



# Percutaneous coronary intervention versus coronary artery bypass grafting among patients with left ventricular systolic dysfunction: a systematic review and meta-analysis

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**Background:** Current guidelines have shown the superiority of coronary artery bypass grafting (CABG) over medical therapy. However, there is a paucity of data evaluating the optimal revascularization strategy in patients with ischemic left ventricular systolic dysfunction (LVSD).

**Objective:** The authors aimed to evaluate the clinical outcomes of postpercutaneous coronary intervention (PCI) and CABG among patients with LVSD.

**Methods:** The authors performed a systematic literature search using the PubMed, Embase, Scopus, and the Cochrane Libraries for relevant articles from inception until 30 November 2022. Outcomes were reported as pooled odds ratio (OR), and their corresponding 95% CI using STATA (version 17.0, StataCorp).

**Results:** A total of 10 studies with 13 324 patients were included in the analysis. The mean age of patients in PCI was 65.3 years, and 64.1 years in the CABG group. The most common comorbidities included: HTN (80 vs. 78%) and DM (49.2 vs. 49%). The mean follow-up duration was 3.75 years. Compared with CABG, the PCI group had higher odds of all-cause mortality (OR 1.15, 95% CI 1.01–1.31,  $P=0.03$ ), repeat revascularization (OR 3.57, 95% CI 2.56–4.97,  $P<0.001$ ), MI (OR 1.92, 95% CI 1.01–3.86,  $P=0.048$ ) while the incidence of cardiovascular mortality (OR 1.23, 95% CI 0.98–1.55,  $P=0.07$ ), stroke (OR 0.73 95% CI: 0.51–1.04,  $P=0.08$ ), major adverse cardiovascular and cerebrovascular events (OR 1.36, 95% CI 0.99–1.87,  $P=0.06$ ), and ventricular tachycardia (OR 0.79, 95% CI 0.22–2.86,  $P=0.72$ ) was comparable between both the procedures.

**Conclusion:** The results of this meta-analysis suggest that CABG is superior to PCI for patients with LVSD. CABG was associated with a lower risk of all-cause mortality, repeat revascularization, and incidence of myocardial infarction compared with PCI in patients with LVSD.

**Keywords:** acute coronary syndrome, cardiomyopathy, coronary artery bypass grafting, ischemia, percutaneous coronary interventions, revascularization

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Annals of Medicine & Surgery (2023) 85:2849–2857

Received 13 January 2023; Accepted 31 March 2023

Supplemental Digital Content is available for this article. Direct URL citations are provided in the HTML and PDF versions of this article on the journal's website, [www.annalsjournal.com](http://www.annalsjournal.com).

Published online 17 April 2023

<http://dx.doi.org/10.1097/MS9.0000000000000634>

## Introduction

The worldwide prevalence and impact of ischemic heart disease on heart failure is evolving as a result of an aging population, increasingly effective treatment of acute coronary syndrome, and consequently, less extensive myocardial fibrosis<sup>[1]</sup>. Previously, coronary artery bypass graft (CABG), percutaneous coronary intervention (PCI), and medical management were the primary revascularization strategies in patients with ischemic left ventricular systolic dysfunction (LVSD). The STITCH (Surgical Treatment for Ischemic Heart Failure) trial demonstrated a 10-year survival benefit of CABG over medical management alone in these patients<sup>[2]</sup>. However, there was insufficient evidence to support PCI over CABG. Furthermore, earlier PCI trials in LVSD employed bare metal stents compared to the modern drug-eluting stents<sup>[3,4]</sup>. Thus, optimal revascularization strategies for patients with LVSD are primarily based on randomized data comparing CABG to medical therapy<sup>[5–10]</sup>.

The 2018 European Society of Cardiology gives a class I recommendation for CABG and class IIa for PCI patients with LVSD<sup>[11]</sup>. The 2021 guidelines from the American College of Cardiology/ American Heart Association/SCAI give a class I recommendation for CABG in patients with LVSD with an ejection fraction (EF) less than 35% and a class IIa recommendation for an EF 35–50%, but with no provision for PCI<sup>[12]</sup>. Although some recent studies have shown worse survival outcomes with PCI than with CABG, the data has been inconsistent, and further clarity regarding optimal management strategies is required<sup>[3,13–27]</sup>. This study aimed to perform a meta-analysis to compare the long-term outcomes of PCI and CABG among patients with ischemic LVSD and compare all-cause mortality (ACM) and the incidence of repeat revascularization and myocardial infarction (MI).

## Methods

This study was reported in compliance with the Preferred Reporting Items for Systematic Review and Meta-analysis 2020 (PRISMA) Guidelines<sup>[28]</sup>, Supplemental Digital Content 1, <http://links.lww.com/MS9/A67>, and performed according to established methods<sup>[29,30]</sup>.

### Outcome variables

The primary outcome of interest was ACM. The secondary outcomes of interest were 30-day mortality, major adverse cardiovascular and cerebrovascular (MACCE), stroke, MI, repeat revascularization, cardiovascular mortality, and ventricular tachycardia.

### Search strategy

#### Search strategy

We conducted a systematic search in PubMed, Embase, Scopus, and Cochrane Central for articles from their inception until 30 November 2022, using the following keywords and MeSH terms: ‘Percutaneous Coronary Interventions’, ‘Coronary Artery Bypass Grafting’, ‘Revascularization’, ‘ischemic cardiomyopathy’, ‘Coronary intervention’, ‘Left ventricular systolic dysfunction’. MeSH terms were used where appropriate. A detailed search strategy has been uploaded in Supplementary Table 1,

## HIGHLIGHTS

- There is a paucity of data and trials evaluating the optimal revascularization strategy in patients with ischemic left ventricular systolic dysfunction (LVSD).
- Our study shows coronary artery bypass grafting was associated with a lower risk of all-cause mortality, repeat revascularization, and incidence of myocardial infarction compared with postpercutaneous coronary intervention in patients with LVSD.
- Further studies are warranted among LVSD patients to stratify the optimal revascularization procedure across different aspects of race, sex, pathology, and ejection fraction.

Supplemental Digital Content 3, <http://links.lww.com/MS9/A69>. Two authors (V.J. and A.I.) reviewed the abstract and title of the articles for eligibility. The senior author resolved any inclusion-related discrepancy.

### Eligibility criteria and study selection

The studies were eligible to be included in our meta-analysis if the study population were age greater than 18, studies with reduced/low left ventricular EF, studies such as randomized controlled trials, prospective and retrospective studies with a follow-up duration of a minimum of one year, and presence of cardiovascular event data showing the comparison of LVSD-PCI and LVSD-CABG. To decrease the risk of bias inherent in including observational studies, propensity score matching outcomes were included based on given availability. We excluded literature or systematic reviews, letters, studies with a single arm, animal studies, and studies with patients less than 18 years of age were excluded.

### Data extraction and statistical analysis

Data from the eligible studies, such as demographic, study design, comorbidity, follow-up, and outcomes between LVSD-PCI and LVSD-CABG group patients, were extracted to an Excel® 2019 spreadsheet by two authors (V.J. and S.K.).

Baseline continuous variables were summarized in the mean (SD), whereas dichotomous variables were described in frequency or percentage. We performed a conventional meta-analysis for primary and secondary outcomes and adopted the DerSimonian and Laird random-effect model for the study variations<sup>[31]</sup>. Outcomes were reported as pooled odds ratio (OR), standard mean difference, and their corresponding 95% CI. Statistical significance was met if the 95% CI did not cross the numeric ‘1’ and the two-tailed *P*-value was less than 0.05. We considered a two-tailed *P*-value of less than 0.05 to be statistically significant. In addition, we assessed the between-study heterogeneity using the Higgins I-square ( $I^2$ ) test, with  $I^2$  values less than 75% considered mild-moderate and greater than 75% considered high<sup>[32]</sup>. For heterogeneity  $I^2$  greater than 75%, a leave-one-out was utilized to explore the cause of heterogeneity. Sensitivity analysis was performed using leave-one-out meta-analysis. All statistical work, inclusive analysis, and graphical illustrations were conducted using STATA (version 17.0, StataCorp).

**Table 1**  
Baseline characteristic of included studies arranged in form of (PCI/CABG)

References	Sample (n) PCI/CABG	Study Design	Age, years	Male, %	Diabetes	HTN, %	HLD, %	Previous MI, %	Type of stent	LVEF%	Follow-up, Years
Bangalore et al. <sup>[27]</sup>	1063/1063	Registry, Multicenter	66.1/65.6	804/799	450/469	64/59	64/67	63.78/64.25	EES	<35	2.9
Buszman et al. <sup>[26]</sup>	55/54	Prospective	60.1/60.9	44/43	15/12	64/59	64/67	56.7/57.4	DES = 501	<35	1
Iribarne et al. <sup>[21]</sup>	718/955	Retrospective	65.4/65.8	531/709	315/415	55.6/58.7	50/44.3	47.2/69.7	DES, BM	<35	4.3
Jiang et al. <sup>[3]</sup>	142/201	Prospective	59.8/60.5	112/176	71/87	60.8/55.7	30.9/46.9	16.6/20.6	DES	<35	6.2
Kang et al. <sup>[20]</sup>	469/442	Registry, multicenter	66.9/63.6	354/347	235/238	89/85	84.9/84.2	44/45	DES, BMS	<35	5
Marui et al. <sup>[18]</sup>	464/444	Retrospective	70.1/67.8	1905/1920	264/249	84.9/84.2	84.9/84.2	44/45	DES, BMS	<35	4.74
Sun et al. <sup>[19]</sup>	2397/2397	Retrospective	66.5/66	34/50	1256/1244	84.9/84.2	84.9/84.2	44/45	DES, BMS	<35	5.2
Toda et al. <sup>[14]</sup>	48/69	Retrospective	67/62	34/50	20/31	84.9/84.2	84.9/84.2	44/45	DES, BMS	<35	3.7
Hannan et al. <sup>[23]</sup>	1059/1614	Retrospective	66/65	101/111	78/78	86/82	39/40	53/47	DES	<35	1.5
Yang et al. <sup>[13]</sup>	141/141	Retrospective	66/65	101/111	78/78	86/82	39/40	53/47	DES	<35	3

**Quality assessment**

One author (A.I.) independently assessed the quality of the included studies using the Newcastle–Ottawa Scale for cohort studies<sup>[33]</sup>. The details of the quality assessment are presented in Supplementary Table 2, Supplemental Digital Content 3, <http://links.lww.com/MS9/A69>.

**Results**

Our initial comprehensive search identified a total of 2135 articles. After excluding duplicates (1420), 674 studies were further excluded after reviewing the title and abstract, and 41 studies were reviewed in full-text form. However, 31 studies were further excluded based on inclusion criteria. A total of 10 studies qualified for quantitative analysis, where two studies were prospective<sup>[3,26]</sup>, and eight were retrospective<sup>[13–15,18,20,21,23,27]</sup>.

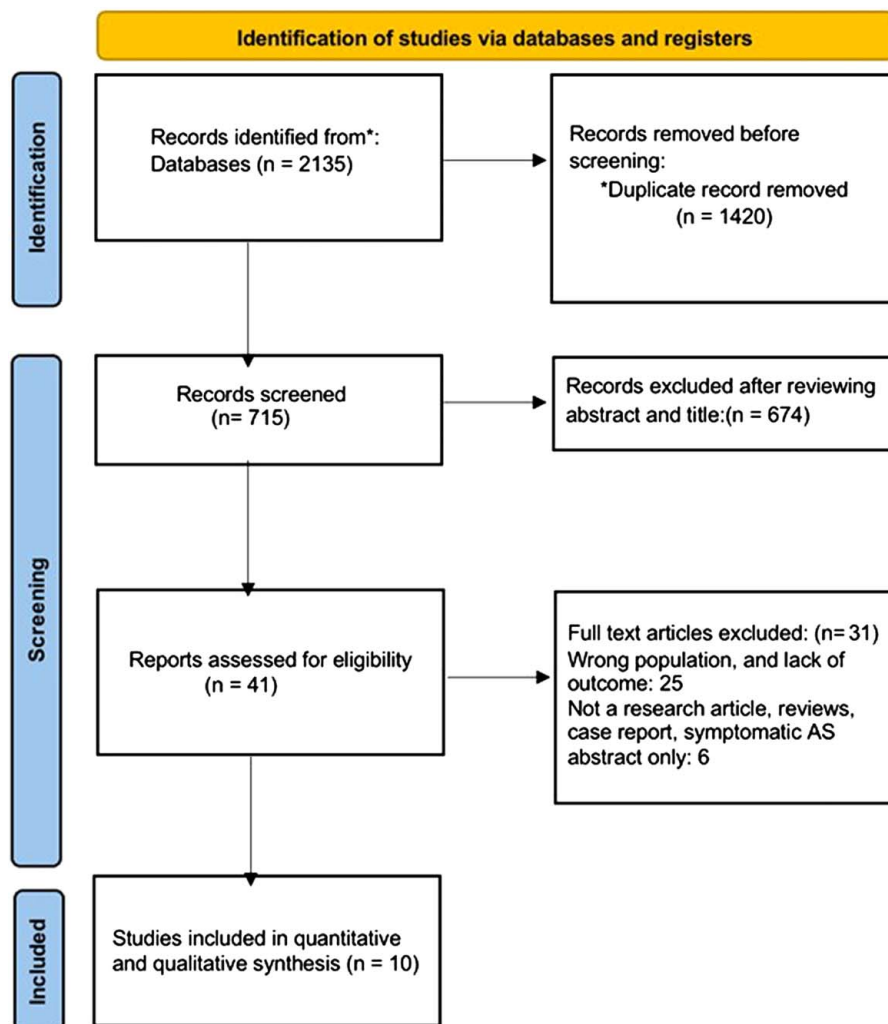
A total of 13 324 patients in 10 studies were included in our analysis: 6245 (47%) in the PCI and 7074 (53%) in the CABG group. The mean follow-up duration was 3.5 years. The mean age was 65.3 years for the PCI group and 64.1 years for the CABG group. Patients were predominantly male (56 vs. 54%) for PCI and CABG, respectively. The most common comorbidity was hypertension (40 vs. 35%) and diabetes mellitus (39 vs. 36%) in PCI and CABG. The study characteristics, demographics, and comorbidities are presented in Table 1. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram is depicted in Figure 1. The quality assessment of the observational studies was a low risk of bias on NOS for all observational studies. (Supplementary Table 2, Supplemental Digital Content 3, <http://links.lww.com/MS9/A69>).

**Meta-analysis of clinical outcomes**

At a mean follow-up of 3.75 years, the PCI group had higher odds of ACM (OR 1.15, 95% CI 1.01–1.31,  $P=0.03$ ,  $I^2=19.16\%$ ), repeat revascularization (OR 3.57, 95% CI 2.56–4.97,  $P<0.001$ ,  $I^2=82.12\%$ ), and MI (OR 1.92, 95% CI 1.01–3.86,  $P=0.048$ ,  $I^2=87.3\%$ ) compared to CABG (Fig. 2A–C). In contrast, the likelihood of cardiovascular mortality (OR 1.23 95% CI 0.98–1.55,  $P=0.07$ ,  $I^2=32.09\%$ ), stroke (OR 0.73 95% CI 0.51–1.04,  $P=0.08$ ,  $I^2=47.7\%$ ) (Fig. 3A, B), MACCE (OR 1.36, 95% CI 0.99–1.87,  $P=0.06$ ,  $I^2=0\%$ ), and ventricular tachycardia (OR 0.79, 95% CI 0.22–2.86,  $P=0.72$ ,  $I^2=0\%$ ) was comparable between both the procedures (Fig. 4A, B).

**Sensitivity analysis and publication bias**

Sensitivity analysis was carried out for outcomes reported by more than 5 studies with a high overall between-study heterogeneity, which includes MI and repeat revascularization. For MI, sensitivity analysis through the leave-one-out method showed that results were nonsignificant between PCI and CABG, except after the removal of the study by Kang et al.<sup>[20]</sup> and Buszman et al.<sup>[26]</sup> (Supplementary Figure 1, Supplemental Digital Content 3, <http://links.lww.com/MS9/A69>). Of note, after the removal of the study by Kang et al.<sup>[20]</sup>, it was observed that patients with PCI had a significantly higher risk of MI compared to that of CABG (OR 2.57, 95% CI 2.18–3.54,  $P<0.001$ ) with a substantial reduction in the heterogeneity from 87 to 0% (Supplementary Figure 2, Supplemental Digital Content 3, <http://links.lww.com/MS9/A69>).



**Figure 1.** Preferred Reporting items for Systematic review and Meta-analysis flow of the search strategy for systematic review and meta-analysis.

links.lww.com/MS9/A69). The results of repeat revascularization remained unaltered in terms of magnitude and direction, suggesting the robustness of primary analysis (Supplementary Figure 3, Supplemental Digital Content 3, <http://links.lww.com/MS9/A69>). The likely cause of heterogeneity in the studies mentioned above was selection bias.

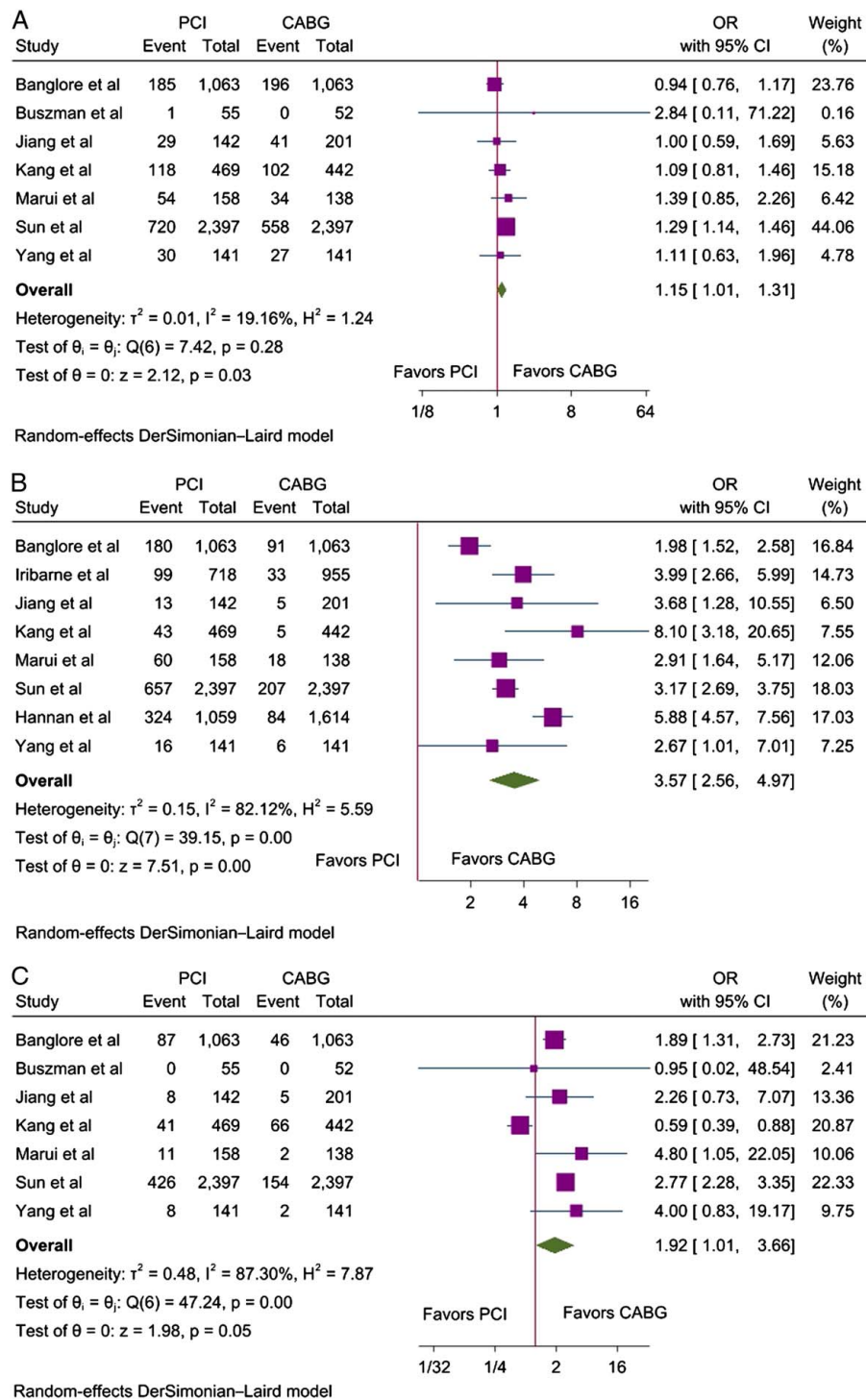
An assessment of publication bias was performed for the primary outcome of the ACM. Visualization of funnel plots showed that there was no funnel plot asymmetry, indicating there was no evidence of publication bias for primary outcomes (ACM) (Supplementary Figure 4, Supplemental Digital Content 3, <http://links.lww.com/MS9/A69>).

## Discussion

This is the most updated and comprehensive systematic review and meta-analysis entailing the superiority of CABG over PCI with LVS dysfunction, showing higher odds of ACM, repeat revascularization, and risk of MI in the PCI group than compared to the CABG group. On the other hand, stroke, MACCE,

ventricular tachycardia, and cardiovascular mortality were comparable between both procedures.

Although there is a plethora of data on patients with CAD and LVSD, current guidelines favor CABG over PCI. The STICH trial has paramount the beneficial effect of CABG in patients with LVEF less than 35%<sup>[2]</sup>. Similarly, European Society of Cardiology guidelines provide class I recommendations in patients with LVEF less than 35%, level of evidence B for left anterior descending disease or multivessel disease, and level of evidence C for left main or equivalent disease<sup>[11]</sup>. Similarly, the American College of Cardiology Foundation/ American Heart Association guidelines points to a reasonable improvement in survival with CABG in patients with LVEF 35–50% and proximal left anterior descending stenosis or multivessel disease (IIa, B) or those with significant CAD and LVEF less than 35% (IIa, B)<sup>[12]</sup>. However, the FREEDOM (Future Revascularization Evaluation in Patients with Diabetes mellitus; Optimal Management of Multivessel Disease)<sup>[34]</sup> showed no difference in mortality between PCI and CABG in patients with LVEF less than 40%; similar results were demonstrated in other trials like



**Figure 2.** Forest plots of outcomes: (A) All-cause mortality, (B) Repeat revascularization, (C) Myocardial Infarction. CABG, coronary artery bypass grafting; PCI, postpercutaneous coronary intervention.

SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) and the AWESOME trails<sup>[35,36]</sup>.

The dual function of CABG can explain the superiority of CABG over PCI in LVSD. It helps in revascularization and, along with it, improves left ventricular function (LVF) postoperatively. Revascularization by CABG and PCI increased LVF by 15 and

5%, respectively, after one year<sup>[37]</sup>. However, the previous PCI followed by CABG is an independent predictor of mortality<sup>[38]</sup>. Although PCI can restore LVF, its magnitude is comparatively lower<sup>[39]</sup>. With ameliorated LVEF, patients are less likely to endure complications due to heart failure and benefit from improved physical fitness levels<sup>[16]</sup>. CABG bypasses a larger

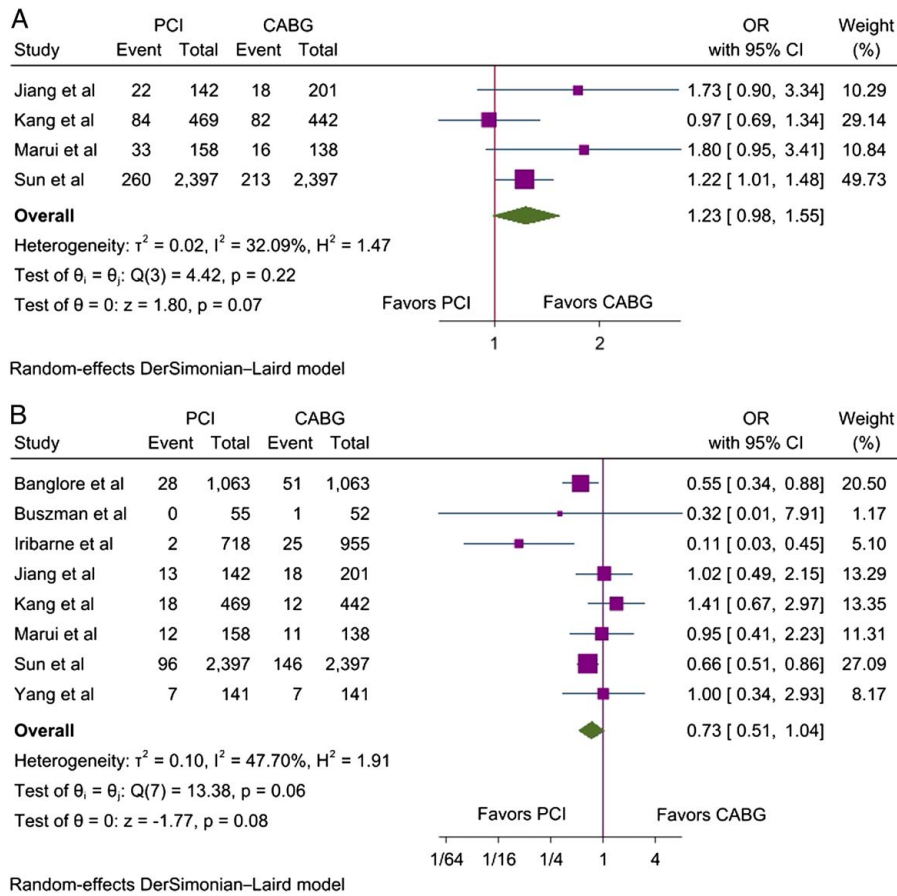


Figure 3. Forest plot of outcomes: (A) Cardiovascular mortality, (B) Stroke. CABG, coronary artery bypass grafting; PCI, postpercutaneous coronary intervention.

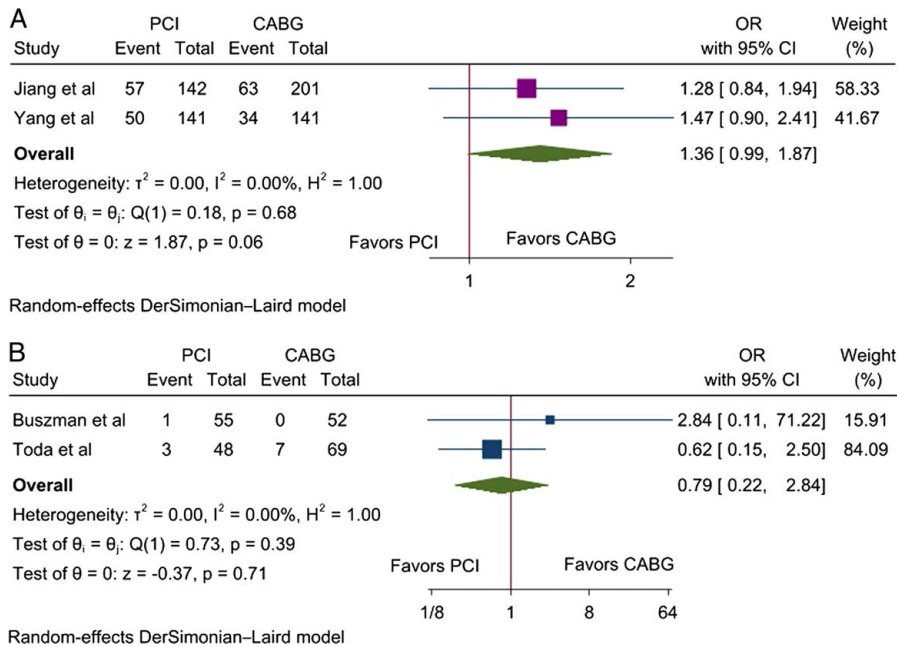


Figure 4. Forest plots of outcomes: (A) MACCE, (B) Ventricular Tachycardia. CABG, coronary artery bypass grafting; PCI, postpercutaneous coronary intervention.

extent of obstructive lesions, thus minimizing the effect of progressive disease in the proximal vessel. Using internal mammary arteries can maintain the long-term patency of the channels, providing better protection. In contrast, PCI checks short segments of severe stenosis that progressive plaque can form new significant lesions and even rupture. Patients with low LVEF will be less tolerant of repeated myocardial insult from restenosis or thrombosis than those without LVD. Hence, patients with viable tissue and LVF would benefit from CABG to restore ventricular dysfunction and prevent further ischemic damage.

The SYNTAX trial showed that compared to CABG, PCI required repeated revascularization<sup>[35]</sup>. Patients in the PCI arm undergoing repeated revascularization had a greater risk of the composite outcome of death, stroke, and MI than compared to patients not undergoing repeated revascularization. On the other hand, there was no difference noted in the CABG arm. In terms of repeat revascularization, the difference between PCI and CABG arms might be dynamic due to changing practice and availability. With the advancement of technology, the guidance of intravascular ultrasonography and second-generation drug-eluting stents have declined the revascularization rates<sup>[40,41]</sup>. Similarly, the development of arterial grafts compared to venous grafts for CABG has been associated with reduced repeat revascularization<sup>[42]</sup>. Our analysis, however, should have considered this factor in account, hence, the relatively older studies may not be accurately justified in context to the current practices.

Similarly, a recent meta-analysis by Galo *et al.*<sup>[43]</sup> showed a significantly increased risk for MI in the PCI arm compared to the CABG arm for left main coronary artery disease. In CABG, a graft is inserted beyond the lesion, prompting complete revascularization compared to stenting in PCI. Thereby allowing CABG to play the protagonist by preventing future ischemic changes arising from the culprit lesions at proximal segments, consequently declining the probability of MI<sup>[44]</sup>. Despite new advances in PCI therapeutic modality, it still needs to overcome the benefit of CABG compared to its methodology. Moreover, the significant risk reduction of MI with CABG over time makes it more favorable, especially considering high-risk patients. As MI is associated with periprocedural PCI, it is recommended to measure pre and postcardiac troponin levels. Such an event is a strong independent predictor for 1-year post-PCI ACM<sup>[45]</sup>. CABG is superior when compared to PCI for patients with LVSD.

### **Recommendation for future research**

Further large multicenter trials are needed among patients with LVSD to stratify the appropriate revascularization strategies and superiority over one another. Baseline EF, and biomarkers roles must be evaluated for predictors of worse outcomes. Along with that, racial and sex-based analysis are needed to understand the role of both in the outcomes of both procedures.

### **Clinical implications for health managers and policymakers**

In consistent with our findings, CABG must be favored over PCI for LVSD patients. However, factors including the cost-benefit ratio, the CABG operating centers and skilled surgeon, and contraindications for CABG must be kept in mind before making a decision.

### **Limitations**

All studies included in our meta-analysis were observational, and the possibility of selection and confounding bias could not be ruled out. In addition, access to the patient's data could have been more feasible, including data regarding adherence to medical therapy, interventional method, incomplete versus complete revascularization, disease complexity, and SYNTAX scores. Lastly, data on mortality and stent thrombosis were unavailable in several studies; hence, a separate analysis could not be performed. More prospective studies and clinical trials should be conducted to verify and cover the limitations of our meta-analysis.

### **Conclusion**

CABG is superior when compared to PCI for patients with LVSD. CABG was associated with a lower risk of ACM, repeat revascularization, and incidence of MI compared with PCI in patients with LVSD.

### **Ethical approval**

NA.

### **Consent**

NA.

### **Source of funding**

None.

### **Authors contribution**

V.J: conceptualization; V.J: methodology; S.P.A, V.J: formal analysis and investigation; A.B.S., V.J., A.I.: writing - review and editing. All authors contributed equally in the writing - original draft preparation.

### **Conflict of interest disclosure**

The authors declare that they have no financial conflict of interest with regard to the content of this report.

### **Research registration unique identifying number (UIN)**

1. Name of the registry: PROSPERO.
2. Unique Identifying number or registration ID: CRD42022360919.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): NA.

### **Guarantor**

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## Data availability statement

All data related to this study has been uploaded in the supplementary files and will be made available upon reasonable request from the corresponding author.

## Provenance and peer review

Not commissioned, externally peer-reviewed.

## Acknowledgment

None.

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