Peertechz


Medical Group

Journal of Cardiovascular Medicine and Cardiology

DOI:http://dx.doi.org/10.17352/jcmc

ISSN: 2455-2976 CC By

Nuremanguli Abudukeremu[1§], Zi-Xiang Yu[1§], Yi-Ning Yang[1,2], Siew-Pang Chan[3,4], Xiao-Mei Li[1,2], Fen Liu[2], Yi-Tong Ma[1,2*]

[1]Department of Coronary Artery Disease, The First Affiliated Hospital of Xinjiang Medical University, Urumqi, Xinjiang, China
[2]Xinjiang Key Laboratory of Cardiovascular Disease Research, Urumqi, Xinjiang, China
[3]Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[4]Cardiovascular Research Institute, National University Heart Centre, Singapore

[§]The authors contribute equally to the manuscript

**Received:** 24 October, 2018
**Accepted:** 05 November, 2018
**Published:** 06 November, 2018

***Corresponding author:** Yi-Tong Ma, Department of Coronary Artery Disease, The First Affiliated Hospital of Xinjiang Medical University, No.137 Liyushan Road, Urumqi, Xinjiang, China 830054, China, Tel: +86 991 4366169; Fax: +86 991 4366169; E-mail: myt-xj@163.com

**Keywords:** Coronary artery disease; Left ventricular dysfunction; Percutaneous coronary intervention; Mortality

https://www.peertechz.com

Check for updates

Research Article

# An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction

## Abstract

**Background:** Coronary artery disease (CAD) is the most common cause of left ventricular dysfunction (LVD). Conflicting evidence exists with regards to available treatments and patient prognosis. Revascularization may improve ventricular function while coronary artery bypass surgery (CABG) has significantly improved survival. The effectiveness of percutaneous coronary intervention (PCI) has also not been thoroughly investigated to date.

**Objectives:** To ascertain the in-hospital and long-term (≥1 year) outcomes of CAD patients with LV systolic dysfunction (ejection fraction ≤40%) after PCI according to a meta-analysis.

**Methods:** A systematic literature search and a series of random-effect meta-analyses were conducted to evaluate the short- and long-term outcomes of PCI of the selected studies. Single-center studies and those that did not report evidence on long-term mortality were excluded in the analysis. All statistical tests were performed with 95% confidence intervals. A p-value of less than 0.05 was considered statistically significant.

**Results:** A total of 25 studies involving 5,471 patients (78% males, average age 65.1 years) were identified. The average follow-up duration was approximately 27 months. The majority of patients had multi-vessel disease (68%), hypertension (66%), hypercholesterolemia (59%), and prior myocardial infarction (MI) (58%). The meta-analysis showed that the in-hospital occurrence of major adverse cardiac events (MACE), deaths, MI, and repeat revascularization (RR) after PCI were controlled at 4%, 2%, 2%, and 1%, respectively. The pooled estimates for long-term outcome were 40% MACE, 20% deaths, 4% MI, and 21% RR. There was no significant difference in mortality risk when PCI was compared with CABG (p=0.71).

**Conclusion:** PCI carries acceptable short- and long-term outcomes for CAD patients with LV systolic dysfunction.

## Introduction

Coronary artery disease (CAD) is the most common cause for left ventricular dysfunction (LVD). Patients with CAD and reduced LV systolic function present a challenge to current treatment modalities, although coronary artery bypass grafting (CABG) has traditionally been the preferred revascularization strategy for patients with reduced LV systolic function [1,2].

However, controversy persists in light of the published results that compare clinical outcomes after PCI or CABG for revascularization of coronary lesions in patients with LV systolic dysfunction [1,3,4]. In general, PCI for patients with decreased left ventricular ejection fraction may result in higher mortality rates in the short- and long-term [5-8], increased risk for nonfatal myocardial infarction (MI) [6], and a greater need for repeat revascularization (RR) [9]. On the other hand, the high perioperative mortality rate after CABG among patients with CAD and LV systolic dysfunction [10,11], suggests that PCI may be a better option. It is also noteworthy that revascularization with PCI for patients suffering from left main stem disease has shown similar safety and efficacy outcomes when compared with CABG at 1 year [12]. A number of studies



**Citation:** Abudukeremu N, Yu ZX, Yang YN, Chan SP, Ma YT, et al. (2018) An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction. J Cardiovasc Med Cardiol 5(4): 073-080.
DOI: http://doi.org/10.17352/2455-2976.000076

also demonstrated equivalent mid- and long-term outcomes between CABG and PCI for patients with CAD and LV systolic dysfunction [1,3,13-15].

While there are several studies confirming the efficacy of PCI for CAD patients with severe LV dysfunction, it is timely and relevant to conduct a comprehensive systematic review and meta-analysis to clarify this issue.

## Methods

### Search strategy

To identify relevant published studies concerning CAD patients with LV systolic dysfunction (LVEF ≤40%) who had undergone PCI (e.g., drug eluting stents, bare metal stents), a search of full manuscripts and abstracts with Medical Subject Headings (MeSH) terms was conducted on the electronic database PubMed, with no language or other methodological restrictions (authors, study design, location, and sample size). The search period was between January 1990 and September 2014. The following terms were searched: "poor left ventricle function," "percutaneous coronary intervention," "revascularization," "LV dysfunction" and "heart failure."

### Study selection criteria

Multi-center studies were eligible for inclusion if the long-term outcomes and all-cause mortality were reported for patients whose LVEF was ≤40. The full-text article of any identified study that appeared initially to meet the above-mentioned criteria was retrieved for closer examination by two reviewers. The final selection was based on consensus. In the event of a disagreement, a third reviewer was summoned to independently determine the article's inclusion in this study. The search strategy is described below:

#1Search poor left ventricle function

#2Search left ventricular dysfunction

#3Search low left ventricular ejection fraction

#4Search heart failure

#5 #1 OR#2 OR#3 OR#4

#6Search percutaneous coronary intervention

#7Search revascularization

#8Search stent implantation

#9Search coronary angioplasty

#10#6 OR#7 OR#8 OR#9

#11#6AND#10

### Data and study quality

The endpoints of concern included in-hospital and long-term (≥1 year) major adverse cardiac events (MACE), mortality, MI, and RR among CAD patients with LV systolic dysfunction (LVEF ≤40%) after PCI. MACE was a composite of all-cause death, MI, and RR. The baseline data, including age, gender, comorbid condition (i.e., hypertension, diabetes, hypercholesterolaemia, stable and unstable angina, prior myocardial infarction [Q wave, Non-Q wave], prior PCI, prior CABG, multi-vessel disease, smoking status, LVEF and follow-up duration) were tabulated by the reviewers. Each identified study was rated with a quality score based the Newcastle-Ottawa Scale [16].

### Statistical analysis

The meta-analysis were performed with the Review Manager (RevMan) software (version 5.3, Cochrane collaboration, http\:ims.cochrane.org/revman/download) and Stata MP Version 14 (Stata Corp., College Station, Texas). Pooled values of the event rates (MACE, mortality, MI, and RR) and 95% confidence intervals were calculated using the random-effects model in anticipation of study heterogeneity. Nevertheless, heterogeneity among the outcomes of enrolled studies was evaluated with Q, based on the chi-squared test. In addition, $I^2$ statistics (ranging from 0% to 100%) were generated to quantify the total variation, consistent with inter-study heterogeneity. A study was deemed to deviate from acceptable homogeneity if the $I^2$ statistic exceeded 50% and when the p-value of the Q-test was below 0.05. Lastly, funnel plots were generated to assess publication bias.

## Results

A total of 717 records were identified in the search process and 41 were thoroughly screened. Thirteen studies were excluded and 28 were assessed for eligibility. The search eventually ended with 25 observational studies (5,471 patients with PCI) satisfying selection criteria. There was no disagreement between reviewers in the selection process, as summarized in figure 1. The features of the included studies are presented in table 1 and patient characteristics in table 2. The quality of the selected studies was remarkable, with 22 (88%) assigned a maximum score of 9. All 25 studies reported long-term mortality (Table 3), of which 16 (64%) provided data on in-hospital mortality (Table 4) and 6 (24%) compared long-term mortality between PCI and CABG.

The pooled estimates of PCI patients' baseline characteristics

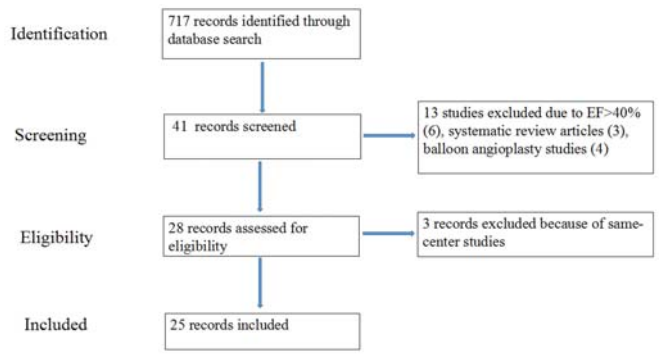


**Figure 1:** Summary of the search process.



**Citation:** Abudukeremu N, Yu ZX, Yang YN, Chan SP, Ma YT, et al. (2018) An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction. J Cardiovasc Med Cardiol 5(4): 073-080.
DOI: http://doi.org/10.17352/2455-2976.000076

**Table 1:** Selected Studies for Meta-Analysis.

| References (publication year) | Total (n=16,168) | Total PCI (n=5471) | Study period | Age-years (mean±SD) | Preprocedural EF (mean±SD)% | Follow-up duration (months) | Quality Score |
|---|---|---|---|---|---|---|---|
| Gioia et al. [13] (2007) | 230 | 128 | 2002/05—2005/05 | 69±10 | 28±6 | 15±9 | 9 |
| Aslam et al. [17] (2005) | 1187 | 149 | 2001/07—2003/06 | 60±10 | 30±10 | 24±10 | 7 |
| Cleland et al. [14] (2011) | 138 | 15 | 2002—2004 | 65(58-70) | 24 | 59 (33-63)[c] | 9 |
| Alidoosti et al. [18] (2008) | 293 | 293 | 2002/03—2004/03 | 56.14 | 35.8±5.4 | ≥12 | 9 |
| Sheiban et al. [19] (2007) | 78 | 78 | 2000/01—2001/12 | 64±7 | 25±2 | 25±6 | 9 |
| Jeevan et al. [20] (2013) | 1436 | 718 | 1995/01—2008/10 | 65.0 | <35 | 180 | 9 |
| Sedlis et al. [3] (2004) | 446 | 152 | 1995-2000 | NA | 28 | 36 | 7 |
| Gabriel et al. [21] (2012) | 5377 | 939 | 2000/01—2009/10 | 68.38±11.31 | 27.5±4.0 | 12 | 9 |
| Brigouri et al. [22] (2009) | 337 | 337 | 1993/04—2004/03 | 68±10 | 28±6[a] | 24 | 9 |
| Di Sciascio et al. [23] (2003) | 80 | 80 | NA | 62±9 | 40±9 | 30±14 | 8 |
| Biondi-Zoccai et al. [24](2011) | 975 | 46 | 2002/01—2006/12 | 74.2±9.2 | 25.1±2.9 | 18.2 | 9 |
| Benoit et al. [25] (2013) | 2430 | 202 | 2009—2011 | 60.3 | <40 | 36 | 9 |
| Divaka et al. [26] (2013) | 301 | 301 | 2005/09—2009/01 | 71±9.50 | 23.6±5.35 | 51 (41-58) | 8 |
| Mario Bollati et al. [27] (2010) | 197 | 21 | 2002/06—2006/10 | 69±10 | 32±7 | 25±17 | 9 |
| Ahn et al. [15] (2010) | 327 | 116 | 2003/04—2009/06 | NA | ≤35 | 36 | - |
| Cho et al. [28] (2009) | 197 | 197 | 2003/07—2007/07 | NA | <40 | 12 | - |
| Naidu et al. [29] (2009) | 754 | 754 | 2001—2006 | NA | 31.3 ; 31.6[b] | 12 | - |
| Marsico et al. [30] (2003) | 125 | 125 | 1999/01—2002/07 | 67±10.3 | 29.7±3 | 17 | 9 |
| Li et al. [31] (2002) | 74 | 74 | 1990/01—1997/12 | 54.7±8.5 | 29±8.6 | 29.1±22.9 | 9 |
| Bukachi et al. [32] (2003) | 41 | 41 | 1995/01—1997/12 | 63±10 | ≤35 | 12 | 9 |
| Keelan et al. [6] (2003) | 166 | 166 | 1997/07—1998/02 | NA | 32 | 12 | 9 |
| Lipinski et al. [33] (2005) | 238 | 171 | 1996/05—1999/03 | 58±12 | 38.4±10 | 60 | 9 |
| Toda et al. [1] (2002) | 117 | 48 | 1992—1997 | 67±11 | 23.7±4.5 | 38±14 | 9 |
| Nusca et al. [34] (2008) | 121 | 121 | 2003/04—2005/10 | 62±12 | 36±8 | 30 (18-51) | 7 |
| Holper et al. [35] (2006) | 503 | 199 | 1997/07—2002/03 | 68.1 | 33.5 | 12 | 8 |

BMS: bare metal stent; DES: drug-eluting stent; EF: ejection fraction; PCI percutaneous coronary intervention.
a. Brigouri et al. [13]: nonsurviving group: 27±5, surviving group: 29±6.
b. Naidu et al. [24]: EF-BMS: 31.3, DES: 31.6; in-hospital mortality-BMS: 2.7%, DES: 1.8%; long-term mortality-BMS: 10.2% (12 months), DES: 9.19% (12 months).
c. Median.

**Table 2:** Baseline Characteristics of Patients of the Selected Studies.

| Variables | Pooled estimate | 95% CI lower | upper |
|---|---|---|---|
| Age (years) | 65.12 | 62.69 | 67.55 |
| Male (%) | 78 | 74 | 82 |
| Hypertention (%) | 66 | 58 | 74 |
| Diabetes (%) | 34 | 30 | 39 |
| Hypercholesterolemia (%) | 59 | 51 | 66 |
| Smoker (%) | 42 | 34 | 50 |
| Prior MI (%) | 58 | 50 | 66 |
| Prior PCI (%) | 24 | 18 | 31 |
| Prior CABG (%) | 27 | 19 | 36 |
| Stable angina (%) | 27 | 16 | 37 |
| Unstable angina (%) | 36 | 28 | 44 |
| Multi-vessel disease (%) | 68 | 60 | 76 |
| LVEF (%) | 30.05 | 28.10 | 32.00 |
| Follow-up duration (months) | 26.91 | 20.41 | 33.41 |

CABG: coronary artery bypass surgery; 95% CI: 95% confidence interval; MI: myocardial infarction; PCI: percutaneous coronary intervention.

are shown in table 2. With an average follow-up period of about 27 months, the mean age of the 5,471 patients was 65 years. The majority (78%) were male subjects and 42% were smokers. The mean EF was 30% prior to PCI and diabetes was reported in 34% of patients. While 66% had hypertension, 59% had hypercholesterolemia and 58% had a history of prior MI. PCI for multi-vessel disease was performed in 68% of patients. Lastly, 24% had undergone PCI and 27% had undergone CABG.

The individual and pooled event rates of the long-term and in-hospital outcomes based on the meta-analysis is summarized in tables 3 and 4 and figures 2 ,3. All but one meta-analysis showed that there was a substantial amount of study heterogeneity according to the Q and $I^2$ statistics.

In terms of long-term MACE, 12 studies were gathered for meta-analysis and the pooled estimate was found to be 40% (95% CI 25%–55%; table 3 and figure 2A). The individual rates of MACE ranged from 8.9% to 81.8%. There was substantial publication bias as evidenced in the funnel plot (Figure 2A).



**Citation:** Abudukeremu N, Yu ZX, Yang YN, Chan SP, Ma YT, et al. (2018) An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction. J Cardiovasc Med Cardiol 5(4): 073-080.
DOI: http://doi.org/10.17352/2455-2976.000076

Table 3: Meta-analysis of long-term outcomes after PCI.

| References (publication year) | MACE (%) | Death (%) | MI (%) | RR (%) |
|---|---|---|---|---|
| Gioia et al. [13] (2007) | 14/128 (10.94) | 10/128 (7.81) | 1/128 (0.78) | 3/128 (2.34) |
| Aslam et al. [17] (2005) | 52/149 (34.90) | 17/149 (11.41) | 2/149 (1.34) | 33/149 (22.15) |
| Brigouri et al. [22] (2009) | 207/332 (62.35) | 83/332 (25.00) | 29/332 (8.73) | 95/332 (28.61) |
| Sheiban et al. [19] (2007) | 35/76 (46.05) | 9/76 (11.84) | 5/76 | 21/76 (27.63) |
| Cleland et al. [14] (2011) | NA* | 4/15 (26.67) | NA | NA |
| Alidoosti et al. [18] (2008) | 26/292 (8.90) | 5/292 (1.71) | 1/292 (0.34) | 20/292 (6.85) |
| Biondi-Zoccai et al. [24] (2011) | 18/43 (41.86) | 15/43 (34.89) | 1/43 (2.33) | 2/43 (4.65) |
| Ahn et al. [15] (2010) | NA | 16/116 (13.79) | NA | NA |
| Cho et al. [28] (2009) | NA | 17/190 (8.95) | NA | NA |
| Naidu et al. [29] (2009) | NA | 72/754 (9.55) | NA | NA |
| Benoit et al. [25] (2013) | NA | 34/199 (17.09) | 16/202 (7.92) | 42/202 (20.79) |
| Divaka et al. [26] (2013) | NA | 100/301 (33.22) | NA | NA |
| Gabriel et al. [21] (2012) | NA | 137/933 (14.68) | NA | NA |
| Jeevan et al. [20] (2013) | NA | 688/718 (95.82) | NA | NA |
| Mario Bollati et al. [27] (2010) | NA | 6/21 (28.57) | 0/21 (0.00) | 11/21 (52.38) |
| Sedlis et al. [3] (2004) | NA | 56/152 (36.84) | NA | NA |
| Marsico et al. [30] (2003) | 55/120 (45.83) | 12/120 (10.00) | 2/120 (1.67) | 41/120 (34.17) |
| Li et al. [31] (2002) | 12/66 (18.18) | 8/66 (12.12) | 1/66 (1.52) | 3/66 (4.55) |
| Bukachi et al. [32] (2003) | 17/37 (45.95) | 2/37 (5.41) | 4/37 (10.81) | 11/37 (29.73) |
| Di Sciascio et al. [23] (2003) | 17/80 (21.25) | 5/80 (6.25) | 4/80 (5.00) | 8/80 (10.00) |
| Keelan et al. [6] (2003) | NA | 16/161 (9.94) | NA | 29/161 (18.01) |
| Lipinski et al. [33] (2005) | 112/171 (65.50) | 32/171 (18.71) | 24/171 (14.04) | 56/171 (32.75) |
| Toda et al. [1] (2002) | 36/44 (81.82) | 16/44 (36.36) | 2/44 (4.55) | 18/44 (40.91) |
| Nusca et al. [34] (2008) | NA | 15/121 (12.40) | NA | NA |
| Holper et al. [35] (2006) | NA | 26/199 (13.07) | NA | 49/199 (24.62) |
| Pooled estimate (95% CI) | 40% (25%–55%) | 20% (4%–36%) | 4% (2%–6%) | 21% (15%–27%) |

PCI percutaneous coronary intervention; MI: myocardial infarction; MACE: major adverse cardiac events; RR: repeat revascularization; 95% CI 95% confidence interval
* NA: Not available

Table 4: Meta-analysis of in-hospital outcomes after PCI.

| References (publication year) | MACE (%) | Death (%) | MI (%) | RR (%) |
|---|---|---|---|---|
| Aslam et al. [17] (2005) | 0/149 (0) | 0/149 (0) | 0/149 (0) | 0/149 (0) |
| Brigouri et al. [22] (2009) | 14/337 (4.15) | 5/337 (1.48) | 9/337 (2.67) | 0/337 (0) |
| Sheiban et al. [19] (2007) | 4/78 (5.13) | 1/78 (1.28) | 3/78 (3.85) | 0/78 (0) |
| Alidoosti et al. [18] (2008) | NA* | 1/293 (0.34) | 1/293 (0.34) | NA |
| Biondi-Zoccai et al. [24](2011) | 4/46 (8.70) | 3/46 (6.52) | 0/46 (0) | 1/46 (2.17) |
| Naidu et al. [29] (2009) | NA | 16/754 (2.12) | NA | NA |
| Gabriel et al. [21] (2012) | 43/939 (4.58) | 30/939 (3.19) | NA | NA |
| Mario Bollati et al. [27] (2010) | NA | 2/21 (9.52) | 0/21 (0) | NA |
| Marsico et al. [30] (2003) | NA | 2/125 (1.60) | 2/125 (1.60) | NA |
| Li et al. [31] (2002) | 3/74 (4.05) | 1/74 (1.35) | 2/74 (2.70) | 0/74 (0) |
| Bukachi et al. [32] (2003) | 10/41 (24.39) | 1/41 (2.44) | 6/41 (14.63) | 3/41 (7.32) |
| Di Sciascio et al. [23] (2003) | 1/80 (1.25) | 0/80 (0) | 1/80 (1.25) | 0/80 (0) |
| Keelan et al. [6] (2003) | NA | 5/166 (3.01) | NA | 2/166 (1.20) |
| Toda et al. [1] (2002) | NA | 4/48 (8.33) | NA | NA |
| Nusca et al. [34] (2008) | 1/121 (0.83) | 0/121 (0) | 2/121 (1.65) | 1/121 (0.83) |
| Holper et al. [35] (2006) | 16/199 (8.04) | 9/199 (4.52) | 8/199 (4.02) | 2/199 (1.01) |
| Pooled estimate (95% CI) | 4% (2%–6%) | 2% (1%–3%) | 2% (1%–3%) | 1% (0%–2%) |

PCI percutaneous coronary intervention; MI: myocardial infarction; MACE: major adverse cardiac events; RR: repeat revascularization; 95% CI: 95% confidence interval
* NA: Not available



Citation: Abudukeremu N, Yu ZX, Yang YN, Chan SP, Ma YT, et al. (2018) An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction. J Cardiovasc Med Cardiol 5(4): 073-080.
DOI: http://doi.org/10.17352/2455-2976.000076

Similarly, the pooled long-term mortality rate based on all 25 selected studies was 20% (95% CI 4%–36%; table 3 and figure 2B) and publication bias could be a major concern (Figure 2B). Long-term rate of MI, based on 14 studies was substantially lower at 4% (95% CI 2%–6%; table 3 and figure 2C). This is not surprising as the majority of the studies reported a mortality rate below 5%. The pooled estimate for the rate of RR based on 16 studies was 21% (95% CI 15%–27%; table 3 and figure 2D). Note that with the exception of MI, all meta-analyses generated wide 95% CIs owing to the large variations in MACE, mortality, and RR rates reported by the individual studies (Table 3).

As shown in table 4, the in-hospital pooled estimate for MACE, mortality, MI, and RR rates were substantially lower compared with the long-term rates. This was expected given the shorter time frames. The pooled estimate in-hospital MACE based on 10 studies was 4% (95% CI 2%–6%; table 4 and Figure 3A). Remarkably, there was substantially less publication bias (Figure 2A) when compared with that of the long-term meta-analysis of MACE described above. The pooled in-hospital mortality rate based on 16 selected studies turned out to be a mere 2% (95% CI 1%–3%; table 4 and figure 3B) and publication bias was not severe (Figure 3B). In-hospital MI rate based on 12 studies was also 2% (95% CI 1%–3%; table 4 and figure 3C). The pooled estimate for the rate of RR based on 10 studies was 1% (95% CI 0%–2%; table 4 and figure 3D), given that half the studies reported no occurrence of RR. The

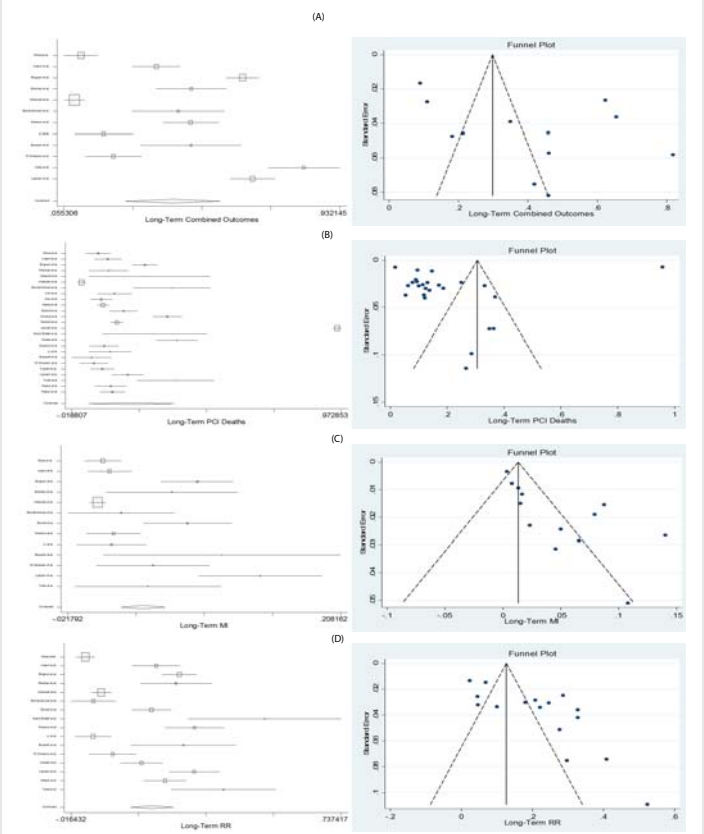


**Figure 2:** Long-term outcomes of PCI.
(A) Meta-analysis and funnel plot for long-term MACE. (B) Meta-analysis and funnel plot for long-term mortality. (C) Meta-analysis and funnel plot for long-term MI. (D) Meta-analysis and funnel plot for long-term RR.

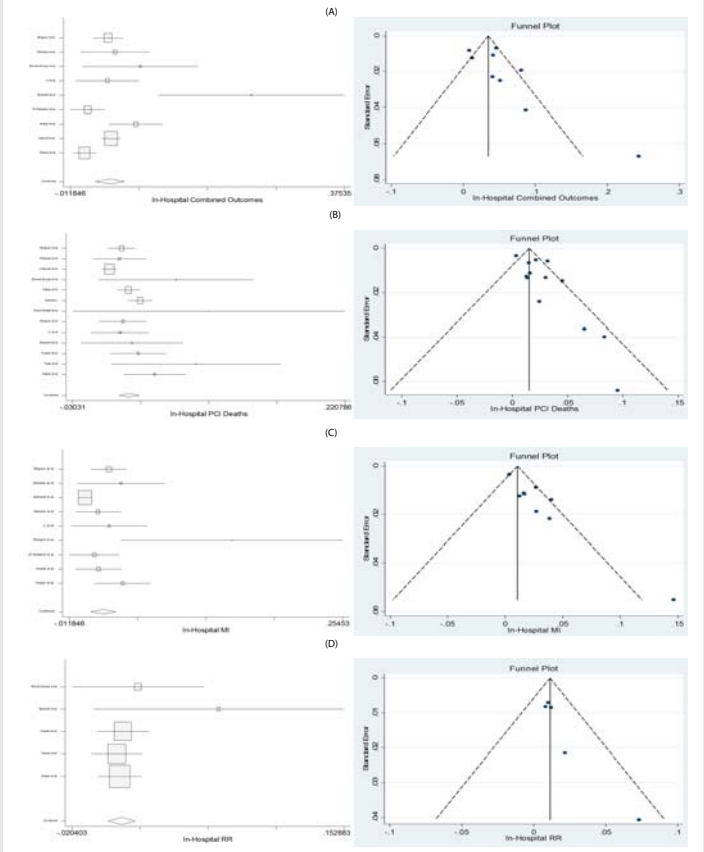


**Figure 3:** In-hospital outcomes of PCI.
(A) Meta-analysis and funnel plot for in-hospital MACE. (B) Meta-analysis and funnel plot for in-hospital mortality. (C) Meta-analysis and funnel plot for in-hospital MI. (D) Meta-analysis and funnel plot for in-hospital RR.

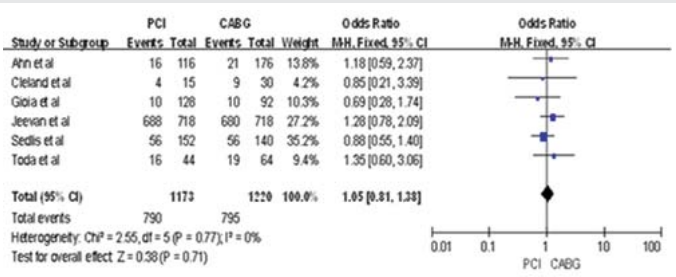


**Figure 4:** Meta-analysis of long-term mortality: percutaneous coronary intervention versus coronary artery bypass surgery.
Meta-analysis for long-term mortality of PCI vs. CABG.
CI, confidence interval; PCI, percutaneous coronary intervention; CABG, coronary artery bypass surgery.

random-effects model was applied throughout for pooling in-hospital outcomes. The results were more credible than that of the long-term outcomes, as the 95% CIs were narrow and publication bias was not a major concern.

Six studies were gathered to compare the long-term mortality of CABG and PCI. As shown in table 5 and figure 4, the pooled odds ratio was 1.05 (95% CI 0.81–1.38), calculated using the fixed-effects model as there was no significant evidence against study homogeneity ($Q_5$ 2.55; $I^2$ 0%). As such, the results suggest that the long-term mortality rate was not significantly higher for patients who had undergone PCI compared with those who underwent CABG.



**Citation:** Abudukeremu N, Yu ZX, Yang YN, Chan SP, Ma YT, et al. (2018) An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction. J Cardiovasc Med Cardiol 5(4): 073-080.
DOI: http://doi.org/10.17352/2455-2976.000076

## Discussion

The presented meta-analyses based on 25 selected observational studies have provided evidential support for PCI as an acceptable treatment for patients with severe LVD. Patients who underwent PCI benefitted from favorable short-term outcomes (2% mortality) and acceptable long-term outcomes (20% mortality) among CAD patients with severe LV systolic dysfunction (EF ≤40%), while the perioperative mortality rate after CABG among patients with CAD and left ventricular systolic dysfunction was 4%–5% [36,37].

The results were consistent with those of the individual selected studies, which reported near 0% in-hospital mortality rates after PCI. For example, Biondi-Zoccai [9] reported similar results (in-hospital MACE 5%, in-hospital mortality 2%, long-term MACE 33%, long-term mortality 11%) for 1,284 patients with an EF ≤50%. In the Heart Failure Revascularization Trial [14], none of the 15 patients who underwent PCI died in the hospital but the long-term mortality rate was 27%. In the SYNTAX trial [12], the 3-year MI rate and RR for three-vessel disease in the PCI group were 7.1% and 19.1%, respectively. In general, the results were also in agreement with a recently-published random-effects meta-analysis involving 4,766 patients with an LVEF ≤40% [11]. It reported a 1.8% in-hospital mortality rate and a 15.6% long-term mortality rate. However, our meta-analysis involved more patients who were followed up in a longer time frame, and with a wider range of high-risk patients characterized by a higher proportion of multi-vessel disease.

This study demonstrated no survival benefit for CABG compared with PCI in patients with severe LV systolic dysfunction (EF ≤40%). Several previous observational studies comparing CABG with PCI also reported similar results [1,3,13–15]. Resent large-scaled trials, which proceeded PCI with more advanced techniques and latest generation of stents,also showed similar survival rates in both groups [38,39]. However, after a long period of follow-up, Jeevan et al. found that CABG was associated with lower rates of RR and improved survival over PCI. In their trial,Lin Jiang and his team demonstrated that Compared with PCI, CABG has a lower risk of cardiac death, repeat revascularization, and MACCE [40]. Another meta-analysis comparing PCI (with drug-eluting stent) with CABG reported a higher mortality rate for the PCI group [41].

The completeness of revascularization was found to be an important predictor of long-term survival and functional status after CABG [42]. However, a randomized study demonstrated that incomplete revascularization by PCI in patients with multi-vessel disease and preserved LVEF did not affect in-hospital mortality and long-term survival, although freedom from angina and RR at 5 years were significantly lower than for patients randomized to CABG [43].

Another alternative treatment for patients with CAD and LV systolic dysfunction is the drug therapy alone. The HEART study performed in patients with myocardial viability and LVD demonstrated that a conservative strategy might not be inferior to an invasive strategy [14]. Another study comparing three treatment strategies for patients with triple-vessel coronary disease and LV systolic dysfunction, revealed that both CABG and PCI were associated with a lower risk of mortality compared with medical therapy alone [40]. A recent meta-analysis of observational data suggests that CABG may offer superior outcomes compared with PCI, with either modality being preferable to medical therapy alone [44].

Most of studies selected for this meta-analysis were conducted many years ago. Technical advances in the field of interventional cardiology with the introduction of new coronary stents and potent antiplatelet therapies have resulted in a marked increase in the complexity of procedures and expanded indications, even in patients considered to be high-risk such as those included in the present study. Newer-generation drug-eluting stents have been developed since the use of the pacilitaxel-eluting stent and have replaced the latter in current clinical practice owing to significant reduction in MI, stent thrombosis, and RR [45].

In actual practice, the reason for avoiding interventional treatments in diseased vessels might be explained by the occurrence of serious medical conditions (e.g., severe LV systolic dysfunction, cancer, old age, and unsuitable anatomic conditions such as chronic total occlusion or severe vessel complexity) [46]. Therefore, a careful evaluation should include appropriate procedural considerations for optimal revascularization strategies.

The meta-analyses concerning the long-term outcomes presented in this study were affected by severe publication bias (see Figure 2 a–d). One possible explanation could be the huge variations in MACE, mortality, MI, and RR. To a large extent, this could be explained by the vast differences in follow-up periods. As such, the results for in-hospital outcomes were more reliable than those reported for the long-term analyses.

The present study remains subject to the inherent caveats of a meta-analysis including publication bias;however, in-depth statistical analysis was carried out to account for these limitations. Given the fact that the present meta-analysis included patients over a long study period and from different organizations around the world, patient-level data were not available and the results were obtained from published pooled data.During the time period of the studies included in the present meta-analysis, there have been significant developments in PCI in terms of improved pharmacotherapy and device technology.This may improve the overall outcomes of CAD patients with LV systolic dysfunction.

### Study limitations

This study has several limitations. First, all the selected studies were observational by nature. As such, care must be taken in interpreting the strength of evidence generated from this meta-analysis. Second, the selected studies were carried out many years ago and not all studies used drug-eluting stents as the routine procedure. As a result, the reported outcomes might not accurately reflect current



**Citation:** Abudukeremu N, Yu ZX, Yang YN, Chan SP, Ma YT, et al. (2018) An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction. J Cardiovasc Med Cardiol 5(4): 073-080.
DOI: http://doi.org/10.17352/2455-2976.000076

practice. With the significant improvement in PCI technology and pharmacotherapy, it is recommended that large-scale randomized studies be conducted. Third, it was impossible to perform multiple meta-regression analyses to adjust for confounding factors, as no individual-level data were available at the time of analysis. It is acknowledged that the considered studies differed considerably in their study populations, the usage of stents, pharmacotherapy, and study duration. Fourth, it was also impossible to compare the results of PCI with medical therapy, which could also be considered appropriate in the absence of anginal symptoms or viability, but may be more appropriate according to specific patient or anatomic features [47].

## Conclusions

Our meta-analysis has shown that PCI has acceptable short- and long-term outcomes in CAD patients with LV systolic dysfunction. There was no significant difference in long-term mortality risk with PCI compared with CABG.

### Disclosure statement

The authors have no conflicts of interest to declare.

### Author contributions

Conceived and designed the experiments: NA. Performed the experiments: NA, SBF. Analyzed the data: NA, SBF. Contributed reagents, materials, or analysis tools: NA,SBF. Contributed to the writing of the manuscript: NA.

### Source of Funding

Supported by the Program for Innovative Research Team, University of Ministry of Education of China (grant No. IRT13094).

## References

1. Toda K, Mackenzie K, Mehra MR, DiCorte CJ, Davis JE, et al. (2002) Revascularization in severe ventricular dysfunction (15% <OR = LVEF<OR = 30%): a comparison of bypass grafting and percutaneous intervention. Ann Thorac Surg 74: 2082–2087. Link: https://goo.gl/iSsxSR

2. Appoo J, Norris C, Merali S, Graham MM, Koshal A, et al. (2004) Long-term outcome of isolated coronary artery bypass surgery in patients with severe left ventricular dysfunction. Circulation 110: II13eII17. Link: https://goo.gl/7Eeh1a

3. Sedlis SP, Ramanathan KB, Morrison DA, Sethi G, Sacks J, et al. (2004) Outcome of percutaneous coronary intervention versus coronary bypass grafting for patients with low left ventricular ejection fractions,unstable angina pectoris, and risk factors for adverse outcomes with bypass (the AWESOME Randomized Trial and Registry). Am J Cardiol 94: 118e120. Link: https://goo.gl/6Hof7r

4. Buszman P, Szkrobka I, Gruszka A, Parma R, Tendera Z, et al. (2007) Tendera M.Comparison of effectiveness of coronary artery bypass grafting versus percutaneous coronary intervention in patients with ischemic cardiomyopathy. Am J Cardiol 99: 36e41. Link: https://goo.gl/AzaWFN

5. Lindsay J Jr, Grasa G, Pinnow EE, Plude G, Pichard AD (1999) Procedural results of coronary angioplasty but not late mortality have improved in patients with depressed left ventricular function. Clin Cardiol 22: 533–536. Link: https://goo.gl/aouyQh

6. Keelan PC, Johnston JM, Koru-Sengul T, Detre KM, Williams DO, et al. (2003) Comparison of in-hospital and one-year outcomes in patients with left ventricular ejection fractions <or = 40%, 41% to 49%, and >or = 50%having percutaneous coronary revascularization. Am J Cardiol 91: 1168–1172. Link: https://goo.gl/Umgg6j

7. Wallace TW, Berger JS, Wang A, Velazquez EJ, Brown DL (2009) Impact of left ventricular dysfunction on hospital mortality among patients undergoing elective percutaneous coronary intervention. Am J Cardiol 103: 355–360. Link: https://goo.gl/EuY159

8. Goto M, Kohsaka S, Aoki N, Lee VV, Elayda MA, et al. (2008) Risk stratification after successful coronary revascularization. Cardiovasc Revasc Med 9: 132–139.

9. Biondi Zoccai G, Moretti C, Abbate A, Lipinski MJ, De Luca G, et al. (2007) Percutaneous coronary stenting in patients with left ventricular systolic dysfunction: a systematic review and meta-analysis. EuroIntervention 3: 409–415.

10. Velazquez EJ, Lee KL, Deja MA, Jain A, Sopko G, et al. (2011) Coronary-artery bypass surgery in patients with left ventricular dysfunction.N Engl J Med 364: 1607–1616. Link: https://goo.gl/Pc5H7L

11. Kunadian V, Pugh A, Zaman AG, Qiu W (2012) Percutaneous coronary intervention among patients with left ventricular systolic dysfunction: a review and meta-analysis of 19 clinical studies. Coron Artery Dis 23: 469-79. Link: https://goo.gl/Arb8w7

12. Morice MC, Serruys PW, Kappetein AP, Feldman TE, Stahle E, et al. (2010) Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery(SYNTAX) trial. Circulation 121: 2645–2653. Link: https://goo.gl/9a2gFG

13. Gioia G, Matthai W, Gillin K, Dralle J, Benassi A, et al. (2007) Revascularization in severe left ventricular dysfunction: outcome comparison of drug-eluting stent implantation versus coronary artery by-pass grafting.Catheter Cardiovasc Interv 70:26–33. Link: https://goo.gl/Gbi6tV

14. Cleland JG, Calvert M, Freemantle N, Arrow Y, Ball SG, et al. (2011) The Heart Failure Revascularisation Trial (HEART). Eur J Heart Fail 13: 227–233. Link: https://goo.gl/MCsrEg

15. Ahn JM, Park D, Park GM, Kim YG, Choi HO, et al. (2011) Comparison of drug-eluting stents vs. coronary artery bypass grafting for patients with multivessel disease ans severely compromised ventricular dysfunction. J Am Coll Cardiol 2010; 56:B76.Heart Fail 13: 773–784.

16. Wells G, Shea B, O'Connell D, Petersen J, Welch V, et al. (2012) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Ottawa: Ottawa Hospital Research Institute. Available: Link: https://goo.gl/DEVLUT

17. Aslam F, Blankenship JC (2005) Coronary artery stenting in patients with severe left ventricular dysfunction. J Invasive Cardiol 17: 656–658.

18. Alidoosti M, Salarifar M, Zeinali AM, Kassaian SE, Dehkordi MR, et al. (2008) Short- and long-term outcomes of percutaneous coronary intervention in patients with low, intermediate and high ejection fraction. Cardiovasc J Afr 19: 17–21. Link: https://goo.gl/3xqyqL

19. Sheiban I, Moretti C, Biondi Zoccai G, Rosano GM, Sciuto F, et al. (2007) Short- and long-term outcomes of percutaneous coronary interventions in patients with severe left ventricular dysfunction. EuroIntervention 3: 359–364. Link: https://goo.gl/Lmh3bA

20. Nagendran J, Norris CM, Graham MM, Ross DB, Macarthur RG, et al. (2013) APPROACH Investigators. Coronary revascularization for patients with severe left ventricular dysfunction. Ann Thorac Surg 96: 2038-2044. Link: https://goo.gl/3dBsFh



**Citation:** Abudukeremu N, Yu ZX, Yang YN, Chan SP, Ma YT, et al. (2018) An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction. J Cardiovasc Med Cardiol 5(4): 073-080.
DOI: http://doi.org/10.17352/2455-2976.000076

21. Sardi GL, Gaglia MA Jr, Maluenda G, Torguson R, Laynez-Carnicero A, et al. (2011) Outcome of percutaneous coronary intervention utilizing drug-eluting stents in patients with reduced left ventricular ejection fraction. Am J Cardiol. 109: 344-51. Link: https://goo.gl/AvBDQ4

22. Briguori C, Aranzulla TC, Airoldi F, Cosgrave J, Tavano D, et al. (2009) Stent implantation in patients with severe left ventricular systolic dysfunction. Int J Cardiol 135: 376–384. Link: https://goo.gl/RfFphq

23. Di Sciascio G, Patti G, D'Ambrosio A, Nusca A (2003) Coronary stenting in patients with depressed left ventricular function: acute and long-term results in a selected population. Catheter Cardiovasc Interv 59: 429–433. Link: https://goo.gl/3PxSCB

24. Biondi-Zoccai G, Sheiban I, Moretti C, Palmerini T, Marzocchi A, et al. (2011) Appraising the impact of left ventricular ejection fraction on outcomes of percutaneous drug-eluting stenting for unprotected left main disease: insights from a multicenter registry of 975 patients. Clin Res Cardiol 100: 403–411. Link: https://goo.gl/wcGXZs

25. Daneault B, Généreux P, Kirtane AJ, Witzenbichler B, Guagliumi G, et al. (2012) Comparison of Three-year outcomes after primary percutaneous coronary intervention in patients with left ventricular ejection fraction <40% versus ≥40% (from the HORIZONS-AMI trial). Am J Cardiol 111: 12-20. Link: https://goo.gl/Dc6vus

26. Perera D, Stables R, Clayton T, De Silva K, Lumley M, et al. (2013) BCIS-1 Investigators. Long-term mortality data from the balloon pump-assisted coronary intervention study (BCIS-1): a randomized, controlled trial of elective balloon counterpulsation during high-risk percutaneous coronary intervention. Circulation 127: 207-12. Link: https://goo.gl/nsL1SU

27. Bollati M, Gerasimou A, Sillano D, Biondi-Zoccai G, Garrone P, et al. (2010) Results of percutaneous drug-eluting stent implantation for unprotected left main coronary disease according to left ventricular systolic function. Catheter Cardiovasc Interv 75: 586-93. Link: https://goo.gl/T7kVor

28. Cho Y-K, Shin H-W, Kinm H-T, Kim I-C, Park H-S, et al. (2009) Percutaeous coronary intervention in patients with severe left ventricular dysfunction. Am J Cardiol 103: 55.

29. Naidu SS, Faith S, Vlachos H, Holper E, Wilensky RL, et al. (2009) Safety of drug eluting stents in patients with severe left ventricular dysfunction: one year data from the NHLBI dynamic registry. J Am Coll Cardiol 53: A76.

30. Marsico F, Morenghi E, Parenti DZ, Milone F, Maiello L, et al. (2003) Immediate and late results of coronary angioplasty in patients with severe left ventricular dysfunction. Ital Heart J 4: 838–842.

31. Li C, Jia G, Guo W, Li W (2002) Stent supported coronary angioplasty in patients with severe ventricular dysfunction. Chin Med J (Engl) 115: 355–358. Link: https://goo.gl/nB5cLQ

32. Bukachi F, Clague JR, Waldenstrom A, Kazzam E, Henein MY (2003) Clinical outcome of coronary angioplasty in patients with ischaemic cardiomyopathy. Int J Cardiol 88: 167–174.

33. Lipinski MJ, Martin RE, Cowley MJ, Goudreau E, Malloy WN, et al. (2005) Improved survival for stenting vs. balloon angioplasty for the treatment of coronary artery disease in patients with ischemic left ventricular dysfunction. Catheter Cardiovasc Interv 66: 547–553. Link: https://goo.gl/w2AnrA

34. Nusca A, Lipinski MJ, Varma A, Appleton DL, Goudreau E, et al. (2008) Safety of drug-eluting stents in patients with left ventricular dysfunction undergoing percutaneous coronary intervention. Am J Cardiol 102: 679-82.

35. Holper EM, Blair J, Selzer F, Detre KM, Jacobs AK, et al. (2006) Percutaneous Transluminal Coronary Angioplasty Registry and Dynamic Registry Investigators. The impact of ejection fraction on outcomes after percutaneous coronary intervention in patients with congestive heart failure: an analysis of the National Heart, Lung, and Blood Institute Percutaneous Transluminal Coronary Angioplasty Registry and Dynamic Registry. Am Heart J 151: 69-75. Link: https://goo.gl/oj65wy

36. Velazquez EJ, Lee KL, Deja MA, Jain A, Sopko G, et al. (2011) Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med 364: 1607–1616. Link: https://goo.gl/Azf5Zu

37. Kunadian V, Zaman A, Qiu W (2011) Revascularization among patients with severe left ventricular dysfunction: a meta-analysis of observational studies. Eur J Heart Fail 13: 773–784. Link: https://goo.gl/wWFipQ

38. Hawranek M, Zembala MO, Gasior M (2018) Comparison of coronary artery bypass grafting and percutaneous coronary intervention in patients with heart failure with reduced ejection fraction and multivessel coronary artery disease. Oncotarget 9: 21201-21210. Link: https://goo.gl/eXBpPe

39. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Hannan EL (2016) Revascularization in Patients With Multivessel Coronary Artery Disease and Severe Left Ventricular Systolic Dysfunction: Everolimus-Eluting Stents Versus Coronary Artery Bypass Graft Surgery. Circulation 133: 2132-2140. Link: https://goo.gl/nwJVCf

40. Jiang L, Xu L, Song L, Gao Z, Tian J, et al. (2018) Comparison of three treatment strategies for patients with triple-vessel coronary disease and left ventricular dysfunction. J Interv Cardiol 31: 310-318. Link: https://goo.gl/yKqxT7

41. Cui K, Zhang D, Lyu S, Song X, Yuan F, et al. (2018) Meta-Analysis Comparing Percutaneous Coronary Revascularization Using Drug-Eluting Stent Versus Coronary Artery Bypass Grafting in Patients With Left Ventricular Systolic Dysfunction. Am J Cardiol S0002-9149(18)31628-X. Link: https://goo.gl/cPRvtW

42. Luciani GB, Montalbano G, Casali G, Mazzucco A (2000) Predicting long-term functional results after myocardial revascularization in ischemic cardiomyopathy. J Thorac Cardiovasc Surg 120: 478–89. Link: https://goo.gl/UA9uJe

43. Bourassa MG, Kip KE, Jacobs AK (1999) Is a strategy of intended incomplete percutaneous transluminal coronary angioplasty revascularization acceptable in nondiabetic patients who are candidates for coronary artery bypass graft surgery? J Am Coll Cardiol 33: 1627–36. Link: https://goo.gl/mP9gvq

44. Wolff G, Dimitroulis D, Andreotti F (2017) Survival benefits of invasive versus conservative strategies in heart failure in patients with reduced ejection fraction and coronary artery disease: a meta-analysis. Circ Heart Fail 10: e003255. Link: https://goo.gl/q63JLL

45. Stefanini GG, Holmes DR Jr (2013) Drug-eluting coronary-artery stents. N Engl J Med 368: 254–265. Link: https://goo.gl/aeq24A

46. Hannan EL, Wu C, Walford G, Holmes DR, Jones RH, et al. (2009) Incomplete revascularization in the era of drug-eluting stents:impact on adverse outcomes. JACC Cardiovasc Interv 2: 17-25. Link: https://goo.gl/PezLM6

47. Hueb W, Lopes NH, Gersh BJ, Soares P, Machado LA, et al. (2007) Five-year follow-up of the Medicine, Angioplasty,or Surgery Study (MASS II): a randomized controlled clinical trial of 3 therapeutic strategies for multivessel coronary artery disease. Circulation 115: 1082-1089. Link: https://goo.gl/dNeHWA






**Citation:** Abudukeremu N, Yu ZX, Yang YN, Chan SP, Ma YT, et al. (2018) An Updated Systematic Review and Meta-analysis of the Short- and Long-term Outcomes of Percutaneous Coronary Intervention for Patients with Severe Left Ventricular Systolic Dysfunction. J Cardiovasc Med Cardiol 5(4): 073-080.
DOI: http://doi.org/10.17352/2455-2976.000076