

Clinical Outcomes of Patients with Coronary Artery Diseases and Moderate Left Ventricular Dysfunction: Percutaneous Coronary Intervention versus Coronary Artery Bypass Graft Surgery

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Purpose: Percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) are two revascularization strategies for patients with coronary artery disease (CAD) and left ventricular dysfunction. However, the comparisons of effectiveness between the two strategies are insufficient. This study is aimed to compare the effectiveness between PCI and CABG among patients with moderate left ventricular dysfunction.

Patients and Methods: A total of 1487 CAD patients with moderate reduced ejection fraction ($36\% \leq EF \leq 40\%$), who underwent either PCI or CABG, were enrolled in a real-world cohort study (No. ChiCTR2100044378). Clinical outcomes included short- and long-term all-cause mortality, rates of heart failure (HF) hospitalization and repeat revascularization. Propensity score matching was used to balance the two cohorts.

Results: PCI was associated with lower 30-day mortality rate (hazard ratio [HR] [95% CI], 0.35 [0.15–0.83]; $P=0.02$). At a mean follow-up of 4.5 years, PCI and CABG had similar all-cause death (HR [95% CI], 0.82 [0.56–1.20]; $P=0.30$) and heart failure (HF) hospitalization (HR [95% CI], 0.93 [0.54–1.60]; $P=0.79$), but PCI had higher risk of repeat revascularization (HR [95% CI], 8.62 [3.67–20.23]; $P<0.001$). Improvement in EF measured at 3 months later after revascularization was also similar between PCI and CABG (P for interaction=0.87).

Conclusion: CAD patients with moderate reduced EF who had PCI had lower short-term mortality rate but higher risk of repeat revascularization during follow-up than patients who had CABG. PCI showed comparable long-term survival, HF hospitalization risk, and EF improvement.

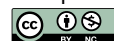
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Introduction

Left ventricular (LV) dysfunction constitutes an independent risk factor of poor prognosis in patients with coronary artery disease (CAD). Revascularization including coronary artery bypass grafting (CABG)¹ and percutaneous coronary intervention (PCI)^{2–4} may improve long-term outcomes by attenuating the ischemic state and reversing LV remodeling.^{5–7} However, no randomized trial compares the effectiveness of PCI and CABG in patients with CAD and LV dysfunction.⁸ Patients with varying extent of LV dysfunction may have different characteristics and response to treatment.⁹ The 2012 American College of Cardiology Foundation/American Heart Association guidelines state that magnitude of LV systolic dysfunction is one of factors for the choice of revascularization strategy.¹⁰

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For patients with severe LV dysfunction, ie, with an ejection fraction (EF) of 35% or less, observational studies have indicated better survival with CABG than PCI,^{11–13} or comparable survival with CABG.^{14–16} However, no study compares the effectiveness of PCI and CABG in patients with moderate LV dysfunction, ie, with an EF between 36% and 40%.

In the present study, the effectiveness of CABG versus PCI with drug-eluting stent (DES) on short- and long-term mortality rate, HF hospitalization, and repeat revascularization was compared among patients with CAD and moderately reduced EF, using real-world data from a large hospital in China.

Patients and Methods

Patient Selection and Definitions

The study protocol was approved by the ethics committee and registered in Chinese Clinical Trial Registry (No. ChiCTR2100044378). Patients who underwent CABG or PCI with DES because of CAD in Beijing Anzhen Hospital from January 1, 2005, to December 31, 2014 were screened. Patient with an EF between 36% and 40% assessed by echocardiography one month before PCI or CABG was included. The database created by the institution also collected the information including patient basic information, medical history, echocardiography data, electrocardiography data and therapy. The date of the procedure is called the index date. Follow-up data were acquired by medical records and phone contact. Patient selection, as well as patient attrition due to different exclusion criteria, is documented in [Figure 1](#).

Left main disease was defined as 50% or greater diameter stenosis by visual assessment in the left main vessel. Multivessel disease was defined as the presence of stenosis 70% or greater of the coronary luminal diameter in more than 1 of the 3 major epicardial vessels.

An anatomical definition of complete revascularization was used in this analysis. Complete revascularization was defined as successful PCI (residual stenosis <30%) of all angiographically significant lesions (ie, $\geq 70\%$ diameter stenosis) in 3 coronary arteries and their major branches, determined visually by the cardiologist who performed the index diagnostic catheterization procedure. A staged procedure (n=21) within 90 days after discharge was acceptable. For CABG procedures, grafting to every primary coronary artery with 70% or greater diameter stenosis was accepted as complete revascularization.

The initial echocardiography data was defined as measured within 30 days before PCI or CABG which includes EF, LV end-diastolic dimension (LVEDD), LV end-systolic dimension (LVESD), and mitral regurgitation (MR). The follow-up echocardiography data was defined as measurement reassessed at least 3 months after revascularization.^{17,18} For patients who had repeat echocardiography measurements, the first available measurement that was 3 months after revascularization was used. Echocardiography measurements beyond 12 months after revascularization were excluded. MR was graded semi-quantitatively in an integrative manner as none/trace (0), mild (1), moderate (2), and severe (3).¹⁹

Outcomes

The primary outcomes of the study were both short-term (≤ 30 days after the procedure) and long-term all-cause mortality rates. Secondary outcome measures were HF hospitalization, repeat revascularization, and cardiac death. We also assessed major adverse cardiac events as long-term all-cause death, HF hospitalization, and repeat revascularization.

A death was considered of cardiac origin unless a noncardiac cause could be identified because it was obvious. When death occurred in the index hospitalization of revascularization, it was termed cardiac death.

HF hospitalization was defined as the first readmission with a primary diagnosis of HF after discharge from the index procedure. Repeat revascularization included any unplanned repeat PCI or repeat CABG, or both. Similar to the initial procedure, a staged PCI was allowed when it was performed within 90 days after discharge and before myocardial infarction. All staged PCIs were excluded as repeat revascularization.

Statistical Analysis

Continuous variables were expressed as mean (SD) and were a comparison of the PCI cohort with the CABG cohort through use of *t*-test or 1-way analysis of variance. Cumulative incidences were estimated with Kaplan–Meier method and compared using the Log rank test. Baseline characteristics between the PCI group and the CABG group differed ([Table 1](#)). Therefore, propensity score matching was performed with use of a 1-to-1 matching protocol without replacement and a caliper width equal to 0.01 of the SD of the logit of the propensity score.²⁰ Standardized differences were estimated for all baseline covariates before and after

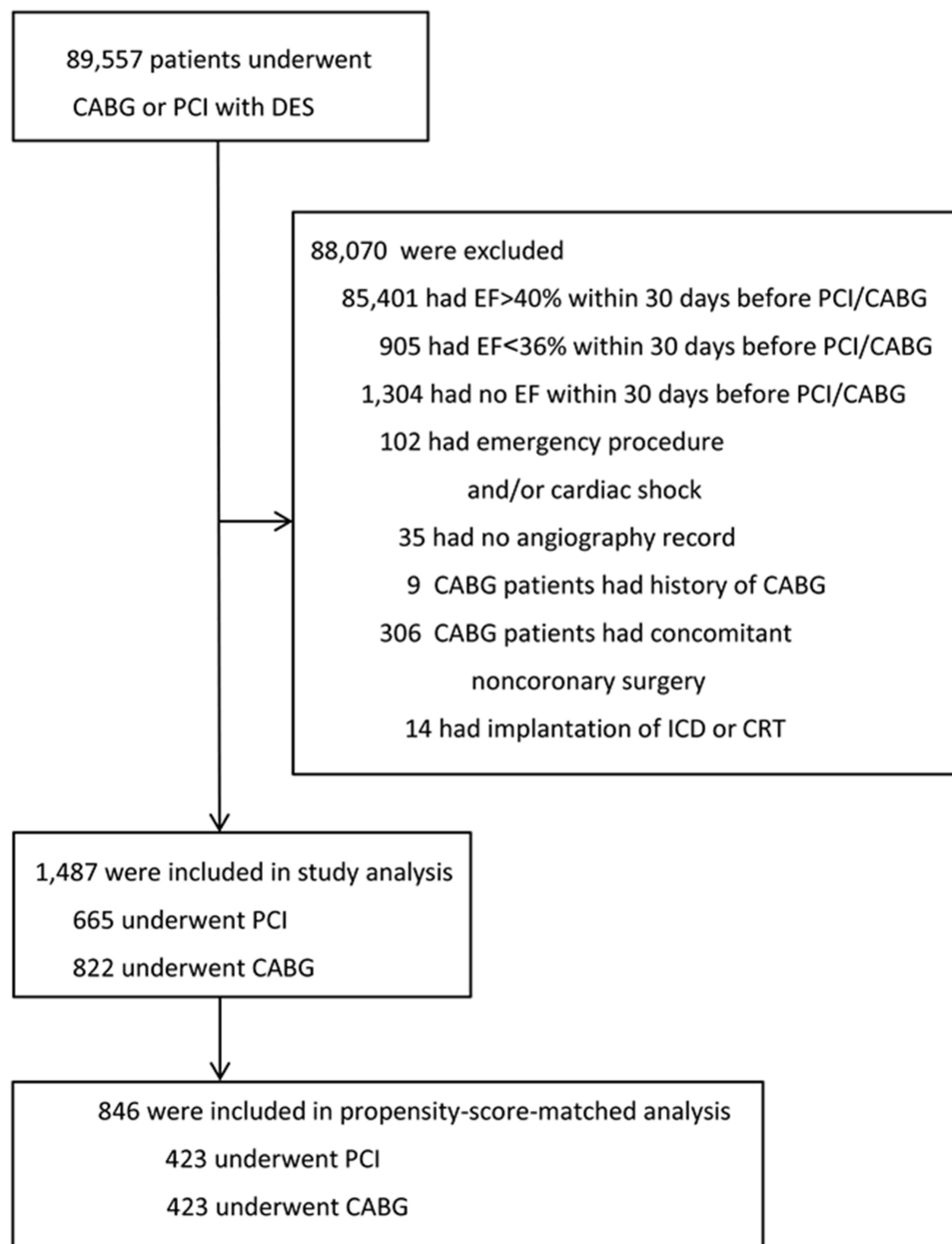


Figure 1 Patient selection process and study protocol. CABG indicates coronary artery bypass grafting.

Abbreviations: CRT, cardiac resynchronization therapy; DES, drug-eluting stent; EF, ejection fraction; ICD, implantable cardioverter-defibrillator; PCI, percutaneous coronary intervention.

matching. A value of less than 10.0% in standardized difference suggested balance in a given covariate between the 2 cohorts. In the matched cohort, the risks of outcomes were analyzed using a Cox proportional hazards regression model.

All statistical analyses were based on 2-tailed tests. *P* values less than 0.05 were considered statistically significant. Statistical analyses were performed with Stata version 14.0 (StataCorp LLC).

Results

Baseline Characteristics

We identified 1487 CAD patients with an initial EF between 36% and 40% who met our inclusion criteria (Figure 1). Of these patients, 665 (44.7%) underwent PCI with DES and 822 (55.3%) underwent CABG (Table 1). Before propensity score matching, differences were observed in baseline characteristics between the 2 groups. One-to-one propensity score matching resulted in a matched sample of 846 patients

Table 1 Baseline Characteristics Before and After Propensity Score Matching in Patients with Initial EF Between 36% and 40%

Patient Characteristics	Prematching ^a		Postmatching ^a		Standardized Difference, %	Standardized Difference, %
	CABG (n=822)	PCI (n=665)	CABG (n=423)	PCI (n=423)		
Age, y						
Mean (SD)	66.44 (9.85)	65.34 (11.44)	65.70 (10.35)	65.77 (10.87)	10.4	-0.6
Distribution						
<59, No. (%)	199 (24.2)	210 (31.6)	123 (29.1)	119 (28.1)	19.8	2.5
60-69, No. (%)	303 (36.9)	197 (29.6)	137 (32.4)	139 (32.9)		
70-79, No. (%)	245 (29.8)	187 (28.1)	127 (30.0)	127 (30.0)		
≥80, No. (%)	75 (9.1)	71 (10.7)	36 (8.5)	38 (9.0)		
Male Sex, No. (%)	678 (82.5)	555 (83.5)	347 (82.0)	351 (83.0)	-2.6	-2.5
Current smoking	256 (31.1)	240 (36.1)	134 (31.7)	145 (34.3)	-10.5	-5.5
Hypertension, No. (%)	413 (50.2)	395 (59.4)	247 (58.4)	238 (56.3)	-18.5	4.3
Diabetes, No. (%)	311 (37.8)	220 (33.1)	151 (35.7)	153 (36.2)	9.9	-1.0
eGFR, mean (SD), mL/min/1.73m ²	83.80 (24.97)	83.46 (22.80)	82.77 (22.71)	83.42 (23.36)	1.4	-2.8
Cerebral vascular disease, No. (%)	88 (10.7)	52 (7.8)	29 (6.9)	39 (9.2)	10.0	-8.7
History of MI, No. (%)	413 (50.2)	306 (46.0)	213 (50.4)	205 (48.5)	8.5	3.8
Atrial fibrillation, No. (%)	36 (4.4)	36 (5.4)	22 (5.2)	24 (5.7)	-4.8	-2.1
Preoperative EF, mean (SD), %	38.78 (1.40)	38.83 (1.34)	38.83 (1.37)	38.83 (1.33)	-3.5	-0.1
Mitral regurgitation (Moderate or severe), No. (%)	104 (12.7)	86 (12.9)	57 (13.5)	60 (14.2)	-0.8	-2.1
Left main disease, No. (%)	60 (7.3)	39 (5.9)	30 (7.1)	33 (7.8)	5.8	-2.7
No. of Diseased Vessel						
1, No. (%)	53 (6.3)	230 (34.6)	53 (11.7)	53 (11.7)	92.4	0.5
2, No. (%)	227 (27.6)	244 (36.7)	211 (46.5)	210 (46.3)		
3, No. (%)	542 (65.9)	191 (28.7)	190 (41.9)	191 (42.1)		
Number of stented artery, mean (SD)		1.29(0.55)		1.40 (0.62)		
Number of total conduit, mean (SD)	2.76(0.75)		2.61 (0.78)			
Complete revascularization, No. (%)	586 (71.3)	278 (41.8)	333 (78.7)	109 (25.8)	62.3	124.9

Note: ^aValues are presented as number and percentage of patients unless specified otherwise.

Abbreviations: CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; EF, ejection fraction.

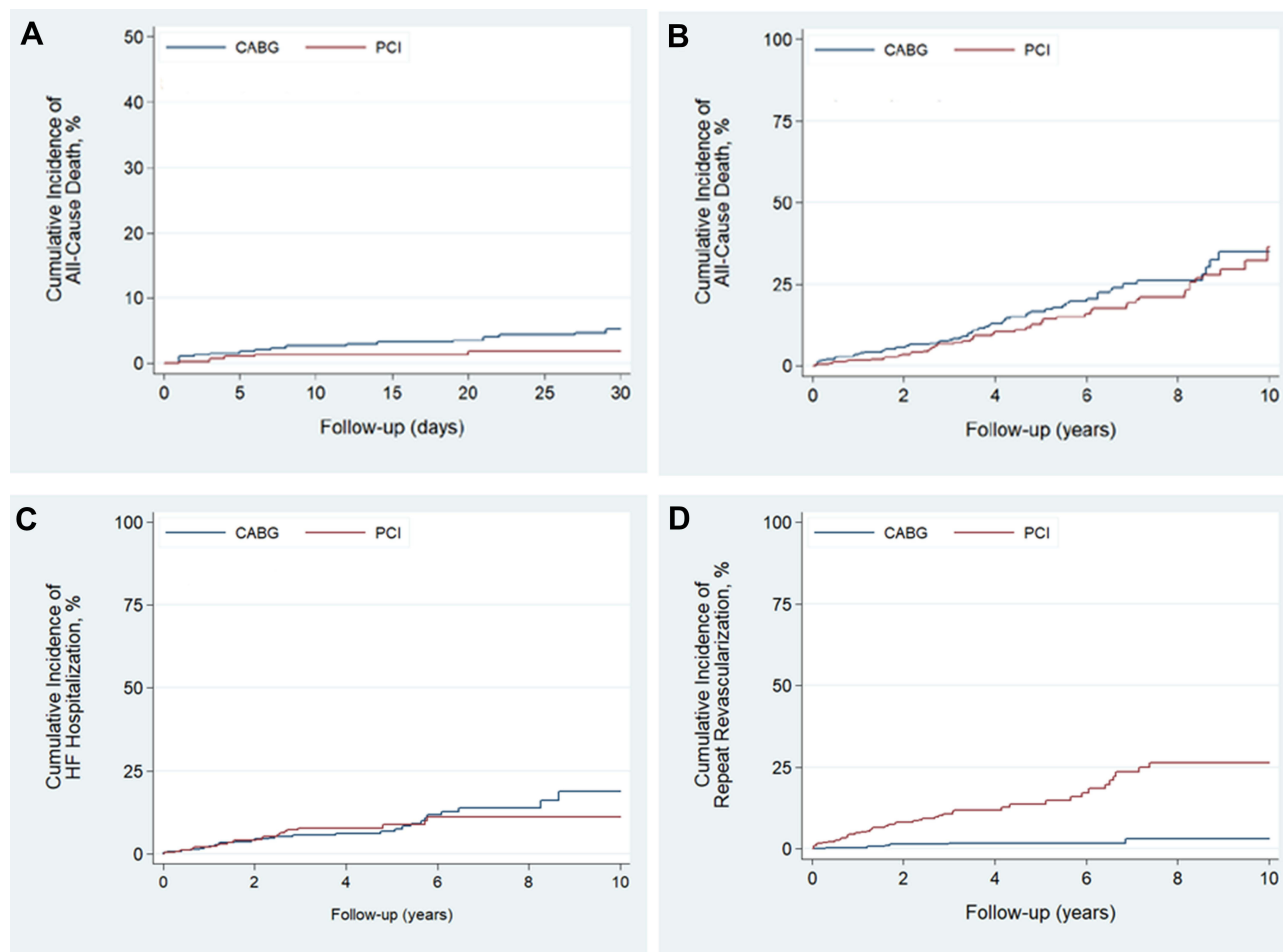


Figure 2 Percutaneous coronary intervention (PCI) versus coronary artery bypass grafting (CABG) for risk of short-term all-cause death (A), long-term all-cause death (B), heart failure (HF) hospitalization (C) and repeat revascularization (D).

with 423 patients in each study cohort of PCI with DES and CABG. In the matched cohort, the proportion with complete revascularization was significantly less in the PCI group (25.8%) than the CABG group (78.7%) (odds ratio [OR] [95% CI], 0.09 [0.07–0.13]; $P < 0.001$) (Table 1).

The mean follow-up was 4.5 years (median, 3.9 years). The maximum follow-up period was 11.6 years, with 82.2% of patients completing the follow-up.

Short-Term Outcomes

There were 7 patients died within 30 days after PCI and 19 in CABG group. PCI was associated with lower risk of 30-day mortality (hazard ratio [HR] [95% CI], 0.35 [0.15–0.83]; $P = 0.02$) (Figure 2A). The risk of 30-day HF hospitalization was similar (HR [95% CI], 0.98 [0.06–15.60]; $P = 0.99$) after PCI and CABG. No unplanned repeat revascularization occurred within 1 month for either group.

Long-Term Outcomes

PCI and CABG were associated with a similar risk of all-cause death (HR [95% CI], 0.82 [0.56–1.20]; $P = 0.30$) (Figure 2B and Table 2). The risk of cardiac death was also similar after PCI and CABG (HR [95% CI], 0.90 [0.59–1.37]; $P = 0.61$) (Table 2).

No significant difference was seen in the long-term risk of HF hospitalization after PCI and CABG (HR [95% CI], 0.93 [0.54–1.60]; $P = 0.79$) (Figure 2C and Table 2).

Initial treatment with PCI was associated with an increased risk of repeat revascularization (HR [95% CI], 8.62 [3.67–20.23]; $P < 0.001$) compared with CABG (Figure 2D and Table 2).

The risk of major adverse cardiac events was similar after PCI and CABG (HR [95% CI], 1.37 [1.03–1.84]; $P = 0.03$) (Table 2).

Table 2 Risk of Long-Term Outcomes in the Propensity Score–Matched Cohort with Preoperative EF Between 36% and 40%

Long-Term Outcomes	No. of Patients	No. of Events	Event Rate, %/y	Hazard Ratio (95% CI)	P value
All-cause death					
PCI	357	50	3.09	0.82(0.56–1.20)	0.30
CABG	357	61	3.76	Reference	
Cardiac death					
PCI	357	42	2.59	0.90(0.59–1.37)	0.61
CABG	357	46	2.83	Reference	
HF hospitalization					
PCI	310	24	1.80	0.93 (0.54–1.60)	0.79
CABG	310	28	1.94	Reference	
Repeat revascularization					
PCI	315	45	3.57	8.62 (3.67–20.23)	<0.001
CABG	315	6	0.40	Reference	
MACE ^a					
PCI	295	101	8.75	1.37 (1.03–1.84)	0.03
CABG	295	84	6.29	Reference	

Note: ^aDefined as all-cause death, HF hospitalization, and repeat revascularization.

Abbreviations: CABG, coronary artery bypass grafting; HF, heart failure; MACE, major adverse cardiac event; PCI, percutaneous coronary intervention.

EF Improvement

To compare EF improvement and LV remodeling after PCI and CABG, we performed propensity score matching among 596 individuals who had echocardiography between 3 and 12 months after PCI or CABG, resulting in 178 matched pairs. Echocardiography was performed an average of 5.3 (3.2–6.9) months after PCI and 6.4 (4.8–9.2) months after CABG. EF was improved to a similar degree in patients treated with PCI and CABG ($P=0.87$ for interaction) (Table 3). LV size was also reduced to

a similar degree in patients treated with PCI and CABG (LVESD, $P=0.85$ for interaction; LVEDD, $P=0.18$ for interaction). The severity of MR did not improve after PCI or CABG ($P=0.44$ for interaction).

Discussion

Among CAD patients with moderate LV dysfunction ($36 \leq \text{EF} \leq 40\%$) undergoing revascularization in a large cardiac care hospital in China, the patients treated with PCI had a lower 30-day rate but greater risk of repeat revascularization during

Table 3 Left Ventricular Remodeling in Propensity Score–Matched Cohort of 178 Patients

Characteristic	Baseline, Mean (SD)	Follow-Up, Mean (SD)	P value	P value for Interaction
EF, %				
PCI	38.80 (1.33)	46.94 (11.24)	<0.001	0.87
CABG	38.91 (1.31)	47.23 (10.66)	<0.001	
LVESD, mm				
PCI	45.11 (7.38)	41.85 (8.82)	<0.001	0.85
CABG	44.65 (7.06)	41.64 (8.46)	<0.001	
LVEDD, mm				
PCI	57.89 (7.37)	56.83 (7.84)	0.03	0.18
CABG	57.69 (6.59)	55.71 (7.26)	<0.001	
MR grade				
PCI	0.93 (0.79)	0.89 (0.78)	0.53	0.44
CABG	0.90 (0.64)	0.93 (0.66)	0.65	

Abbreviations: CABG, coronary artery bypass grafting; EF, ejection fraction; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; MR, mitral regurgitation; PCI, percutaneous coronary intervention.

follow-up compared with CABG. However, long-term mortality rate, risk of HF hospitalization, and EF improvement were similar following PCI and CABG.

The effectiveness between PCI and CABG among CAD patients has been compared for several years according to the revascularization indication and severity of coronary diseases. For patients with unprotected left main coronary artery stenosis,²¹ PCI resulted in comparable mortality, stroke, and MI compared with CABG. PCI was associated with higher rates of repeat revascularization. For patients with multivessel disease,²² CABG was associated with lower mortality, MI and repeat revascularization. Risk-adjusted mortality temporally decreased significantly after CABG but not after PCI across all revascularization indication.^{23,24}

For patients with CAD and LV dysfunction, regarding whether and how best to revascularize have not been clearly established. The Surgical Treatment for Ischemic Heart Failure (STICH) trial randomized 1212 patients with an EF of 35% or less to receive optimal medical therapy with or without CABG.²⁵ The benefits of CABG were indicated. However, the first trial evaluating the role of PCI for ischemic ventricular dysfunction (REVIVED-BCIS2)²⁶ is still underway. To date, the long-term outcomes of PCI compared with CABG have not been evaluated in randomized trial. Subgroup analysis (abnormal LV function) of a collaborative analysis of individual patient data from ten randomized trials indicated similar risk of mortality between PCI and CABG among patients with multivessel disease.²⁷ Observational studies analyzing patients with the EF less than 36%, 40% or 50% had controversial results. Some studies^{11–13,28} have suggested survival is worse after PCI in comparison to CABG, while others^{2,14–16} have demonstrated similar survival. The degree of left ventricular dysfunction is a known determinant of both short-term and long-term adverse outcome events in patients undergoing CABG²⁹ or PCI.³⁰ Thus our study, in contrast to previous studies, compared the effectiveness of PCI versus CABG in patients with EF among 36% to 40% only. Our findings show PCI was associated with lower risk of 30-day mortality but had similar long-term mortality rate in comparison with CABG in patients with moderate left ventricular dysfunction.

No randomized study has compared the outcomes of complete revascularization with incomplete revascularization in CAD patients after either PCI or CABG.³¹ For patients with LV dysfunction, achieving complete revascularization by PCI or CABG is often not feasible due to coronary anatomical factors, patient comorbidities and procedural considerations.

Similar with other studies,^{13,14} in our study, the rate of complete revascularization in patients undergoing PCI was significantly lower than that in patients undergoing CABG. Complex anatomy and limitation of contrast agent administration in PCI procedure might be potential reasons. During the long-term follow-up, PCI was associated with an increased risk of repeat revascularization compared with CABG.

Few data are available, to our knowledge, that comparing the effects of 2 revascularization strategies on EF improvement among patients with ischemic LV dysfunction. In the present study, we found that PCI was associated with similar extent of EF improvement and reverse LV remodeling as with CABG. The relative factors associated with EF recovery after revascularization need to be further investigated.

Limitations

This was a nonrandomized observational study from a single center. The follow-up date came from medical records and phone contact that was not completely followed up for all patients. Therefore, as with any other observational studies, ours might be limited from selection biases. We attempted to minimize such bias using propensity score matching. Moreover, we did not have data on both the coronary anatomical risk score (ie, Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery score), which is a useful tool to assess the risk of revascularization, and the myocardial viability test. Medications during follow-up indicate the status of optimal medical therapy for HF, which has an important effect on long-term outcome regardless of coronary revascularization strategy for patients with ischemic HF.³² Our study could not incorporate any of these factors because of lack of relevant data. Thus, similar with other studies,^{11,12,14–16,28} these variables could not be included in analysis.

Conclusion

Among patients with moderate LV dysfunction (36% ≤ EF ≤ 40%), PCI with DES and CABG had similar long-term risk of death, risk of HF hospitalization, and EF improvement. However, PCI was associated with a higher risk of repeat revascularization and a lower risk of short-term death. At the expense of increased risk of repeat revascularization, PCI with DES for selected patients with moderate LV dysfunction may be an alternative to CABG.

Data Sharing Statement

The datasets are available from the corresponding author (Jinghua Liu) upon reasonable request.

Ethical Approval and Informed Consent

The Ethics Committee of the Beijing Anzhen Hospital approved the study. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki. Because this was a retrospective cohort study and waiver of informed consent will not adversely affect the rights and welfare of the subjects, written informed consent from the patients was waived. Patient data confidentiality was protected.

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Disclosure

All authors declare that they have no conflict of interest.

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