The outcome of early rehabilitation therapy for the patient after percutaneous coronary intervention: a systematic review and meta-analysis

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ABSTRACT

Background: Acute myocardial infarction (AMI) is one of the leading causes of mortality, morbidity and physical disability worldwide. The chief treatment for AMI is primary percutaneous coronary intervention (PCI). However, the effectiveness of early rehabilitation therapy after PCI patients still lacks documentation. Therefore, a meta-analysis has assessed the patient’s outcome of early rehabilitation therapy after PCI.

Methods: The searching protocol was carried out using several databases, such as PubMed, ScienceDirect, and Google Scholar, to identify relevant topics in June 2022. This study used the Preferred Reporting Items for Systematic Review and Meta-Analysis 2020 (PRISMA) guidelines.

Result: There were nine studies included in this systematic review and meta-analysis. All of the reviewed studies were written in English. Most of the included studies were carried out in China. Most of the included studies were carried out in China. The mean age of the patient were all above 18 years. The total participants were 858 patients with PCI. There was a significant difference in 6-minute walk distance (MD = 85.64; 95% CI = 78.68–92.60; p < 0.01); left ventricle ejection fraction (LVEF) (MD = 5.97; 95% CI = 5.30–6.63; p < 0.01) and body mass index (BMI) score (MD = 1.43; 95% CI = 0.86–2.0; p < 0.01) between groups in overall analysis.

Conclusion: Early rehabilitation in patients with PCI has better outcomes (6-minutes walk distances, LVEF, and BMI score) than in the control group.

Keywords: Percutaneous coronary intervention, rehabilitation therapy, 6 Minute Walking test, Ejection Fraction, outcome.


INTRODUCTION

The World Health Organization (WHO) statistical report in 2021 showed that cardiovascular disease causes approximately 4.6 million deaths, or a quarter of all deaths annually in Southeast Asia.1,2 People with hyperlipidemia are estimated to be more than 1.2 million annually diagnosed with acute myocardial infarction (AMI).1 The AMI conditions with the highest mortality and morbidity rates are often found in patients with ST-segment elevation myocardial infarction (STEMI).3

Patients with STEMI are plaque ruptures that partially or completely close the arteries and result in extensive heart muscle damage. The great treatment for STEMI patients is primary percutaneous coronary intervention (PCI).4 Primary PCI has been shown to contribute to high revascularization success rates, earlier discharge, and fewer subsequent cardiac events. Moreover, PCI has reduced morbidity and mortality following AMI events; however, fully allowing the condition to recover remains a problem today.3 This recovery effort is better done by undergoing a rehabilitation therapy program after PCI as early as possible.5–9 It has been shown to have helped reduce mortality and the recurrence rate of heart attacks.7,8,10–12

Early rehabilitation has also been credited with relieving patients’ symptoms, improving functional capacity and perceived quality of life, and supporting medical care during and after hospitalization.5,7,8,13,14 However, most patients undergo rehabilitation during their stay in the hospital, and only for a short time. We were interested in assessing the six-minute walking test and LV ejection fraction (LVEF) of early rehabilitation therapy after PCI in patients with AMI. Thus, this study aimed to evaluate the outcome of early rehabilitation therapy in patients after percutaneous coronary intervention/PCI.

METHODS

Data search

The searching protocol was carried out using several databases, such as PubMed, ScienceDirect, and Google Scholar, to identify relevant topics up to June 2022. The formula search employed Boolean “AND” or “OR” with “rehabilitation therapy”, “percutaneous coronary intervention”, “six-minute walking test”,...
and “ejection fraction” as keywords. We also inspected the references in identified studies to search for similar and relevant studies.

**Selection criteria**

Studies included must meet the following criteria such as: (1) The result reported any outcome of early rehabilitation therapy for the patient after PCI measure with either a six-minute walking test or ejection fraction; (2) the researchers calculated the number of population into categories (intervention and comparator/control); (3) non-randomized trial (cross-sectional, cohort, and case-control study design) or randomized controlled trial (RCT); and (4) English-language studies. The study selection, quality evaluation, and data extraction were done independently by all reviewers. The issue between the reviewers was settled by consensus among the fourth reviewers. This study was designed using the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines.15

**Outcome definition**

The major outcomes of this study included a six-minute walking test, left ventricle ejection fraction (LVEF), and BMI after early rehabilitation therapy in a patient with percutaneous coronary intervention in the form of mean difference (MD; 95%CI). First, the reviewers independently retrieved the baseline characteristics, exposures, and outcomes of included studies, including the name of authors, publication year, study design, country location, mean age and the number of people who participated.

We also assess the risk of bias in included studies using the Modified Newcastle Ottawa Scale (NOS) for non-randomized study design, which has three components: Patient selection (five points), group comparability (two points), and exposure determination (three points). Measurement in the selection components includes Proper case definition, case representativeness, control group selection, and definition. Measurement in the comparability components includes Research controls for the most and extra factor. Measurement in the exposure domain has Exposure determination, method of cases and controls determination, and rate of non-response. The overall score varied from 0 (worst) to 10 (best). The overall quality was rated as good quality (3 or 4 stars in the selection domain and 1 or 2 stars in the comparability domain and 2 or 3 stars in the outcome/exposure domain); fair quality (2 stars in the selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome/exposure domain), and poor quality (0 or 1 star in selection domain or 0 stars in comparability domain or 0 or 1 stars in outcome/exposure domain). Cochrane risk-of-bias tool for randomized trials ver. 2 (RoB 2) was also used to assess the risk of bias in randomized controlled trial (RCT) studies. All calculations and assessments based on five major domains are carried out automatically on the RoB2 tools.

**Data analysis**

The mean difference was calculated using the fixed-model analysis with a 95% confidence interval (CI) and a significant p-value of 0.05. Heterogeneity was measured using the Q-test, with a p<0.05. A funnel plot was used to measure publication bias for each outcome based on the symmetricity of each plot (qualitative measurement). The meta-analysis was performed using Review Manager ver. 5.4.

**RESULT**

**Search result**

In the study search process, we collected 75,473 studies from online databases (PubMed, ScienceDirect, and Google scholar) and six studies originating from the previous review version identified by the authors. A total of 7,047 studies were obtained for the title and abstract screening process, resulting in 16 studies that could be assessed for eligibility. Furthermore, nine studies were excluded cause by unmatched the inclusion and exclusion criteria, resulting in further analysis using seven newly included studies. We also retrieved two studies from the previous review version, resulting in nine studies in our analysis. The entire literature search process follows the PRISMA Guideline and is summarized through a flow chart as follows (Figure 1).

**Outcomes of studies**

Data characteristics and major outcomes of all studies that meet the inclusion criteria are compiled in Table 1. All reviewed studies were written in English, most of which were carried out in China. The mean age of the patient were all above 18 years. The total participants were 858 patients with PCI.

**Quantitative analysis**

Nine studies were included in the quantitative analysis of comparative 6-minute walk distance, left ventricle ejection fraction (LVEF), and body mass index (BMI) between the experimental and control group using 858 patients, including 434 in the experimental group. The mean difference between both techniques was assessed using the fixed model analysis. Our calculation was used to evaluate evidence of heterogeneity. Our analysis showed a significant difference in 6-minute walk distance between groups in overall analysis (MD = 85.64; 95% CI = 78.68–92.60; p < 0.01). Our calculation also showed significant difference in LVEF (MD = 5.97; 95% CI = 5.30–6.63; p < 0.01) (Figure 3) and BMI score (MD = 1.43; 95% CI = 0.86–2.00; p < 0.01) (Figure 4) between both groups.

**Heterogeneity Publication bias**

Q-Test was used to evaluate evidence of heterogeneity. Our analysis showed that the mean difference in 6-minute walk distance, left ventricle ejection fraction (LVEF), and body mass index (BMI) was significant heterogeneity (p<0.05) supported by the I2 test value >50%. Moreover, the publication bias of each outcome was described in the figures below.

**DISCUSSION**

Based on several studies in the last decade, technological advances in the cardiovascular field have provided intervention therapy for AMI patients and have produced many success.16–19 One is early rehabilitation therapy which can accelerate functional recovery and a patient’s quality of life. This result is consistent with and strongly suggested by the results of this study, which, based on a meta-analysis of several studies related
to early post-PCI rehabilitation therapy, showed significantly increased scores of 6-minute walking distance and LVEF.

The outcomes and safety of early rehabilitation programs in cardiovascular disease have been investigated previously.\(^8\)–\(^{11}\),\(^{14}\),\(^{20}\)–\(^{24}\) In RCT, Cai et al.\(^8\) found that cardiac rehabilitation in patients who had undergone PCI led to substantial improvements in recurrent angina, total exercise time and tolerance, and ST segment pattern. While the findings of Sunamura et al.\(^25\) showed that early rehabilitation could improve 10-year survival in patients with AMI who have undergone primary PCI. Unfortunately, most of this rehabilitation is only done in the short term, during hospitalization (≤3 months).\(^26\) These results are consistent that early rehabilitation therapy after AMI had no adverse effect on myocardial remodeling.

Based on the results, we obtained a 6-minute walk distance based on each study showed a significant difference compared to the control group the mean difference = 85.64 (95%CI: 78.68–92.60; I²: 79%; p < 0.01). Based on Zhang et al.,\(^10\) the 6MWT of the rehabilitation group showed improvement in phase II (t=4.013, P<0.001) and phase III (t=4.995, P<0.001). The findings of Jalinek et al.\(^19\) that 6MWT distance in both groups at baseline and after six weeks was significant (p=0.001). That 6-week early rehabilitation program benefits both patient groups in terms of exercise capacity, cardiorespiratory function and autonomic nervous system modulation of heart rate. Averstrom et al.\(^21\) also found that the mean 6MWT distance increased significantly more in the intervention group than in the control group, with a mean difference of 38 minutes at follow-up (95%CI: 14.62; p = 0.003).

Echocardiographic results in this study showed that after PCI intervention, the difference in LVEF in the group undergoing early rehabilitation was higher than in the control group (MD= 5.97; 95%CI= 5.30–6.63; I²: 92%; p<0.01) which was different statistically significant. Research from Vasiliauskas et al.\(^18\) reported that The Doppler echocardiographic findings revealed significant (p<0.05) improvement in ejection fraction and left ventricular and atria morphometric data. Relatively similar findings with Zhang et al.\(^10\) that the Left ventricular ejection fraction (LVEF) of the rehabilitation group showed improvement in phase II (t=4.963, P<0.001) and phase III (t=11.802, P<0.001). Based on an RCT from Cai et al.\(^8\) LVEF increased in the exercise group but not in the control group at six months. These results indicate that the program does not lead to myocardial remodeling in the long term. However, the increased LVEF may indicate that early post-PCI rehabilitation therapy restored myocardial function better than the control group. However, studies with larger samples are still needed to validate these observations. Based on a meta-analysis of echocardiographic examinations of the group consistently undergoing rehabilitation therapy for six months from day 14 after PCI, LVEF significantly increased.

Based on this, it is very important to improve cardiopulmonary function and prevent recurrence of myocardial infarction after AMI,\(^2\),\(^6\),\(^20\),\(^27\) and rehabilitation therapy improves both effectively. After completing this rehabilitation therapy, several recent studies are investigating methods to maximize the effects of rehabilitation programs as early as possible.

Early rehabilitation therapy is still not widely used because of difficulties in the hospital implementation, monitoring, and follow-up.\(^9\),\(^10\),\(^16\),\(^24\),\(^25\) However, this protocol has proven to be feasible based on the results of our analysis; all patients in this cardiac rehabilitation therapy group completed the program and felt the benefits outweigh the side effects. In addition, the success of this program cannot be separated from the close cooperation between cardiologists, general practitioners, study participants and their families. Thus, early rehabilitation therapy has beneficial outcomes in improving cardiac function and quality of life of patients after experiencing AMI and can be a recommendation to carry out this rehabilitation therapy in AMI patients after PCI.

Figure 1. PRISMA Flowchart.
Table 1. Data characteristics.

<table>
<thead>
<tr>
<th>No.</th>
<th>Author, Year</th>
<th>Study Design</th>
<th>Country</th>
<th>Total Population</th>
<th>Mean age±S.D</th>
<th>Main Results</th>
<th>Quality of study/risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Jelinek, 2013</td>
<td>Cohort</td>
<td>Australia</td>
<td>25</td>
<td>62.5 ± 9.9</td>
<td>The 6MWT distance in both groups at baseline and after six weeks is significant (p&lt;0.001). The 6-weeks CR program benefits both patient groups in terms of exercise capacity, cardiorespiratory function and autonomic nervous system modulation of heart rate.</td>
<td>Good quality</td>
</tr>
<tr>
<td>2.</td>
<td>Xiao, 2021</td>
<td>Cohort</td>
<td>China</td>
<td>82</td>
<td>60.2 ± 9.2</td>
<td>At 12 months, left ventricular ejection fraction and 6-minute walk distance in the rehabilitation group were significantly greater than those in the control group (both p &lt;0.01), and laboratory values also improved. The left ventricular ejection fraction (LVEF) of the rehabilitation group showed improvement in phase II (t=4.963, P&lt;0.001) and phase III (t=11.802, P&lt;0.001). The 6MWT of the rehabilitation group showed improvement in phase II (t=4.013, P&lt;0.001) and phase III (t=4.995, P&lt;0.001).</td>
<td>Good quality</td>
</tr>
<tr>
<td>3.</td>
<td>Zhang, 2018</td>
<td>Randomized controlled trial</td>
<td>China</td>
<td>65</td>
<td>70.3 ± 10.7</td>
<td>The left ventricular ejection fraction is significant (p &lt; 0.05) at six months of follow-up in the exercise group compared with the control group. The mean 6MWT distance increased significantly more in the intervention group than in the control group, with a mean difference of 38 minutes at follow-up (95% confidence interval 14.62, p = 0.003).</td>
<td>Low risk of bias</td>
</tr>
<tr>
<td>4.</td>
<td>Zheng, 2008</td>
<td>Randomized controlled trial</td>
<td>China</td>
<td>27</td>
<td>N.A.</td>
<td>The left ventricular ejection fraction is significant (p &lt; 0.05) at six months of follow-up in the exercise group compared with the control group. The mean 6MWT distance increased significantly more in the intervention group than in the control group, with a mean difference of 38 minutes at follow-up (95% confidence interval 14.62, p = 0.003).</td>
<td>Low risk of bias</td>
</tr>
<tr>
<td>5.</td>
<td>Arevstrom, 2019</td>
<td>Randomized controlled trial</td>
<td>Sweden</td>
<td>25</td>
<td>66 (62-71)</td>
<td>The left ventricular ejection fraction (LVEF) of the rehabilitation group showed improvement in phase II (t=4.963, P&lt;0.001) and phase III (t=11.802, P&lt;0.001). The 6MWT of the rehabilitation group showed improvement in phase II (t=4.013, P&lt;0.001) and phase III (t=4.995, P&lt;0.001).</td>
<td>Low risk of bias</td>
</tr>
<tr>
<td>6.</td>
<td>Cai, 2021</td>
<td>Randomized controlled trial</td>
<td>China</td>
<td>30</td>
<td>55 ± 9</td>
<td>LVEF increased in the exercise group but not the control group at six months. The LVEF difference is significant between the intervention and control groups (p=0.008) at week 4. LVEF score is higher in the intervention group. During the follow-up (33 ± 7 months) trained patients had a significantly lower event rate than controls (11.9 vs. 32.2%, RR: 0.71, 95% confidence interval [CI]: 0.60 to 0.91, p&lt;0.008) and a lower rate of hospital readmission (18.6 vs. 46%, RR: 0.69, 95% CI: 0.55 to 0.93, p&lt;0.001). Training group patients showed significant (p&lt;0.05) improvement in exercise capacity, oxygen consumption and ventilating equivalents after six months. The Doppler echocardiographic findings revealed significant (p&lt;0.05) improvement in ejection fraction and left ventricular and atria morphometric data.</td>
<td>Low risk of bias</td>
</tr>
<tr>
<td>7.</td>
<td>Xu, 2016</td>
<td>Randomized controlled trial</td>
<td>China</td>
<td>26</td>
<td>55.8 ± 9.7</td>
<td>The LVEF difference is significant between the intervention and control groups (p=0.008) at week 4. LVEF score is higher in the intervention group. During the follow-up (33 ± 7 months) trained patients had a significantly lower event rate than controls (11.9 vs. 32.2%, RR: 0.71, 95% confidence interval [CI]: 0.60 to 0.91, p&lt;0.008) and a lower rate of hospital readmission (18.6 vs. 46%, RR: 0.69, 95% CI: 0.55 to 0.93, p&lt;0.001). Training group patients showed significant (p&lt;0.05) improvement in exercise capacity, oxygen consumption and ventilating equivalents after six months. The Doppler echocardiographic findings revealed significant (p&lt;0.05) improvement in ejection fraction and left ventricular and atria morphometric data.</td>
<td>Low risk of bias</td>
</tr>
<tr>
<td>8.</td>
<td>Belardinelli, 2001</td>
<td>Randomized controlled trial</td>
<td>Italy</td>
<td>59</td>
<td>53 ± 11</td>
<td>Low risk of bias</td>
<td>Low risk of bias</td>
</tr>
<tr>
<td>9.</td>
<td>Vasiliauskas, 2007</td>
<td>Randomized controlled trial</td>
<td>Lithuania</td>
<td>95</td>
<td>58.49 ± 4.3</td>
<td>Low risk of bias</td>
<td>Low risk of bias</td>
</tr>
</tbody>
</table>
Early rehabilitation in patients with PCI has better outcomes (6-minute walk distances, LVEF, and BMI score) than in the control group. Our meta-analysis concluded that the outcome of early rehabilitation therapy significantly improved the physical stamina and cardiac function of AMI patients who underwent PCI.

CONCLUSION

Early rehabilitation in patients with PCI has better outcomes (6-minute walk distances, LVEF, and BMI score) than in the control group. Our meta-analysis concluded that the outcome of early rehabilitation therapy significantly improved the physical stamina and cardiac function of AMI patients who underwent PCI.

DISCLOSURE

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Author Contribution
All authors contributed equally in conducting the study and preparing the manuscript.

Conflict of Interest
All authors stated no conflict of interest regarding publishing this manuscript.

Ethical Consideration
None.

REFERENCES


