presents mixed findings, and the ideal timing for CR initiation remains unclear, particularly in patients undergoing primary percutaneous coronary intervention (pPCI) for ACS (16-19).

This study aimed to evaluate the short-term effects of CR in patients with ACS treated with pPCI, specifically focusing on comparing the functional outcomes of those who commenced CR one month versus two months after the procedure. The findings are anticipated to inform more tailored rehabilitation strategies and contribute to improved long-term outcomes in this high-risk population.

Methods

Study Design

The study was designed as a randomized, controlled, parallel-group clinical trial conducted at Farshchian Heart Hospital in Hamadan Province, Iran, from March 2021 to March 2022 (corresponding to 1400–1401 in the Iranian calendar). The study protocol, registered under the IRCT registration number IRCT20151123025202N18, received approval from the local ethics committee and was registered in a clinical trials registry prior to participant enrollment.

Participants

Eligible participants were adult patients (≥ 18 years) diagnosed with acute coronary syndrome (ACS) who underwent successful pPCI at Farshchian Heart Hospital. The inclusion criteria were: (1) hemodynamic stability post-pPCI; (2) full consciousness and cooperation; and (3) willingness to provide written informed consent. The exclusion criteria included: (1) hemodynamic instability; (2) resting systolic blood pressure (BP) >180 mmHg or diastolic BP >110 mmHg; (3) uncontrolled malignant arrhythmias; (4) major respiratory disease; or (5) physical inability to engage in exercise-based rehabilitation.

Sample Size

Based on data from Johnson et al. (20), we estimated that 27 participants per group would be required to detect a significant difference in change in MET between the early (3.0 ± 1.6) and delayed (1.8 ± 1.5) CR groups ($\alpha=0.05$, power=0.80). To account for an anticipated 10% attrition rate, we planned to enroll 30 patients per group. However, due to logistical constraints, including limited rehabilitation center capacity, only 20 participants were recruited into each group (total $N=40$). Consequently, the achieved sample size was lower than originally planned and may have reduced the study's ability to detect modest between-group differences.

Randomization and Allocation

Participants were randomized in a 1:1 ratio utilizing block randomization with a block size of 4, resulting in a total of 10 blocks for 40 participants. The random sequence was generated using Excel by an independent statistician who was not involved in participant recruitment or outcome assessment. Each participant was assigned a unique study code. Allocation was concealed through the use of sequentially numbered, sealed, opaque envelopes prepared by the same independent researcher. The envelopes were opened only after participants completed baseline assessments.

Interventions

Participants were randomized into two groups based on the timing of CR initiation following pPCI. Group A commenced the CR program one month after pPCI, whereas Group B began the program two months post-procedure. Both groups received an identical, structured outpatient CR protocol consisting of 12 supervised sessions delivered over four weeks (three sessions per week). Each session lasted approximately 60 to 90 minutes and was conducted under the supervision of a physiatrist and a multidisciplinary rehabilitation team. The program included a warm-up phase, followed by 40 minutes of aerobic exercise (using a treadmill or stationary bicycle) under continuous heart rate and ECG monitoring, a cool-down period, and then a combination of resistance training for upper and lower limbs and flexibility/stretching exercises. The intensity of aerobic activity was individually tailored for each participant based on baseline exercise stress test results and the Borg Rating of Perceived Exertion scale. Vital signs, including heart rate and blood pressure, were

measured at the start, midpoint, and end of each session to ensure safety and optimal training progression.

Outcomes

The primary outcomes of the study were functional capacity and quality of life following the completion of the cardiac rehabilitation program. Functional capacity was assessed using exercise stress testing, with a specific focus on METs, maximum heart rate (HR max), and heart rate recovery (HRR). Quality of life was measured using the validated Short Form-36 (SF-36) questionnaire, which evaluates eight dimensions of physical and mental well-being and generates a total score ranging from 0 (worst health status) to 100 (best possible health status). Secondary outcomes included changes in LVEF and parameters of diastolic function, evaluated through transthoracic echocardiography. Diastolic function indices included the E/A ratio, E'/A' ratio, E/E' ratio, and systolic tissue Doppler velocity (S'). These echocardiographic parameters were selected to provide insight into the structural and functional impact of rehabilitation on cardiac performance.

Data Collection and Instruments

Baseline demographic and clinical characteristics, including age, sex, cardiovascular risk factors, and procedural details of primary PCI, were obtained from patient records or through direct interviews at enrollment. Quality of life was assessed using the SF-36 questionnaire, which was administered in person by trained personnel both before and after the completion of the 12-session rehabilitation program. Echocardiographic evaluations were performed at baseline and following the final rehabilitation session according to standardized protocols, with interpretation conducted by a cardiologist who was blinded to group allocation. Exercise stress testing was conducted at both time points under the supervision of a physiatrist and trained technicians. To minimize measurement bias, all data collectors and outcome assessors were blinded to group assignment. Data entry and validation were carried out independently by two researchers to ensure accuracy and completeness.

Statistical Analysis

Data were analyzed using SPSS version 25. Descriptive statistics, including means and standard deviations, were calculated for continuous variables, while frequencies and percentages were computed for categorical variables. To compare baseline demographic and clinical characteristics between the two groups (rehabilitation starting one month vs. two months after PCI), the Chi-square test (or Fisher's exact test where appropriate) was employed for categorical variables, and independent samples t-tests were utilized for normally distributed continuous variables. For the evaluation of within-group changes before and after rehabilitation (pre-post comparisons), paired t-tests were applied to normally distributed variables, such as SF-36 quality of life scores, echocardiographic parameters, and exercise test outcomes. Between-group comparisons of changes (differences in pre- and post-intervention values)

were assessed using independent samples t-tests for continuous variables with a normal distribution. Variables that did not meet normality assumptions were analyzed using non-parametric alternatives (e.g., Mann-Whitney U test); however, all presented variables in this study were analyzed parametrically. All tests were two-tailed, and a P -value < 0.05 was considered statistically significant. Since block randomization ensured balanced baseline characteristics and no significant differences were observed between groups at enrollment, advanced adjustment methods such as ANCOVA were not deemed necessary.

Results

A total of 45 participants were assessed for eligibility, of whom 5 were excluded (4 did not meet the inclusion criteria and 1 declined participation), resulting in 40 participants being randomized. Twenty participants were allocated to the intervention group, all of whom received the assigned intervention, completed follow-up, and were included in the primary outcome analysis. Similarly, 20 participants were allocated to the control group, all of whom received the assigned intervention, completed follow-up, and were included in the primary outcome analysis (Figure 1).

Baseline demographic and anthropometric characteristics were comparable between the one-month and two-month rehabilitation groups, with no meaningful differences in age, height, weight, or BMI (Table 1).

Similarly, the distribution of sex, comorbidities, cardiovascular history, smoking status, and family history of cardiac disease did not differ significantly between groups (Table 2), indicating well-balanced baseline profiles.

Cardiac function and quality-of-life measures exhibited improvement following rehabilitation in both groups. Although the one-month group demonstrated a marginally greater numerical increase in LVEF and SF-36 scores, these differences were not statistically significant, indicating comparable effectiveness of the two program durations (Table 3). Figure 2 visually compares LVEF and SF-36 scores before and after rehabilitation across the two groups.

Diastolic function patterns were broadly similar between groups at baseline and after rehabilitation, with no statistically significant differences in the distribution of dysfunction grades (Table 4). Both groups demonstrated a modest shift toward improved diastolic function following rehabilitation; however, the magnitude of change did not differ significantly.

Exercise-related physiological parameters, including maximum heart rate, heart rate recovery, and MET capacity, exhibited comparable trajectories in both groups (Table 5). Both groups demonstrated slight improvements across sessions; however, none of the between-group comparisons achieved statistical significance. Figure 3 illustrates these trends, revealing parallel patterns of change throughout the rehabilitation program.

Echocardiographic indices reflecting diastolic and systolic function were comparable between the one-month and two-month rehabilitation groups at baseline, with no

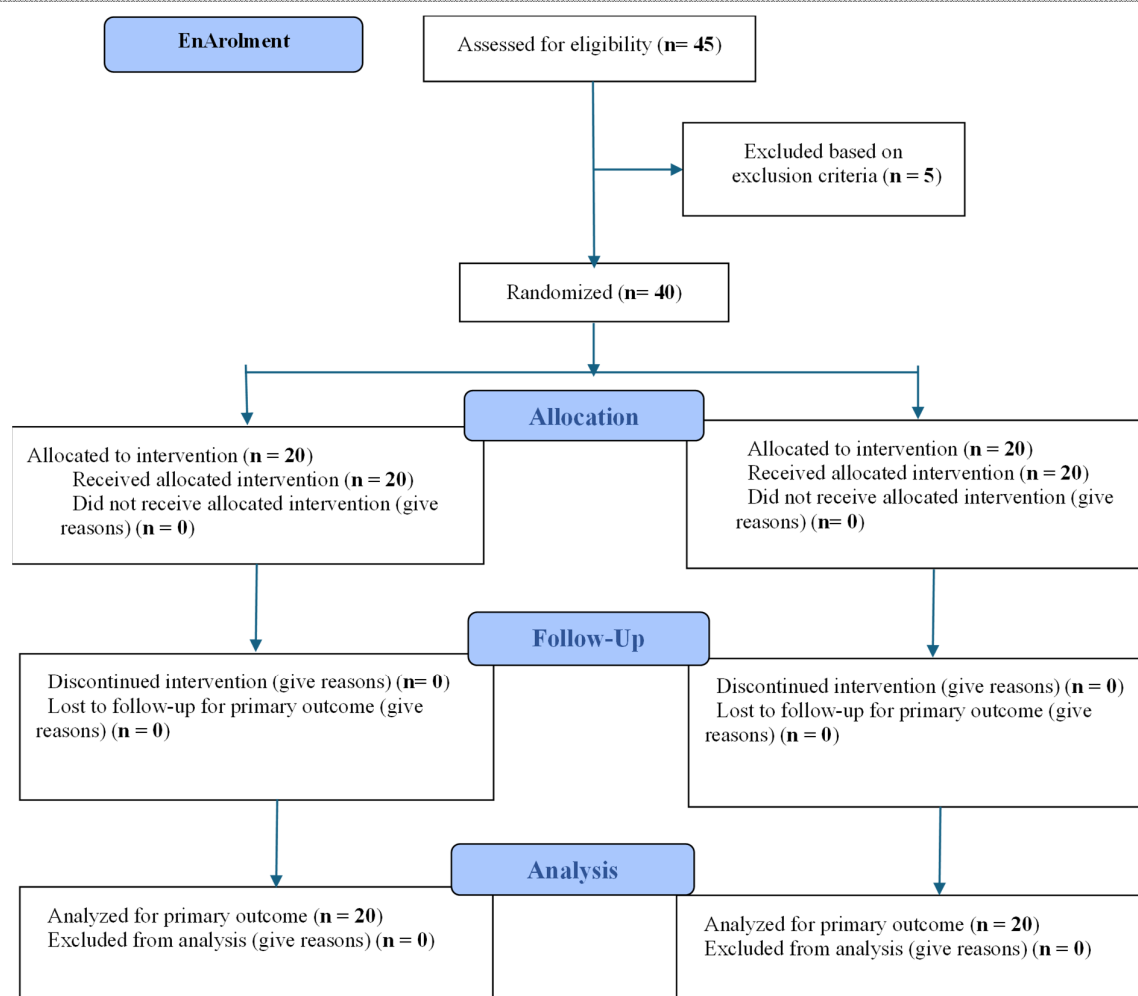


Figure 1. CONSORT 2025 Flow Diagram

Table 1. Mean and standard deviation of age, height, weight, and BMI in patients with cardiac conditions undergoing rehabilitation, stratified by the timing of rehabilitation initiation.

Variable	One Month After PCI (mean $\pm$ SD)	Two Months After PCI (mean $\pm$ SD)	P-value*
Age (years)	58.85 $\pm$ 9.91	57.85 $\pm$ 8.75	0.737
Height (cm)	162.30 $\pm$ 18.04	167.85 $\pm$ 6.20	0.285
Weight (kg)	79.60 $\pm$ 22.31	73.55 $\pm$ 11.16	0.201
BMI (kg/m ²)	27.83 $\pm$ 4.80	26.07 $\pm$ 3.46	0.192

* Independent samples t-test

meaningful differences observed across transmitral flow parameters (E, A, E/A), tissue Doppler velocities (E', A', S'), or derived ratios (E'/A', E/E'). Following rehabilitation, both groups exhibited small, non-significant shifts in these measures, and no between-group differences emerged for any parameter (Table 6). Overall, the echocardiographic profile indicates that the timing of program initiation—one versus two months after PCI—did not differentially influence diastolic or systolic functional indices (Table 6).

Discussion

Evidence regarding the impact of cardiac rehabilitation (CR) following myocardial infarction (MI) or cardiac surgery remains inconclusive. While some studies report no

significant effect of CR on mortality, psychological outcomes, cardiovascular risk factors, quality of life, or recurrence of cardiac events (21, 22), others have demonstrated that CR can significantly reduce mortality, improve survival, and lower the incidence of recurrent MI, coronary interventions, angina, restenosis, and hospitalizations (23–25). Building on the established benefits of CR, the present study specifically examined whether the timing of CR initiation, at one versus two months post-primary PCI, affects short-term functional outcomes in post-MI patients.

In the present study, no significant difference was observed in the mean LVEF between the initiation of cardiac rehabilitation at 1 and 2 months post-PCI. A clinical trial conducted by Zhang and colleagues (2018) in China,

Table 2. Baseline demographic and clinical characteristics of participants based on the timing of cardiac rehabilitation initiation.

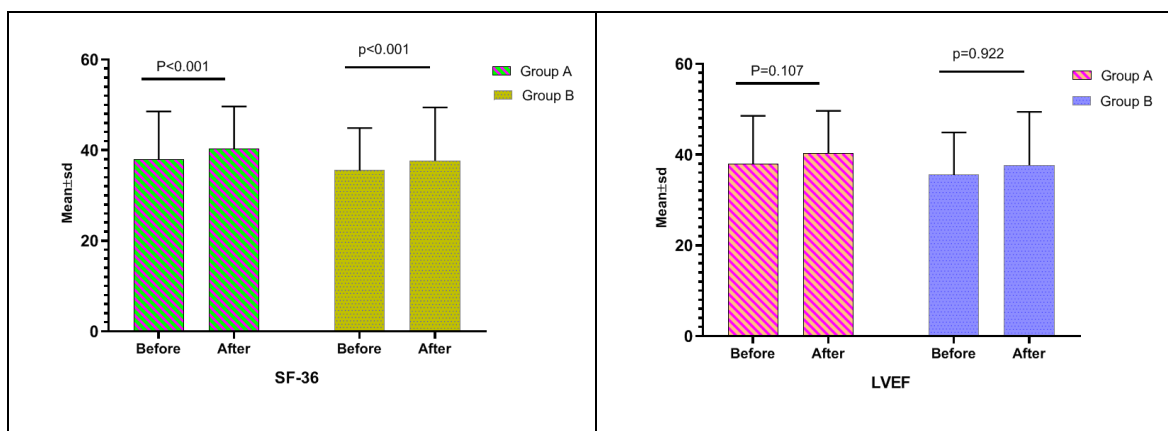
Variable	One Month After PCI n (%)	Two Months After PCI n (%)	P-value*
Sex			0.731
Male	13 (65.0%)	15 (75.0%)	
Female	7 (35.0%)	5 (25.0%)	
History of comorbidities			0.880
No	3 (15.0%)	4 (20.0%)	
Yes	17 (85.0%)	16 (80.0%)	
Previous myocardial infarction			0.633**
No	18 (90.0%)	17 (85.0%)	
Yes	2 (10.0%)	3 (15.0%)	
Prior cardiac intervention			0.605**
No	19 (95.0%)	17 (85.0%)	
Yes	1 (5.0%)	3 (15.0%)	
Smoking status			0.490
Non-smoker	15 (75.0%)	13 (65.0%)	
Smoker	5 (25.0%)	7 (35.0%)	
Family history of cardiac disease			0.342
No	9 (45.0%)	12 (60.0%)	
Yes	11 (55.0%)	8 (40.0%)	

Chi-square test and Fisher's exact test are statistical methods used for analyzing categorical data. Fisher's exact test is specifically employed when the expected cell count is less than 5.

Table 3. Comparison of mean LVEF and SF-36 quality of life scores before and after CR in two groups stratified by rehabilitation initiation time.

Timepoint	One Month After PCI (mean $\pm$ SD)	Two Months After PCI (mean $\pm$ SD)	P-value*
Left ventricular ejection fraction (LVEF)			
Before Rehabilitation	38.00 $\pm$ 10.56	37.50 $\pm$ 9.93	0.878
After Rehabilitation	40.25 $\pm$ 9.38	37.65 $\pm$ 11.76	0.444
SF-36 quality of life			
Before Rehabilitation	60.80 $\pm$ 5.99	63.35 $\pm$ 4.72	0.737
After Rehabilitation	65.85 $\pm$ 6.67	67.05 $\pm$ 5.96	0.192

* Independent samples t-test

**Figure 2.** Comparison of mean SF-36 quality of life and LVEF scores before and after cardiac rehabilitation in two groups based on timing of rehabilitation initiation.

which compared the presence and absence of rehabilitation in 130 STEMI patients who underwent PCI, indicated that the rehabilitation group experienced better outcomes in terms of LVEF improvement during phases II and III compared to the control group (25). Additionally, a systematic review and meta-analysis by Zhang and colleagues (2019), which examined the effect of exercise post-PCI on cardiac function and cardiovascular side effects in CAD patients across ten randomized controlled trials involving 1,274 subjects (636 in the exercise group and 638 in the control group), revealed a significant im-

provement in LVEF in the exercise group (24). In the current study, both groups underwent cardiac rehabilitation, albeit with a 1- and 2-month interval post-PCI. The discrepancy in results may be attributed to differences in study methodology or sample size.

Quality of life, assessed using the SF-36 questionnaire, improved significantly in both groups following CR; however, no significant between-group difference was observed. This finding aligns with the results reported by West et al. (2012), which indicated no significant quality-of-life differences between the CR and control groups

Table 4. Frequency of diastolic dysfunction assessed by echocardiography during the initial and final cardiac rehabilitation sessions in two groups stratified by the timing of rehabilitation initiation.

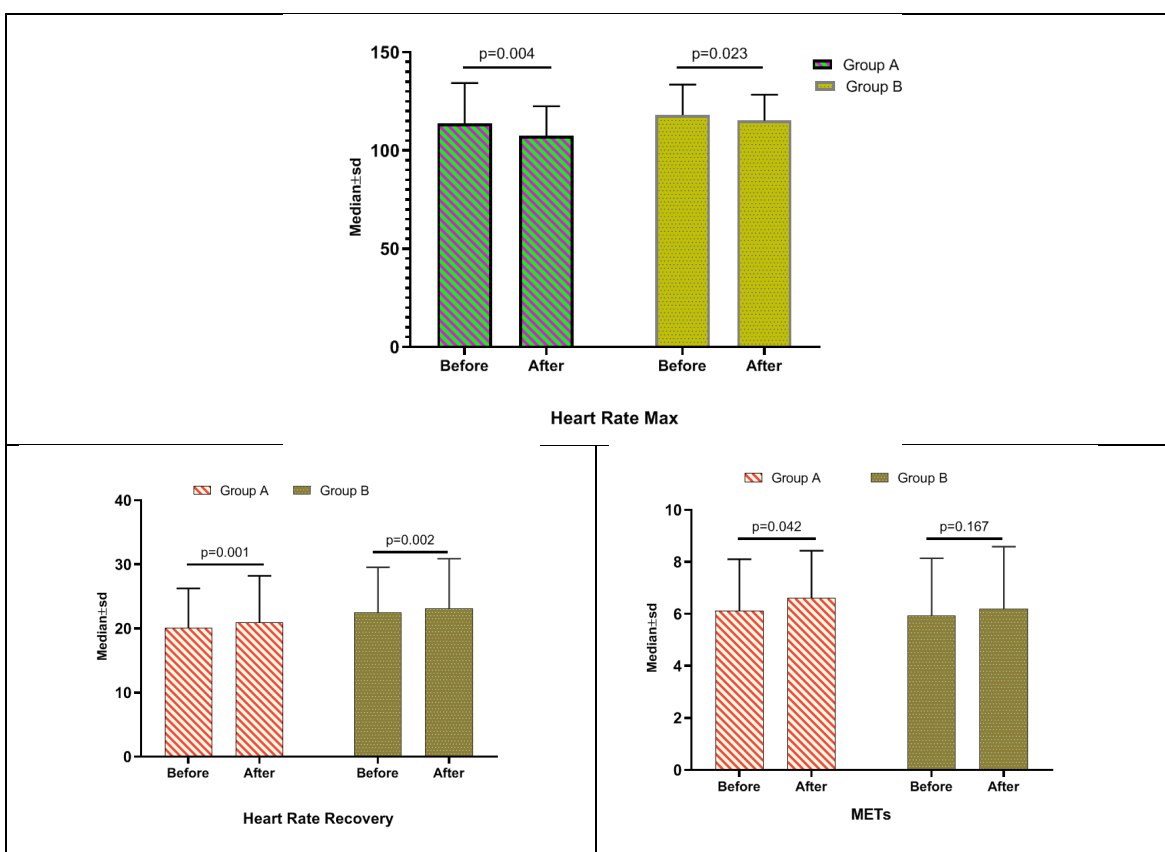
Diastolic Dysfunction Grade	One Month After PCI, n (%)	Two Months After PCI, n (%)	P-value*
Before Rehabilitation			0.407
None	0 (0%)	0 (0%)	
Grade 1	18 (90%)	15 (75%)	
Grade 2	2 (10%)	5 (25%)	
After Rehabilitation			0.506
None	3 (15%)	3 (15%)	
Grade 1	15 (75%)	12 (60%)	
Grade 2	2 (10%)	5 (25%)	

* Fisher's exact test

Table 5. Comparison of maximum heart rate (Heart Rate Max), heart rate recovery, and MET before and after cardiac rehabilitation in two groups based on the timing of rehabilitation initiation.

Timepoint	One Month After PCI (mean $\pm$ SD)	Two Months After PCI (mean $\pm$ SD)	P-value*
Maximum heart rate (Heart Rate Max)			
Before Rehabilitation	113.60 $\pm$ 20.76	118.00 $\pm$ 15.55	0.453
After Rehabilitation	107.45 $\pm$ 15.04	115.20 $\pm$ 13.12	0.091
Heart rate recovery			
Before Rehabilitation	20.05 $\pm$ 6.19	20.95 $\pm$ 7.25	0.675
After Rehabilitation	22.50 $\pm$ 7.05	23.10 $\pm$ 7.78	0.800
Metabolic equivalent of task (MET)			
Before Rehabilitation	6.12 $\pm$ 1.98	5.92 $\pm$ 2.22	0.765
After Rehabilitation	6.60 $\pm$ 1.83	6.20 $\pm$ 2.39	0.556

* Independent samples t-test

**Figure 3.** Comparison of changes in maximum heart rate, heart rate recovery, and MET between the first and last cardiac rehabilitation sessions in two groups based on the timing of rehabilitation initiation (one month versus two months after PCI).

post-MI (26). Our results suggest that while CR enhances patient-reported outcomes, the timing of initiation within the 1–2-month window may not critically influence these improvements.

In the present study, a significant difference was observed in the mean METs before and after rehabilitation in patients who began rehabilitation 1 month post-PCI ($P=0.042$); however, no significant difference was found

Table 6. Mean $\pm$ SD of echocardiographic parameters before and after CR in two groups based on the timing of rehabilitation initiation.

Parameter	Timepoint	One Month After PCI (mean $\pm$ SD)	Two Months After PCI (mean $\pm$ SD)	P-value
E (cm/s)	Before Rehabilitation	0.655 $\pm$ 0.011	0.622 $\pm$ 0.025	0.588
	After Rehabilitation	0.565 $\pm$ 0.012	0.586 $\pm$ 0.020	0.671
A (cm/s)	Before Rehabilitation	0.534 $\pm$ 0.017	0.497 $\pm$ 0.015	0.453
	After Rehabilitation	0.629 $\pm$ 0.015	0.549 $\pm$ 0.015	0.095
E/A ratio	Before Rehabilitation	0.89 $\pm$ 0.11	0.95 $\pm$ 0.18	0.111
	After Rehabilitation	0.956 $\pm$ 0.36	1.18 $\pm$ 0.68	0.186
E' (cm/s)	Before Rehabilitation	0.091 $\pm$ 0.005	0.113 $\pm$ 0.011	0.423
	After Rehabilitation	0.113 $\pm$ 0.019	0.109 $\pm$ 0.010	0.934
A' (cm/s)	Before Rehabilitation	0.205 $\pm$ 0.016	0.161 $\pm$ 0.013	0.343
	After Rehabilitation	0.244 $\pm$ 0.022	0.249 $\pm$ 0.015	0.940
E'/A' ratio	Before Rehabilitation	0.685 $\pm$ 0.438	0.730 $\pm$ 0.420	0.741
	After Rehabilitation	1.14 $\pm$ 0.78	0.756 $\pm$ 0.97	0.565
E/E' ratio	Before Rehabilitation	8.20 $\pm$ 2.44	7.96 $\pm$ 4.57	0.838
	After Rehabilitation	7.78 $\pm$ 2.89	7.58 $\pm$ 3.89	0.846
S' (cm/s)	Before Rehabilitation	0.095 $\pm$ 0.015	0.090 $\pm$ 0.009	0.444
	After Rehabilitation	0.105 $\pm$ 0.016	0.102 $\pm$ 0.010	0.934

in those starting 2 months post-PCI. Additionally, no significant difference in MET changes was observed between the two groups initiating rehabilitation at 1 and 2 months post-intervention. An observational study by Johnson and colleagues (2014) in the USA examined the relationship between the timing of cardiac rehabilitation initiation after cardiac events or surgery and its outcomes. The study found that patients with a delay of less than 30 days had a higher maximum MET level compared to those with a delay greater than 30 days. The authors concluded that delays in starting cardiac rehabilitation are directly related to patient outcomes, with initiation within 15 days post-intervention providing the greatest benefit in terms of weight and exercise performance improvement (27). In the present study, the first group began rehabilitation 30 days post-surgery and the second group 60 days post-surgery, which aligns with Johnson's findings that earlier rehabilitation initiation had a greater impact on increasing METs.

In the present study, the frequency of diastolic dysfunction was lower in the group commencing cardiac rehabilitation one month post-surgery compared to the group starting two months post-surgery. However, no significant difference was observed between the two groups regarding the frequency of diastolic dysfunction assessed by echocardiography during the first and last rehabilitation sessions. Consistent with the findings of this study, a systematic review and meta-analysis by Zhang and colleagues (2019) reported no significant difference in left ventricular end-diastolic (LVED) frequency between patients with or without exercise (24). The distinction lies in the fact that, in the current study, both groups underwent cardiac rehabilitation, differing only in the timing of initiation.

Heart rate recovery is a well-established cardiac marker utilized to evaluate the risk of sudden cardiac death. Physical exercise and rehabilitation contribute to improved heart rate recovery (28). In the present study, the mean heart rate recovery significantly increased in both groups commencing rehabilitation at 1 and 2 months post-PCI compared to pre-rehabilitation levels; however, no significant

difference was observed between the two groups. A study conducted by Kalka and colleagues (2016) in Poland, which compared 89 cardiac patients undergoing 6 months of rehabilitation with 35 non-rehabilitated patients, found that the HRR parameter significantly increased in the rehabilitation group compared to the control group (28).

In the present study, the mean Heart Rate Max decreased from 113 to 107 bpm in Group A and from 118 to 115 bpm in Group B following rehabilitation. Although both groups demonstrated reductions in Heart Rate Max after rehabilitation, no significant between-group difference was observed. Elshazly et al. (2018), in a study of patients undergoing cardiac rehabilitation after acute myocardial infarction, reported an average reduction of 2.8 bpm in Heart Rate Max; however, this change was not statistically significant (29). Some studies suggest that reducing the waiting time for cardiac rehabilitation can lead to greater improvements in patients' exercise capacity (30). Fell and colleagues (2016), in a review on the timing of cardiac rehabilitation initiation, reported a median start time of 58 days. They recommended optimal start times of 28 days post-MI, 28 days post-MI-PCI, and 42 days post-CABG, with observed initiation times of 38 days for MI, 35 days for MI-PCI, 33 days for PCI, and 55 days for CABG. They indicated that each day of delay in starting rehabilitation reduces the likelihood of improvement in fitness-related measures by 1% (31). This randomized, controlled trial employed a parallel-group design with balanced baseline characteristics, thereby enhancing internal validity. The intervention adhered to evidence-based protocols and was registered under IRCT20151123025202N18. However, several limitations should be acknowledged: outcomes were assessed only immediately post-rehabilitation, without medium- or long-term follow-up; hard clinical endpoints and psychological variables were not evaluated; quality of life was measured using a generic tool (SF-36) without disease-specific instruments; both groups received the same protocol with relatively delayed initiation (≥ 1 month), limiting insights into the benefits of very early CR; and the single-center

design with limited demographic diversity may affect generalizability. Future multicenter studies with earlier CR initiation and broader outcome measures are recommended. A potential limitation of this study is the increased risk of type I error (alpha error), which may arise due to multiple comparisons across diverse outcomes.

Conclusion

In this study, initiating cardiac rehabilitation one month versus two months after primary PCI did not result in significant differences in short-term outcomes, including quality of life, LVEF, diastolic function, maximum heart rate, MET, or heart rate recovery. These findings suggest that moderate delays in the initiation of rehabilitation may not substantially impact early functional outcomes. However, the small sample size, short-term follow-up, and absence of hard clinical or psychological endpoints limit the generalizability of these results. Future studies with larger populations and extended follow-up are needed to determine the optimal timing for the initiation of cardiac rehabilitation.

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Conflict of Interests

The authors declare that they have no competing interests.

Authors' Contributions

Lobat Majidi (LM): Conceptualization; Methodology; Supervision; Writing-original draft; Project administration.

Ashkan Dabiri (AD): Investigation (data collection); data curation; validation; visualization; writing review and editing.

Mohammadreza Nikoo (MN): Formal analysis; Statistical analysis; Software; Validation; Writing-review & editing.

Azadeh Mozayanimonfared (AM): Resources; Clinical oversight; Methodology (clinical aspects); Critical revision of the manuscript; Writing—review & editing.

Azar Pirdehghan (AP) and Saeed Ghiasvandi (SGH): Ethics coordination; Project administration; Supervision; Interpretation of results; Writing-review & editing. All authors substantially contributed to the study's design and interpretation, and all authors read and approved the final manuscript.

Ethical Considerations

The study protocol was reviewed and approved by the local ethics committee of Farshchian Heart Hospital. All procedures adhered to the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment. To ensure confidentiality, all data were anonymized before

analysis, and no identifiable information was stored or reported.

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Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

AI Use Statement

Generative artificial intelligence (AI) tools were used solely for language editing and improving the clarity and readability of the manuscript. The authors reviewed and approved all AI-assisted content and take full responsibility for the accuracy, integrity, and originality of the manuscript. AI tools were not used to generate or interpret the study data, perform statistical analyses, or make scientific conclusions.

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