Percutaneous Coronary Intervention Versus Coronary Artery Bypass Graft among Patients with Coronary Artery Disease and Left Ventricular Systolic Dysfunction: A Meta-Analysis

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Abstract

Background
There is an absence of randomized controlled trials (RCTs) comparing types of revascularization in patients with coronary artery disease (CAD) in the presence of left ventricular systolic dysfunction (LVSD). Our aim was to compare the outcomes of percutaneous coronary intervention (PCI) versus coronary artery graft bypass (CABG) among patients with CAD and LVSD.

Methods
The PubMed online database (from 1976 to November, 2014) and EMbase (from 1974 to November, 2014) were searched. Studies comparing the outcomes of PCI versus CABG among patients with left ventricular dysfunction (ejection fraction <50%) were included. Random- and fixed-effect models were used depending on between-study heterogeneity.

Results
Due to absence of RCTs on this topic, twelve observational studies including 5,494 patients were included. PCI was associated with a lower risk of short-term mortality (Risk ratio [RR], 0.51, 95% confidence interval [CI], 0.26-1.00) but a higher risk of long-term mortality (RR, 1.21, 95%CI, 1.05-1.40) and repeat revascularization (RR, 4.18, 95%CI, 1.92-9.12) compared with CABG. No significant difference in composite outcomes (RR, 1.26, 95%CI), myocardial infarction (RR, 0.63, 95% CI, 0.17-2.41) and cerebrovascular accident ((RR, 0.61, 95%CI, 0.18-2.01) was observed between PCI vs. CABG.

Conclusions
Due to the absence of any RCTs on this topic, a meta-analysis of observational studies was performed. It suggested PCI was associated with a better short-term prognosis but an increased risk of long-term mortality compared with CABG. Further well-designed RCT’s are needed to verify this conclusion.

Keywords: Percutaneous coronary intervention; Coronary artery bypass graft; Left ventricular systolic dysfunction; Meta-analysis


Introduction
Coronary artery disease (CAD) remains the most common cause of left ventricular systolic dysfunction. Since the first coronary artery bypass graft (CABG) surgery was introduced in 1964, surgeons have attempted to perform CABG in patients with CAD complicated by left ventricular systolic dysfunction (LVSD). In early observational studies, revascularization in those selected patients seemed to be superior to conventional medical therapy1. With improvements in drug eluting stents (DES), especially new-generation DES (n-DES), and adjuvant pharmacotherapy, percutaneous coronary intervention (PCI) was found to be non-inferior to CABG in selected patients2. The recently published
European guidelines recommended PCI to be I class in three-vessel disease or left main disease with SYNTAX scores less than 22. However, revascularization for CAD with LVSD was mostly implemented via CABG in the early observational and randomized controlled trials (RCT)\(^1\)\(^\text{,}^4\). Then the question raises: Does PCI produce similar effects to CABG in these patients? In this meta-analysis, our aim was to compare PCI versus CABG among patients with CAD and LVSD.

**Methods**

**Data search**

The PubMed online database (from 1976 to November, 2014) and EMBase (from 1974 to November, 2014) were searched using the terms “cardiac failure” or “heart failure” or “left ventricular dysfunction”, and “revascularization” or “coronary artery bypass graft” or “percutaneous coronary intervention” or “percutaneous transluminal angioplasty” or “percutaneous transluminal angioplasty balloon” or “percutaneous transluminal coronary angioplasty”. References of relevant studies and review articles were checked for additional studies.

**Study Selection**

Two reviewers screened potential articles according to pre-specified inclusion and exclusion criteria. The definition of LVEF for distinguishing the HF with reduced EF and HF with preserved EF varied widely. To include as many studies as possible, we chose EF≤50% as an inclusion criterion for LVSD in the primary analysis. Thus, the inclusion criteria were that the study compared PCI versus CABG among patients with left ventricular systolic dysfunction (EF ≤50%). The exclusion criteria were reviews, meta-analysis, editorials and small sample studies (n<50).

**Data Extraction**

Two authors extracted data independently. A standardized data extraction form was used to collect eligible studies on the publication year, country, type of report, follow-up duration, the total number of patients, participant characteristics and main outcomes. Baseline characteristics including age, sex, hypertension, diabetes, left ventricular ejection fraction (EF), prior PCI, prior CABG, angiographic characteristics and complete revascularizations was extracted.

**Quality Assessment**

The quality of non-randomized studies was assessed using the Newcastle–Ottawa quality scale\(^5\), which mainly included three broad perspectives: the selection of the study groups, the comparability of groups and the outcome collected.

**Study Outcome Definition**

The primary outcome was all-cause mortality. The secondary outcome was myocardial infarction (MI), repeat revascularization (PCI or CABG), cerebrovascular accident (CVA) and composite outcome of death, MI, CVA and repeat revascularization. In-hospital or 30-day events was regarded as short-term outcome while long-term events was defined from 1 year to 5 year. To reduce bias to the maximal extent, we used the results with adjustment or propensity score matched groups to obtain the synthesized outcome.

**Data Synthesis**

The relative ratios (RRs) were pooled using the fixed effects model or DerSimonian and Laird random effects model in

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**Publication Bias and Sensitivity analysis**

Potential publication bias was examined for by constructing a funnel plot and the Egger’s test. If an asymmetrical funnel plot was observed, the contour enhanced funnel plots combined with the trim and fill method was performed to distinguish asymmetry due to publication bias from other factors.

Sensitivity analysis was conducted by repeating meta-analysis according to different pre-specified decision nodes including randomized effect model, peer-review articles and adjusted results. Furthermore, according to the recent ACC/AHA guidelines for chronic heart failure, in which EF≤40% was used as the diagnostic criterion for HF with reduced EF, we reran the meta-analysis in studies with the cut-off of EF ≤40%.

**Results**

**Literature Search and Study Selection**

Initially 8202 records in Pubmed and 7008 in Embase were obtained (Figure 1). Due to the lack of RCTs addressing this question, a total of 10 non-randomized studies\(^2\)\(^\text{–}^\text{,}^\text{16}\) and 4 conference abstracts\(^1\)\(^\text{–}^\text{,}^\text{16}\) were eligible for our inclusion criteria. But two studies (one was peer-review article\(^1\), the other abstract\(^1\)) had the same population, we chose the peer-reviewed article and discarded the other conference abstract. One abstract\(^16\) had no available results to measure. Hence, we included 12 studies\(^7\)\(^\text{–}^\text{,}^\text{18}\) recruiting 5494 individuals for this meta-analysis.

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**Figure 1. Flow diagram of study selection.**

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**The Study and Patients Characteristics**

The characteristics and quality assessment of the included studies were shown in Table 1. Table 2 showed the pooled baseline characteristics based on the methods of
revascularization. Most of most of studies did not report the data of myocardial viability except Saakyan et al and Cleland et al. Patients in PCI group were more likely to have experienced previous CABG. More complex vessel disease and complete revascularization were observed in CABG group. There was no significant difference in preoperative EF and history of disease between groups.

### Primary Outcome

Twelve studies reported long-term all-cause mortality in HF patients undergoing PCI versus CABG while five studies described short-term mortality. For long-term mortality, PCI was associated with significantly higher risk of death (pooled Relative ratio [RR], 1.21, 95% confidence interval [CI], 1.05-1.40; Figure 2) compared with CABG. In contrast there was lower short-term mortality in PCI (pooled RR, 0.51, 95% CI, 0.26-1.00; Figure 2). There was no evident heterogeneity between studies (I²=0%, 0.3%).

### Composite outcomes

The incidence of composite outcome (death, MI, CVA and repeat revascularization) was evaluated in four studies. No significant difference was observed between the two procedures (RR, 1.26, 95% CI, 0.92-1.73; Table 3). Moderate heterogeneity was observed between studies (I²=45.8%).

### Myocardial infarction

Three studies contributed to the analysis of short-term MI while three to long-term MI. Patients receiving either PCI or CABG showed non-significant difference in both short and long-term MI (pooled RR, 0.63, 95% CI, 0.17-2.41; RR, 0.83, 95% CI, 0.22-3.13; Table 3). I² indicated low heterogeneity in the pooled analysis (I²=12.4, 0%).

### Repeat revascularization

Five studies reported the outcome of the long-term repeat revascularization. There was significantly higher incidence of repeat revascularization in PCI compared with CABG (pooled RR, 4.18, 95%CI, 1.92-9.12; Table 3). I² indicated low heterogeneity in the pooled analysis (I²=17.8%).

### Cerebrovascular accident

Short-term and long-term CVA was analyzed in three and two studies respectively. There was a non-significant tendency towards a lower risk of CVA event in PCI group (pooled RR, 0.36, 95% CI, 0.10-1.32; 0.61, 0.18-2.01; Table 3). I² indicated low heterogeneity in the pooled analysis (I²=32.2%, 8.1%).

### Sensitivity analysis and Publication bias

We conducted a sensitivity analysis for the primary outcome according to pre-specified decision nodes including randomized
effect model, peer-review articles, defined EF less than 40% or adjusted results. The sensitivity analysis showed the results were robust (Table 4). Due to only the long-term mortality being evaluated in more than 10 studies, we conducted funnel plots to probe into the potential publication bias regarding the endpoint. The asymmetry funnel plots were observed by both visual inspection and Egger’s test (P= 0.012). And then the contour enhanced funnel plot in conjunction with trim-and-fill method displayed most “missing” studies would be expected in the non-significant area (Figure 4), which added credence to the possibility that the asymmetry was due to publication bias21.

Discussion
To the best of our knowledge, this is the most comprehensive meta-analysis focusing on the type of revascularization for CAD complicated by LVSD. Our meta-analysis has demonstrated that CABG contributed to significantly lower long term all-cause mortality compared to PCI in patients with CAD and LVSD. Furthermore, PCI was associated with a higher rate of repeat revascularization. Interestingly, there was lower early death in PCI group, and CVA events occurred more frequently in GABG group. A potential for publication bias was observed in the contour enhanced funnel plot.

Several studies explored the optimal strategy of revascularization for CAD patients with depressed LV function. A meta-analysis of observational studies suggested that revascularization brought benefit to those patients with image-examined viable but dysfunctional myocardium2, whereas three following RCTs (STICH, Table 2

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>PCI</th>
<th>CABG</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>64.5 (11.1) (n=274)</td>
<td>62.7 (10.9) (n=266)</td>
<td>0.06</td>
</tr>
<tr>
<td>Male</td>
<td>973/1233 (78.9)</td>
<td>1005/1225 (82.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>753/1166 (64.6)</td>
<td>709/1125 (63.0)</td>
<td>0.44</td>
</tr>
<tr>
<td>Diabetes</td>
<td>452/1257 (36.0)</td>
<td>462/1245(37.1)</td>
<td>0.55</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>607/1042 (58.3)</td>
<td>592/1005 (58.9)</td>
<td>0.56</td>
</tr>
<tr>
<td>Smoking</td>
<td>324/1005 (32.2)</td>
<td>350/1033 (33.9)</td>
<td>0.43</td>
</tr>
<tr>
<td>Prior CVA</td>
<td>98/983 (10.0)</td>
<td>96/979 (9.8)</td>
<td>0.90</td>
</tr>
<tr>
<td>Prior MI</td>
<td>668/1085 (61.6)</td>
<td>647/1056 (61.3)</td>
<td>0.89</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>181/1159 (15.6)</td>
<td>154/1140 (13.5)</td>
<td>0.12</td>
</tr>
<tr>
<td>Prior CABG</td>
<td>154/1159 (13.3)</td>
<td>85/1140 (7.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LVEF</td>
<td>28.5 (6.0) (n=274)</td>
<td>28.3 (6.7) (n=264)</td>
<td>0.76</td>
</tr>
<tr>
<td>Three vessel disease</td>
<td>740/1138 (65.0)</td>
<td>775/1133 (68.4)</td>
<td>0.09</td>
</tr>
<tr>
<td>Left main disease</td>
<td>132/949 (13.9)</td>
<td>265/1129 (23.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Complete revascularization</td>
<td>278/437 (63.6)</td>
<td>401/468 (85.7)</td>
<td>&lt;0.004</td>
</tr>
</tbody>
</table>

Table 2. Pooled Characteristics of Patients
Data are presented as number (percentage) or mean (standard difference). PCI, indicates percutaneous coronary artery disease; CABG, coronary artery bypass graft; LVEF, left ventricular ejection fraction; CVA, cerebrovascular accident; MI, myocardial infarction;
Table 3. Summary of pooled short-term and long-term outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Heterogeneity</th>
<th>Meta-analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>I², %</td>
<td>Effect</td>
</tr>
<tr>
<td>Short-term outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>5</td>
<td>0.3</td>
<td>0.51</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3</td>
<td>12.4</td>
<td>0.63</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>3</td>
<td>32.2</td>
<td>0.36</td>
</tr>
<tr>
<td>Long-term outcome</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>12</td>
<td>12.4</td>
<td>2.51</td>
</tr>
<tr>
<td>Composite outcomes</td>
<td>4</td>
<td>45.8</td>
<td>1.26</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>3</td>
<td>0</td>
<td>0.83</td>
</tr>
<tr>
<td>Repeat revascularization</td>
<td>5</td>
<td>17.8</td>
<td>4.18</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>2</td>
<td>8.1</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Table 4. Sensitivity Analysis of long-term mortality between PCI vs. CABG

<table>
<thead>
<tr>
<th>Decision nodes</th>
<th>Heterogeneity</th>
<th>Meta-analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total study (Fixed effect model)</td>
<td>0</td>
<td>0.513</td>
</tr>
<tr>
<td>No abstract included</td>
<td>13.4</td>
<td>0.323</td>
</tr>
<tr>
<td>LVEF&lt;40%</td>
<td>1.9</td>
<td>0.423</td>
</tr>
<tr>
<td>Only adjusted results included</td>
<td>0</td>
<td>0.748</td>
</tr>
<tr>
<td>Randomized effect model</td>
<td>0</td>
<td>0.513</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; LVEF, left ventricular ejection fraction

More complex vessel disease is seen in the patients with CAD and LVSD. In STICH, patients with three vessel disease or proximal left anterior descending stenosis accounted for 60% and 68%, respectively. Our pooled baseline characteristics also showed the proportion of three vessel disease was more than 60%. Complete revascularization was significantly more common in patients undergoing CABG than PCI (85.7% vs 63.6%). Garcia et al showed that complete revascularization was associated with lower long-term mortality and repeat revascularization in patients with multi-vessel CAD. This may explain why lower long-term mortality and repeat revascularization was observed in HF patients undergoing CABG when compared with PCI. There are several reasons for the different rates of complete revascularization between PCI and CABG: first, chronic total occlusion occurs frequently in these patients, which limits the success rate of CR using PCI.

This may be the most important reason for more incomplete revascularization rate in the PCI group; secondly sicker patients with significant comorbidities are more likely to undergo IR via PCI. This is particularly true in the case of observational studies, where the treatment strategies cannot be controlled by investigators. Considering that potential selection bias may be introduced, we did a sensitivity analysis from data of multivariable adjustment, which still supported the superiority of CABG for long-term mortality. Owing to most of the included studies using early-generation DES, among these patients less is known about the effect of n-DES, which has been reported to address the concerns of very late stent thrombosis during long-term follow-up. Moreover, a recent network meta-analysis suggested that only CABG and n-DES were likely to correlate with a survival benefit compared with strategy of initial medical treatment. Hence further trials should be performed to confirm this in the setting of HF.

Notably, PCI was associated with a significantly lower short-term mortality. This finding is in line with the recent study in which Yanai et al suggested that PCI was associated with lower risk of mortality, bleeding, and acute kidney injury. Patients with CAD and LVSD are more vulnerable to complications of general anesthesia, cardiopulmonary bypass, median sternotomy, and long bed stays, which may contribute to the poorer short-term prognosis in the CABG group. Edwards et al suggested that CABG conferred a higher peri-procedural stroke risk. Moreover, Gioia et al also reported that half of hard events in CABG group occurred in the perioperative period, and the mortality advantage of PCI lasted up to 6 months. Meanwhile, most of patients with CAD and LVSD were elderly. Ben-Gal et al demonstrated that Octogenarian CABG patients experienced a higher risk of early mortality compared with PCI (9.9% versus 2.5%, P = .01). Our results showed a significantly lower short-term mortality with PCI and better long-term outcomes of CABG in those patients with CAD and LVSD. The question is if we can manage selected patients, especially those with complex vessel disease, by combining the advantages of the two procedures — the hybrid coronary revascularization (HCR), which is increasingly popular in the era of emphasis on the Heart Team. This type of procedure offers less surgical trauma than conventional CABG but greater complete revascularization than PCI. The
in-hospital MACE rates was considerably lower in HCR group than CABG\textsuperscript{30}. Several studies have demonstrated HCR provided advanced superior perioperative and late outcomes in patients with high surgical risk\textsuperscript{11-33}. Even so, some practical and logistical issues in the HCR remained to be solved. Further studies are needed to examine its feasibility in this condition.

Limitations
Our meta-analysis has several limitations. (1) Owing to absence of RCTs on this topic, we only included non-randomized studies. In spite of low heterogeneity within the studies and confirmation with the adjusted and the sensitivity analyses that displayed the robustness of the results, selection bias inevitably existed in the analysis. Caution should be taken to interpret the results. (2) The contour enhanced funnel plot combined with the trim and fill method implied publication bias mainly contributed to the asymmetry funnel. However adjusted results by trim and fill analysis was similar to the crude RR. Egger tests for funnel plot asymmetry are unsuitable for the meta-analysis of other outcomes that included less than ten studies. (3) Events were defined from 1 year to 5 year in order to incorporate more studies. (4) Significant improvements in both DES and surgery have emerged over time, but we cannot carry out a subgroup for the comparison between those new and old techniques, so we cannot know the precise comparison of effects in the modern era of new equipment and surgical techniques.

Conclusions
In selected patients with CAD in presence of LVSD requiring revascularization, there is weak evidence from cohort studies that CABG might be superior to PCI for long-term prognosis. However, PCI seems to contribute to a better short-term prognosis compared with CABG. However, due to significant publication bias and non-randomized studies in this meta-analysis, further randomized trials are needed to verify the conclusion.

Declarations of Interest
The authors declare no conflicts of interest.

Acknowledgements
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References


[34] Shewan LG, Coats AJJS, Henein M. Requirements for ethical publishing in biomedical journals. International Cardiovascular Forum Journal 2015;2:2 DOI: 10.17987/icfj.v2i1.4