

Evaluate the Outcome of Mortality and Clinical Endpoints of Cardiac Rehabilitation and Statin Therapy after Acute Coronary Syndrome and Coronary Artery Bypass Grafting: A Systematic Review and Meta-Analysis

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Evaluate the Outcome of Mortality and Clinical Endpoints of Cardiac Rehabilitation and Statin Therapy after Acute Coronary Syndrome and Coronary Artery Bypass Grafting: A Systematic Review and Meta-Analysis

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Abstract

Background and aim: In the present study, we tried to provide sufficient evidence to evaluate the effectiveness of Cardiac Rehabilitation in patients with coronary artery disease after Acute Coronary Syndrome and Coronary Artery Bypass Grafting. Therefore, the present study was conducted to evaluate the Outcome of Mortality and Clinical Endpoints of Cardiac Rehabilitation and Statin Therapy after Acute Coronary Syndrome and Coronary Artery Bypass Grafting.

Method: From the electronic databases, PubMed, Scopus, Web of Science, EBSCO and Embase have been used to perform a systematic literature over the last ten years between 2011 and May 2021. Newcastle-Ottawa Scale and Cochrane Collaboration's tool used to assess quality of the cohort studies and randomized control trial studies, respectively. Hazard ratio with 95% confidence interval, fixed effect model and Mantel-Haenszel method were calculated. The Meta analysis have been evaluated with the statistical software Stata/MP v.16 (The fastest version of Stata).

Result: In the first step of selecting studies 904 studies were selected to review the abstracts, in the second step, the full text of 168 studies was reviewed. Finally, thirteen studies were selected. Hazard ratio of Total mortality after Acute Coronary Syndrome and Coronary Artery Bypass Grafting between Cardiac Rehabilitation group and no-Cardiac Rehabilitation group was 1.33 (HR, 1.33 95 % CI 1.20, 1.46; p=0.00) and 0.52 (HR, 0.52 95 % CI 0.33, 0.71; p=0.00), respectively.

Conclusion: mortality was reduced in Cardiac Rehabilitation after Acute Coronary Syndrome and Coronary Artery Bypass Grafting.

Key words: Coronary Artery Bypass Grafting, Acute Coronary Syndrome, Acute Coronary Syndrome, mortality, Statin Therapy

Introduction

Numerous studies have been performed on Cardiac Rehabilitation (1-7), but insufficient evidence has been provided for the beneficial effects of Cardiac Rehabilitation in patients with coronary artery disease, as Cardiac Rehabilitation varies from country to country and there is no universally accepted minimum standard for judging quality. There is no Cardiac Rehabilitation, so discussing the effectiveness of this method is challenging (8-10). Over the past two decades, surgery, intervention therapies, and medications have had an impact on how quality care is provided to patients who have experienced cardiac rehabilitation (11, 12). Studies of prospective, high-volume, randomized clinical trials examining the effects of Cardiac Rehabilitation are scarce (13-15). As a result, other strong studies that have used this method should be considered (16, 17). In the present study, we tried to provide sufficient evidence to evaluate the effectiveness of Cardiac Rehabilitation in patients with coronary artery disease after Acute Coronary Syndrome and Coronary Artery Bypass Grafting. Therefore, the present study was conducted to evaluate the Outcome of Mortality and Clinical Endpoints of Cardiac Rehabilitation and Statin Therapy after Acute Coronary Syndrome and Coronary Artery Bypass Grafting.

Methods

Search strategy

From the electronic databases, PubMed, Scopus, Web of Science, EBSCO, and Embase have been used to perform a systematic literature over the last ten years between 2011 and September 2021. The reason for choosing studies in the last ten years is to be able to provide sufficient evidence in this area and use newer studies. Therefore, a software program (Endnote X8) has been utilized for managing the electronic titles.

Searches were performed with mesh terms:

("Cardiac Rehabilitation/classification"[Mesh] OR "Cardiac Rehabilitation/instrumentation"[Mesh] OR "Cardiac Rehabilitation/methods"[Mesh] OR "Cardiac Rehabilitation/pharmacology"[Mesh] OR "Cardiac Rehabilitation/statistics and numerical data"[Mesh] OR "Cardiac Rehabilitation/therapy"[Mesh]) OR "Cardiac Rehabilitation"[Mesh] AND ("Heart Diseases"[Mesh] OR "Coronary Disease"[Mesh]) OR "Coronary Artery Bypass"[Mesh] AND "Acute Coronary Syndrome"[Mesh] OR ("Acute Coronary Syndrome/classification"[Mesh] OR "Acute Coronary Syndrome/complications"[Mesh] OR "Acute Coronary Syndrome/diagnosis"[Mesh] OR "Acute Coronary Syndrome/drug therapy"[Mesh] OR "Acute Coronary Syndrome/surgery"[Mesh] OR "Acute Coronary Syndrome/therapy"[Mesh]) OR ("Coronary Artery Bypass/classification"[Mesh] OR "Coronary Artery Bypass/epidemiology"[Mesh] OR "Coronary Artery Bypass/methods"[Mesh] OR "Coronary Artery Bypass/mortality"[Mesh] OR "Coronary Artery Bypass/rehabilitation"[Mesh] OR "Coronary Artery Bypass/statistics and numerical data"[Mesh] OR "Coronary Artery Bypass/therapy"[Mesh]) AND ("Mortality"[Mesh] OR "Mortality, Premature"[Mesh]) OR "Stroke"[Mesh] AND "Myocardial Infarction"[Mesh].

This systematic review has been conducted on the basis of the key consideration of the PRISMA Statement—Perfumed Reporting Items for the Systematic Review and Meta-analysis (18), and PICO strategy (Table 1).

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Selection criteria

Inclusion criteria: Randomized controlled trials studies, controlled clinical trials; Prospective and retrospective cohort studies; in human; in English. In vitro studies, case studies, case reports and reviews; maxillary arch were excluded from the study.

Table 1. PICO OR PECO strategy.

PICO strategy	Description
P	Population/ Patient: patients after hospitalization for Acute Coronary Syndrome and Coronary Artery Bypass Grafting
I	Intervention: Cardiac Rehabilitation
C	Comparison: No-Cardiac Rehabilitation
O	Outcome: mortality and Clinical Endpoints

Data Extraction and analysis method

The data were extracted from the research included years, study design, sample size, intervention group, control group and Follow-up period.

The quality of randomized studies included was assessed using Collaboration’s tool (19). The scale scores for low risk was 1 and for High and unclear risk was 0. Scale scores range from 0 to 6. A higher score means higher quality. Newcastle-Ottawa Scale (NOS) (20) used to assess quality of the cohort studies and case-control studies, This scale measures three dimensions (selection, comparability of cohorts and outcome) with a total of 9 items. In the analysis, any studies with NOS scores of 1- 3, 4- 6 and 7- 9 were defined as low, medium and high quality, respectively.

For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included. Prior to the screening, kappa statistics was carried out in order to verify the agreement level between the reviewers. The kappa values were higher than 0.80.

Odds ratio and Hazard ratio with 95% confidence interval (CI), fixed effect model and Mantel-Haenszel method were calculated. Random effects were used to deal with potential heterogeneity and I^2 showed heterogeneity. I^2 values above 50% signified moderate-to-high heterogeneity. The Meta analysis have been evaluated with the statistical software Stata/MP v.16 (The fastest version of Stata).

Results

In the review of the existing literature using the studied keywords, 976 studies were found. In the initial review, duplicate studies were eliminated and abstracts of 904 studies were reviewed. At this stage, 736 studies did not meet the inclusion criteria, so they were excluded, and in the second stage, the full text of 168 studies was reviewed by two authors. At this stage, 155 studies were excluded from the study due to incomplete data, inconsistency of results in a study, poor studies, lack of access to full text, inconsistent data with the purpose of the study. Finally, thirteen studies were selected (Figure 1).

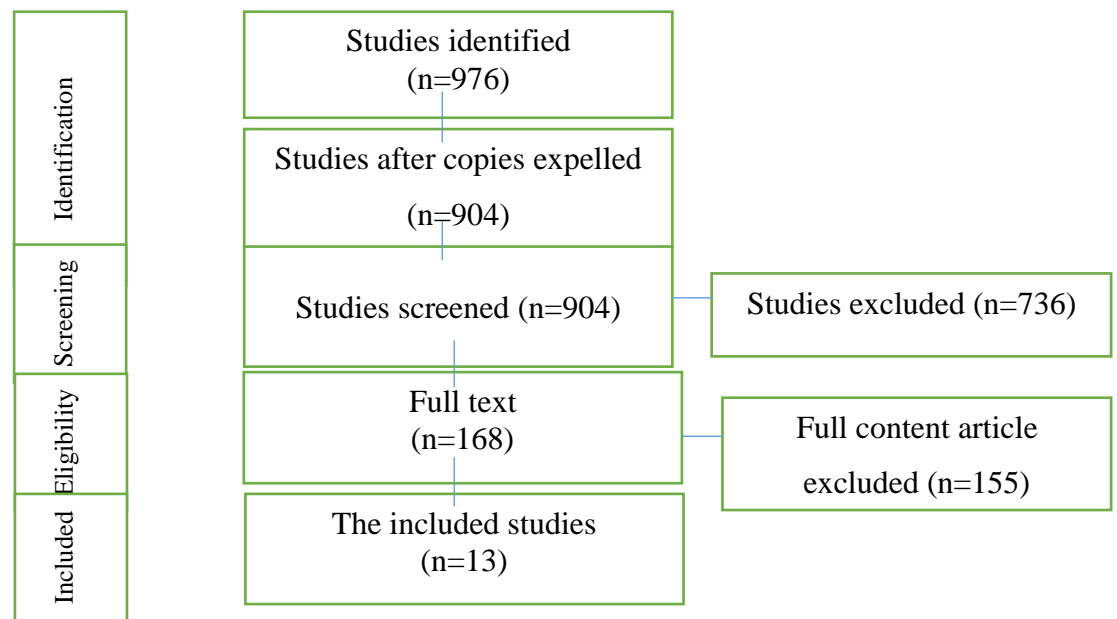


Figure 1. Study Attrition

Table 2. Studies selected for systematic review and meta-analysis.

Studies. Years	Study design	Number of patients		Mean of age	CR duration	CR setting	Follow-up period
		CR	No-CR				
Schlitt et al.,2015 (21)	Retrospective	52 2	124 6	61	NR	In-patient (majority) and outpatient	136
Meurs et al.,2015 (22)	Retrospective	87 8	824	57	9 wk average	Out-patient	6 mo
Vries et al.,2015 (23)	Retrospective	11 01 4	249 05	63.4	6-12 w	Out-patient	4y
Rauch et al.,2014 (24)	Prospective	25 13	104 7	62	3-4w	In-patient	4-12 mo
Prince et al.,2014 (25)	Retrospective	48 8	334	61.6	NR	Out-patient	14 y
Coll-Fernández et al.,2014 (26)	Retrospective	58 2	264	64.4	NR	Out-patient	18 mo
Pack et al.,2013 (16)	Retrospective	58 2	264	64.4	55 d	Out-patient	9 y
Marzolini et al.,2013 (27)	Prospective	42 4	427	64.8	NR	Out-patient	3 y

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Beauchamp et al.,2013 (28)	Retrospective	281	263	60.9	NR	Out-patient	14 y
Martin et al.,2012 (4)	Prospective	2900	2986	60.1	12 w	Out-patient	14 y
Schwaab et al.,2011 (29)	Retrospective	794	679	64.1	3-4w	In-patient	1 y
Kim et al.,2011 (30)	Prospective	69	72	61.9	6-8 w	usual care	1 y
Goel et L.,2011 (2)	Retrospective	964	1431	62.5	3 mo	usual care	6 y

CR: Cardiac Rehabilitation

Table3. Risk of bias assessment (NOS tool)

Study. Years	Selection (5 score)				Comparability (2 score)	Outcome (2 score)		Total score
	representative sample	Sample size	Nonrespondents	Ascertainment of the exposure	Based on design and analysis	Assessment of outcome	Statistical test	
Schlitt et al.,2015 (21)	1	1	1	0	1	0	1	5
Meurs et al.,2015 (22)	1	1	1	0	1	1	1	6
Vries et al.,2015 (23)	1	1	0	2	1	1	1	7
Rauch et al.,2014 (24)	1	1	1	1	2	1	1	8
Prince et al.,2014 (25)	1	1	1	0	2	1	1	7
Coll-Fernández et al.,2014 (26)	1	1	1	1	2	1	1	8
Pack et al.,2013 (16)	1	1	1	1	1	1	1	7
Marzolini et al.,2013 (27)	1	1	1	1	2	1	1	8
Beauchamp et al.,2013 (28)	1	1	1	1	1	1	1	7
Martin et al.,2012 (4)	1	1	1	1	1	1	1	7
Schwaab et al.,2011 (29)	1	1	1	0	1	1	1	6
Kim et al.,2011 (30)	1	1	1	0	1	0	1	5
Goel et L.,2011 (2)	1	1	1	1	1	1	1	7

Characteristics

Thirteen studies (nine retrospective cohort studies, four Prospective cohort studies) have been included in present article. The number of patients in Cardiac Rehabilitation group and control group was 22011 and 34742, respectively; a total was 56753 with mean age of 62.15 years. Other characteristics of the selected studies are reported in Table 2.

Bias assessment

According to NOS tool, threestudies had a total score of 8/9, sixstudies had a total score of 7/9, two studies had a total score of 6/9 and two studies had a total score of 5/9. All studies had high quality excepttwo study that had medium quality(Table3).

Total mortality

Hazard ratio of Total mortality after Acute Coronary Syndrome between Cardiac Rehabilitation group and no-Cardiac Rehabilitationgroup was 1.33 (HR, 1.33 95 % CI 1.20, 1.46; p=0.00)with low heterogeneity($I^2 < 0\%$; p=0.69) (Figure2). There was statistically significant difference between two groups, mortality was reduced in Cardiac Rehabilitation group.

Hazard ratio of Total mortality after Coronary Artery Bypass Grafting between Cardiac Rehabilitation group and no-Cardiac Rehabilitationgroup was 0.52 (HR, 0.52 95 % CI 0.33, 0.71; p=0.00)with high heterogeneity($I^2 = 96.65\%$; p=0.00) (Figure3). There was statistically significant difference between two groups, mortality was reduced in Cardiac Rehabilitation group.

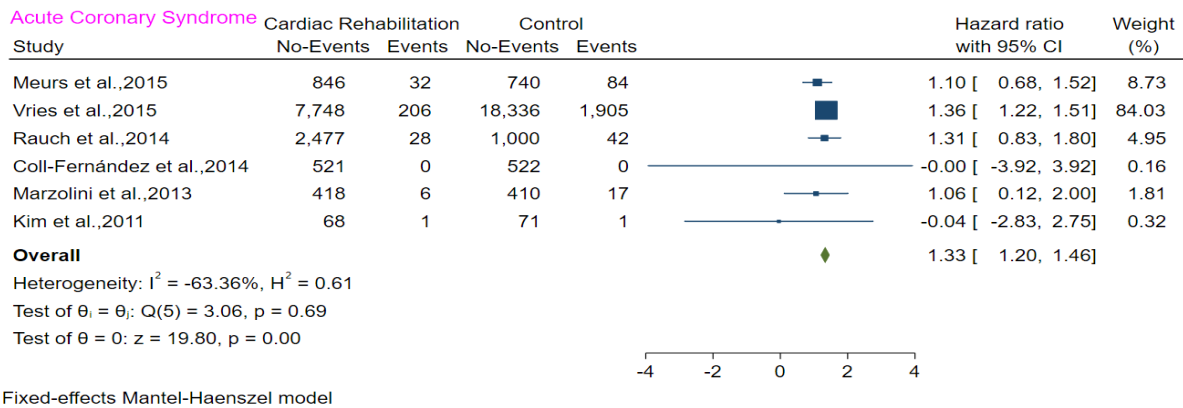


Figure 2. The Forest plot showed Total mortality after Acute Coronary Syndrome

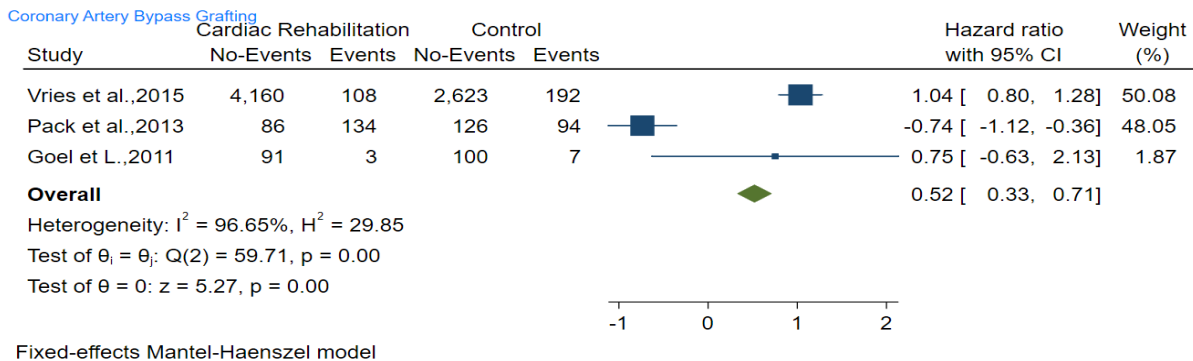


Figure 3. The Forest plot showed Total mortality after Coronary Artery Bypass Grafting

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Hazard ratio of Total mortality in mixed populations between Cardiac Rehabilitation group and no-Cardiac Rehabilitation group was 0.74 (HR, 0.74 95 % CI 0.63, 0.86; $p=0.00$) with high heterogeneity ($I^2=94.90\%$; $p=0.00$) (Figure 4). There was statistically significant difference between two groups, mortality was reduced in mixed populations.

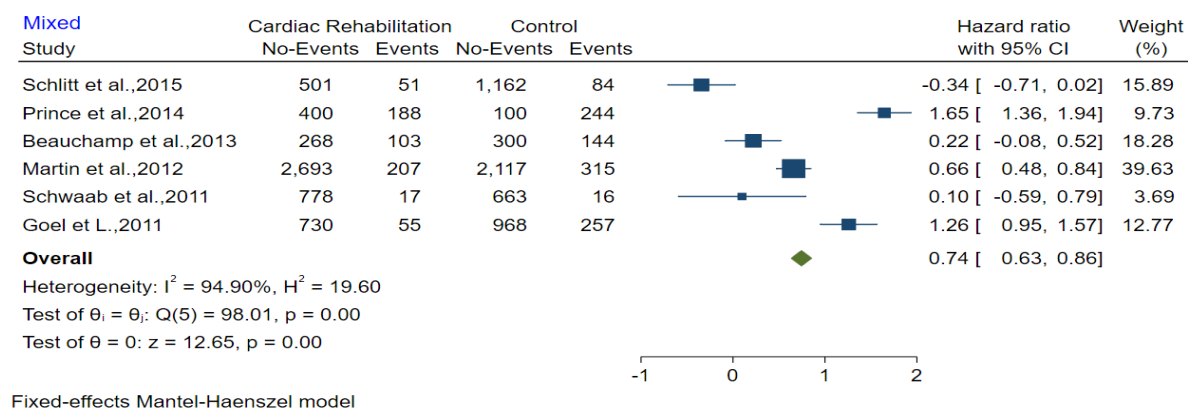


Figure 4. The Forest plot showed Total mortality in mixed populations

Discussion

The aim of current systematic review and meta-analysis study was to evaluate the Outcome of Mortality and Clinical Endpoints of Cardiac Rehabilitation and Statin Therapy after Acute Coronary Syndrome and Coronary Artery Bypass Grafting. In the present study, compared to previous studies, newer studies of the last ten years in 2011 to 2021 have been used. Newer studies provide strong evidence, the quality of all studies is considered high. The reason for choosing the studies of the last ten years is that the evidence shows that since 1995, treatments and drugs have been different compared to clinical practice, and the impact of Cardiac Rehabilitation participation is increasing day by day. The results of meta-analysis showed a significant difference in terms of mortality between the two groups of Cardiac Rehabilitation and non-use of Cardiac Rehabilitation. In Cardiac Rehabilitation group, the mortality rate after Acute Coronary Syndrome and Coronary Artery Bypass Grafting decreased significantly. RCTs were not included in the present study, firstly because in previous studies they had high heterogeneity results and existing RCTs had a high risk of bias. It is better to design stronger RCTs in future studies. The latest Cochrane review, based on RCT studies, did not show a reduction in overall mortality in the subgroup of studies published after 1995. However, cardiovascular mortality decreased significantly in both time periods, before and after 1995(1). The type of Cardiac Rehabilitation and the duration of it, as well as other factors can cause high inconsistencies between the findings. The populations under study are also of great importance in this regard (1, 31-34). Previous Meta-analysis show that the ongoing need for well-designed studies with minimum standards set for cardiac rehabilitation is significant(35, 36). Cardiac Rehabilitation should be carefully considered as it may be considered as the main mechanism in reducing mortality. However, medical supervision, motivation, education, and increased adherence to secondary prophylactic drugs, as shown in some studies, may also have contributed to positive outcomes(37). The present study cannot provide sufficient evidence; however, its results can be used in comparison with other researches and as a basis for RCTs studies. The results of the meta-analysis

show that Cardiac Rehabilitation is a very important therapeutic intervention and can reduce mortality after Acute Coronary Syndrome and Coronary Artery Bypass Grafting.

Conclusion

Cardiac Rehabilitation after Acute Coronary Syndrome and Coronary Artery Bypass Grafting can effectively and significantly reduce mortality. The present study does not provide strong evidence due to the high heterogeneity between the study findings; it is suggested that in order to achieve stronger evidence and better quality studies, the minimum internationally accepted standards for planning, implementing and delivering Cardiac Rehabilitation should be considered.

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