Original Article

Culprit-only versus multivessel percutaneous coronary intervention among STEMI patients complicated by cardiogenic shock in real-world practice: an updated systematic review and meta-analysis

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Background: The recent randomized trials demonstrated that culprit-only percutaneous coronary intervention (CO-PCI) was superior to multivessel PCI (MV-PCI) among ST-segment elevation myocardial infarction (STEMI) patients with multivessel disease (MVD) complicated by cardiogenic shock, yet the real-world scenario remains to be determined.

Methods: Studies that compared CO-PCI versus MV-PCI in STEMI patients with MVD complicated by cardiogenic shock were identified by a systematic search of published articles. Pooled odds ratios (OR) and 95% confidence intervals (CI) were calculated by using random-effects models.

Results: Eventually, 18 observational studies involving 73,528 patients were included. The results showed that CO-PCI was associated with lower risks of short-term renal failure (OR: 0.75; 95% CI: 0.64 to 0.88; I^2=14.7%) and short-term stroke (OR: 0.86; 95% CI: 0.77 to 0.96; I^2=0.0%) compared with immediate MV-PCI. But the risk of short-term myocardial infarction (OR: 1.12; 95% CI: 1.03 to 1.22; I^2=0.0%) was increased. There was no significant difference during long-term follow-up. The results remained consistent after adding the only randomized trial.

Discussion: Based on real-world analyses, our meta-analysis suggested that CO-PCI decreased the risks of renal failure and stroke but increased the risk of myocardial infarction relative to immediate MV-PCI during short-term follow-up in STEMI patients with MVD complicated by cardiogenic shock. If possible in clinical practice, staged MV-PCI can be given a try to decrease the risks of renal failure and stroke associated with immediate MV-PCI and myocardial infarction associated with CO-PCI. However, the conclusions need to be confirmed by further large-scale studies.

Keywords: Multivessel disease (MVD); myocardial infarction; percutaneous coronary intervention (PCI); cardiogenic shock

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Introduction

It is estimated that approximately 5% to 10% of patients with ST-segment elevation myocardial infarction (STEMI) are complicated by cardiogenic shock (1) and the mortality rate of this population is high. The prevalence of multivessel disease (MVD) can approaches as high as 80% in STEMI patients complicated by cardiogenic shock (2), which is higher than that in patients without cardiogenic shock (40–65%) (3,4). MVD is regarded as a risk factor associated with worse outcomes when compared with single-vessel coronary artery disease (3-6). For the treatment of STEMI patients with MVD and cardiogenic shock, the U.S. 2016 appropriate use criteria consider immediate multivessel PCI (MV-PCI), which is defined as revascularization of both infarct related artery (IRA) as well as non-IRA at the same intervention (7). Similarly, the 2017 European Society of Cardiology (ESC) guidelines also recommend non-IRA PCI during the index procedure based on consensus of opinion of the experts (Class IIa, Level C) (8). However, the largest randomized Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK) trial (2) suggested that the 30-day composite of death or renal-replacement therapy were lower with culprit-only PCI (CO-PCI) when compared with immediate MV-PCI, thus challenging the guideline recommendations. However, there was no significant difference between the two groups in the composite of death or renal-replacement therapy during one-year follow-up (9). Based on the CULPRIT-SHOCK trial, the European revascularization guidelines have now downgraded immediate MV-PCI in cardiogenic shock patients from a class I to a class III recommendation (10). Moreover, the recent Taiwan Society of Cardiology for the Management of STEMI also suggests that in STEMI patients with MVD complicated by cardiogenic shock, routine non-IRA revascularization during primary PCI is not recommended (11). However, the results based on real-world registry suggested that the 3-year risk of all-cause mortality was lower with immediate MV-PCI than that with CO-PCI (12). Considering the fact that in the CULPRIT-SHOCK trial, patients were strictly selected and unable to reflect the real-world situation, we sought to conduct a systematic review and meta-analysis based on real-world analyses to determine if CO-PCI is associated with improved clinical outcomes when compared with immediate MV-PCI in real-world situation. Meanwhile, the CULPRIT-SHOCK trial was just powered for the 30-day analysis of the primary composite of all-cause mortality and renal failure, and significant difference exist in study type, therefore, subgroups according to short- (≤30 days) and long-term outcomes (≥6 months) and study type were made to investigate the difference between short- and long-term outcomes. The study has been registered in PROSPERO (https://www.crd.york.ac.uk/PROSPERO/), and the register number is CRD42020183124. This study was carried out in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) 2020 reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1408) (13).

Methods

We searched PubMed, EMBASE, the Cochrane database, Web of Science, clinicaltrial.gov, together with Google Scholar for studies from inception to April 2021. The following key words and Medical Subject Headings (MeSH) terms were used to find potential eligible studies: cardiogenic (MeSH), cardiogenic shock, shock, myocardial infarction (MeSH), percutaneous coronary intervention (MeSH), myocardial revascularization (MeSH), multi-vessel, multivessel, culprit vessel, non-infarct, incomplete revascularization, and complete revascularization. Meanwhile, the presentations at major cardiovascular conferences, the bibliography of original trials, review articles, as well as meta-analyses were also searched to find other eligible studies.

Study selection and data extraction

In the present meta-analysis, eligible studies were required to fulfill the following criteria: (I) study (sub)group included STEMI patients with MVD and complicated by cardiogenic shock; (II) compared CO-PCI versus MV-PCI strategies; (III) at least 10 patients in each treatment group were included; (IV) published in English language. Studies that concerned about patients undergoing coronary artery bypass grafting were ruled out. Two reviewers (Meng-Jin Hu and Wen-Yang Jiang) independently assessed the studies for inclusion, and disagreements were resolved by consensus with third-party adjudication (Jing Xu). Information with regard to the study period, sample size, study design, definition of MVD and cardiogenic shock, exclusion criteria, clinical outcomes, follow-up time, and baseline characteristics of enrolled patients were extracted.

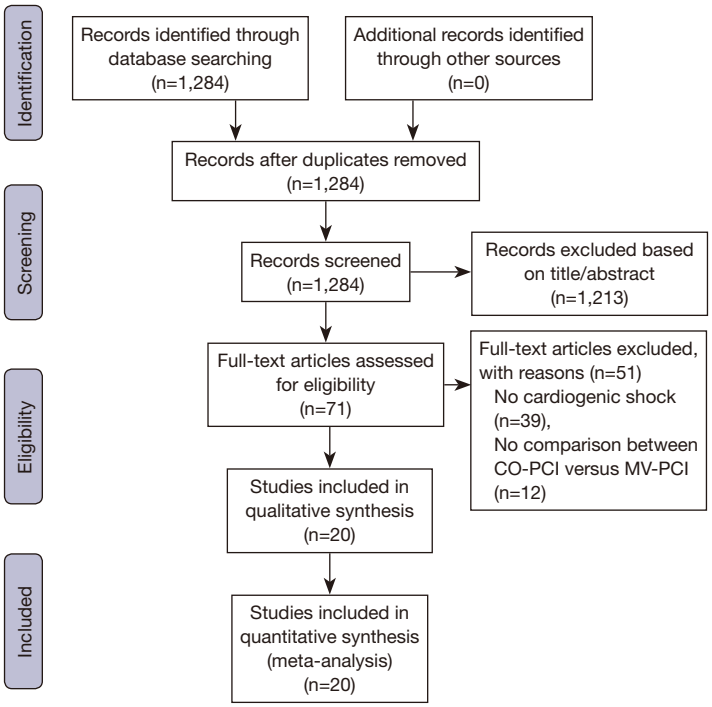

Figure 1 PRISMA flow of the study search and included studies. CABG, coronary artery bypass grafting; CO-PCI, culprit-only percutaneous coronary intervention; MV-PCI, multivessel percutaneous coronary intervention; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Outcomes

The primary outcomes for this meta-analysis were all-cause mortality and renal failure on the basis of the definition of separative studies. Secondary outcomes included MACE (major adverse cardiovascular events), cardiac death, myocardial infarction, heart failure, and any revascularization. Safety outcomes including major bleeding and stroke were also investigated. Subgroup analysis according to short- (≤30 days) and long-term (≥6 months) follow-up were also investigated.

Statistical analysis

We extracted raw, unadjusted statistics from each included study. By using Random-effects models of DerSimonian and Laird, we established summary estimate odds ratio (OR) and 95% confidence interval (CI) for the defined endpoints. Heterogeneity across trials was assessed by using the I^2 statistic, with I^2 less than 25% considered low, 25% to 75% moderate, and I^2 more than 75% high. By using a leave-one-out analysis, the sensitivity analysis was performed to evaluate whether the summary results were affected by a single study. Meanwhile, the only randomized CULPRIT-SHOCK trial (2) was added to the results based on observational studies to find out whether the results were influenced by the randomized trial. Publication bias was assessed quantitatively by Egger's linear regression method test or visually by asymmetry in funnel plots. P value <0.05 was considered statistically significant. The meta-analysis was performed by using STATA software, version 14 (StataCorp., College Station, TX, USA).

Results

Selected studies and characteristics

Our original search yielded 1,284 articles, after excluding 1,213 irrelevant articles according to titles or abstracts, 71 articles with full text were assessed for eligibility. Among the 71 articles, 51 articles were excluded for the following reasons: no cardiogenic shock, n=39, no comparison between CO-PCI versus MV-PCI, n=12. Eventually, a total of 18 observational studies and 2 randomized trials (the same trial) were included in our meta-analysis based on defined inclusion criteria (*Figure 1*). Of the included studies,

MV-PCI was all performed in an immediate procedure. As shown in *Table 1*, among the 73,528 STEMI patients with MVD complicated by cardiogenic shock, 48,611 (66.1%) patients received CO-PCI, whereas only 24,917 (33.9%) patients received immediate MV-PCI. Of the included observational studies, 14 were multicenter studies and 4 were single center studies, 10 were prospective and 8 were retrospective studies. MVD was defined using different criteria including stenosis ≥50% in ≥2 major epicardial coronary arteries, ≥70% in ≥2 major epicardial coronary arteries, or left main (LM) stenosis was also defined as two vessel disease. Baseline characteristics of included patients are detailed in Table S1.

Primary outcomes

Analyses of all-cause mortality revealed that there were no significant differences with CO-PCI compared with immediate MV-PCI during short-term (OR: 0.96; 95% CI: 0.82 to 1.14; I^2=72.2%) and long-term (OR: 1.10; 95% CI: 0.88 to 1.36; I^2=78.0%) follow-up (*Figure 2*). However, CO-PCI strategy could significantly reduce the risk of short-term renal failure (OR: 0.75; 95% CI: 0.64 to 0.88; I^2=14.7%) relative to immediate MV-PCI strategy, without benefit observed during long-term follow-up (OR: 0.84; 95% CI: 0.37 to 1.92; I^2=29.1%; *Figure 3*).

Secondary and safety outcomes

Secondary outcomes including MACE, cardiac death, myocardial infarction, heart failure, and any revascularization as well as safety outcomes including major bleeding and stroke are detailed in *Figure 4*. In summary, there was a trend indicating that CO-PCI decreased short-term (OR: 0.79; 95% CI: 0.62 to 1.02; I^2= NA) but increased long-term MACE (OR: 1.08; 95% CI: 1.00 to 1.18; I^2=0.0% *Figure 4A*) relative to immediate MV-PCI. Meanwhile, CO-PCI could increase the risk of myocardial infarction compared with immediate MV-PCI (OR: 1.12; 95% CI: 1.03 to 1.22; I^2=0.0%; *Figure 4C*). However, the short-term outcomes indicated that CO-PCI could decrease the risk of stroke (OR: 0.86; 95% CI: 0.77 to 0.96; I^2=0.0%; *Figure 4G*). There were no significant differences in other outcomes.

Sensitivity and publication bias analyses

The sensitivity analyses by using a leave-one-out analysis were consistent with the main analyses (Figure S1). The risks of all-cause mortality (Figure S2), renal failure (Figure S3), secondary and safety outcomes (Figure S4) remained concordant after adding the only randomized trial. Moreover, considering the fact that including prospective and retrospective studies in the same analysis may increase the probability of selection bias, a separate analysis of prospective versus retrospective, single center versus multicenter studies was performed. Subgroup analyses of clinical outcomes based on study type can be found in Figure S5. The lower risk of stroke with CO-PCI was mainly confined to retrospective studies (OR: 0.58; 95% CI: 0.34 to 0.99; I^2=0.0%; Figure S5C). CO-PCI could reduce the risk of renal failure both in multicenter (OR: 0.74; 95% CI: 0.65 to 0.85; I^2=11.0%) and prospective studies (OR: 0.75; 95% CI: 0.65 to 0.86; I^2=7.8%) compared with immediate MV-PCI (Figure S5E). There was no evidence of publication bias with funnel plots (Figure S6) or Begg's test (Figure S7) for any of the above outcomes assessed.

Discussion

This meta-analysis that compared CO-PCI versus immediate MV-PCI in STEMI patients with MVD and complicated by cardiogenic shock provides a comprehensive aggregate analysis of the available observational studies to date. In analyses based on real-world data, compared with immediate MV-PCI, CO-PCI reduced short-term risks of renal failure and stroke, whereas the short-term risk of myocardial infarction was also increased. The outcomes of short- and long-term all-cause mortality, MACE, cardiac death, heart failure, revascularization, as well as major bleeding were similar between the two groups. The results remained consistent after adding the only randomized trial.

Cardiogenic shock is a serious condition featured by myocardial dysfunction derived from massive myocardium ischemia, increased diastolic stiffness, as well as rapid development of hypoxia, hypotension, tachycardia, and pulmonary congestion (32). In addition, activation of the inflammatory cascade further exacerbates the development vasodilation, hypotension, and hypoperfusion (33). Therefore, considering the low aortic pressure and high left ventricular end-diastolic pressure in patients complicated by cardiogenic shock, it is speculated that immediate MV-PCI can improve myocardial perfusion and ventricular function, and hence enable patients to recover from cardiogenic shock. However, it is worthwhile to note that immediate MV-PCI may also lead to harm because of the

Table 1 Baseline characteristics of included studies [reproduced with permission from (14)]

First author; year	Study period	Sample size		Study design	Definition of MVD	Definition of cardiogenic shock	Exclusion criteria	Primary endpoint(s)	Follow-up
		CO-PCI	MV-PCI						
Cavender (15); 2009	2004–2007	2,654	433	Multicenter, retrospective	CAD in >1 major artery	SBP <80 mmHg and/or CI <1.8 L/min/m^2 despite maximal treatment, requiring intravenous inotropes and/or an IABP to maintain the SBP >80 mmHg and/or CI >1.8 L/min/m^2	LM, staged PCI, thrombolytics	All-cause death, stroke, renal failure, bleeding	In-hospital
van der Schaaf (16); 2010	1997–2005	124	37	Single center, retrospective	LM stenosis ≥50% or stenosis >50% in ≥1 major non-IRA	SBP ≤90 mmHg for ≥30 min, require vasopressors to maintain BP >90 mmHg, end organ hypoperfusion (e.g., urine output <30 mL, cold/ diaphoretic extremities, altered mental status), and elevated filling pressures (e.g., pulmonary congestion)	NA	All-cause death	1 year
Bauer (17); 2012	2005–2008	254	82	Multicenter, retrospective	stenosis ≥70% in ≥2 major epicardial vessels	SBP ≤90 mmHg for ≥30 min, need inotropes to maintain SBP >90 mmHg, end-organ hypoperfusion, and increased filling pressures	Prior GABG, LM disease	All-cause death	In-hospital
Cavender (18); 2013	2002–2010	32	32	Single center, retrospective	stenosis ≥50% in ≥2 major epicardial vessels	Sustained SBP <90 mmHg, CI <2.2 L/min/m^2, need parenteral inotropic, vasopressor agents or mechanical support to maintain SBP and CI above specified levels	Indications for surgery (e.g., significant valvular heart disease, mechanical complications of MI)	All-cause death	5 years
Mylotte (19); 2013	1998–2010	103	66	Multicenter, prospective	Stenosis ≥70% in a major (≥2.5 mm) non-IRA, distal LM lesion with significant stenosis of the ostia of both the daughter arteries	SBP <90 mmHg for >30 min, require supportive measures to maintain BP ≥90 mmHg, and end-organ hypoperfusion (cool extremities, urine output <30 mL/hr, and a heart rate ≥60 beats/min)	Further resuscitation was futile, other cause of shock, mechanical complication of MI	A composite of all-cause death, death because of cardiogenic shock, and recurrent cardiac arrest, and separative endpoints	6 months
Jaguszewski (20); 2013	2005–2012	158	85	Multicenter, retrospective	stenosis ≥50% in ≥2 major coronary arteries and/or the LM involved	Killip class IV	NA	MACCE, all-cause death, MI, stroke	In-hospital

Table 1 (*continued*)

Table 1 (*continued*)

First author; year	Study period	Sample size		Study design	Definition of MVD	Definition of cardiogenic shock	Exclusion criteria	Primary endpoint(s)	Follow-up
		CO-PCI	MV-PCI						
Yang (21); 2014	2005–2010	278	60	Multicenter, prospective	≥50% stenosis in ≥1 major non-IRA	SBP persistently <90 mmHg, require vasopressors to maintain BP >90 mmHg, hypoperfusion (e.g., urine output <30 mL/hr, cold/diaphoretic extremities, an altered mental status), and increased left ventricular filling pressure (e.g., pulmonary congestion)	No primary PCI, mechanical complications such as ventricular septal defect or mitral regurgitation, LM disease	All-cause death, cardiac death, MI, revascularization, MACE	224 days
Zeymer (22); 2015	2008–2011	562	173	Multicenter, retrospective	>50% stenosis of 2 or 3 major vessels	SBP <90 mmHg, heart rate >100 beats/min, and end organ hypoperfusion	LM disease, prior CABG	All-cause death, MI, stroke, bleeding, dialysis	In-hospital
Park (23); 2015	2006–2012	386	124	Multicenter, prospective	Stenosis ≥50% in ≥1 major non-IRA	SBP <90 mmHg for >30 min, need supportive management to maintain SBP ≥90 mmHg, end-organ hypoperfusion (cool extremities, urine output <30 mL/hr, altered mental status)	Initial vital signs information was missing, NSTEMI	All-cause death, cardiac death, MI, revascularization, MACE	194 days
Hambraeus (24); 2016	2006–2010	263	67	Multicenter, prospective	NA	NA	SVD, prior GABG, missing data for revascularization status and missing time for the procedure	All-cause death, MI, and revascularization	1 year
Zeymer (25); 2017	2009–2012	284	167	Multicenter, post hoc analysis of RCT	Stenosis >50% in ≥2 major coronary vessels	SBP <90 mmHg for >30 min, require catecholamines to maintain BP >90 mmHg, pulmonary congestion; impaired organ perfusion with ≥1 the following criteria: cold—clammy skin and extremities, oliguria with urine output <30 mL/hr, serum lactate >2.0 mmol/L, altered mental status	Severe cerebral deficit, resuscitation >30 min, mechanical causes of cardiogenic shock, shock of other cause, onset of shock >12 hr, severe peripheral artery disease, life expectancy <6 months, age >90 years	All-cause death, MI, renal replacement, bleeding	1 year
McNeice (26); 2018	2008–2014	414	235	Multicenter, retrospective	Stenosis >70% in ≥2 epicardial coronary arteries	SBP <90 mmHg for 30 min, require inotropic or mechanical support to maintain BP and adequate systemic perfusion, secondary to cardiac dysfunction	LM disease	All-cause death	1 year

Table 1 (*continued*)

Table 1 (*continued*)

First author; year	Study period	Sample size		Study design	Definition of MVD	Definition of cardiogenic shock	Exclusion criteria	Primary endpoint(s)	Follow-up
		CO-PCI	MV-PCI						
Lee (12); 2019	2011–2015	399	260	Multicenter, prospective	Stenosis ≥50% ≥1 major non-IRA or LM involved	SBP <90 mmHg for >30 min, need supportive management to maintain SBP >90 mmHg, pulmonary congestion, impaired end-organ perfusion with ≥1 the following criteria: decreased urine output, increased lactic acid level, cool extremities, or altered mental status	Lost to follow-up, symptom onset >12 hr, thrombolysis, suboptimal or failed PCI for IRA	All-cause death, MI, cardiac death, revascularization, stent thrombosis	3 years
Petrovic (27); 2019	2007–2016	142	28	Single center, retrospective	NA	SBP <90 mmHg for 30 min, require vasopressors to maintain SBP ≥90 mmHg; pulmonary congestion or elevated left ventricular filling pressures; tissue perfusion with ≥1 the following criteria: cold, sticky skin, oliguria (<0.5 mL/kg/h), elevated serum lactate (>1.5 mmol/L), altered mental status,	Failed primary PCI or fatal outcome during intervention	In-hospital mortality	In-hospital
Lemor (28); 2020	2016–2019	39	69	Multicenter, prospective,	Stenosis of >70% in 2 or more epicardial coronary arteries	Presence of ≥2 the following criteria: hypotension (SBP <90 mmHg, require inotropes/vasopressors to maintain SBP >90 mmHg); end-organ hypoperfusion (cool extremities, oliguria or anuria, or elevated lactate levels); or hemodynamic criteria of cardiogenic shock (cardiac index <2.2 L/min/m^2 or cardiac power output <0.6 W)	NA	Hospital survival	In-hospital
Khera (29); 2020	2009–2018	41,883	22,418	Multicenter, prospective	Stenosis of 70% or greater in 2 or more epicardial coronary arteries other than the left main, where a stenosis of 50% or more was considered obstructive	Sustained (>30 min) episode of SBP <90 mmHg and/or a CI I<2.2 L/min/m^2 secondary to cardiac dysfunction, require parenteral inotropic or vasopressor agents or mechanical support to maintain blood pressure and CI above those levels	Patients had CABG	In-hospital mortality	1 year

Table 1 (*continued*)

Table 1 (*continued*)

First author; year	Study period	Sample size		Study design	Definition of MVD	Definition of cardiogenic shock	Exclusion criteria	Primary endpoint(s)	Follow-up
		CO-PCI	MV-PCI						
Rathod (30); 2020	2005–2015	561	497	Multicenter, prospective	Stenosis ≥ 75% in ≥2 major epicardial arteries	SBP ≤90 mmHg due to cardiac insufficiency with hypoperfusion (cold extremities, oliguria, altered mental state etc.), not responsive to fluid resuscitation for ≥30 min, with a CI <1.8 L/min/m^2 without support or 2.0 to 2.2 L/min/m^2 with support	Patients with chronic total occlusions	All-cause death	4.1 years
Vergara (31); 2021	1995–2016	159	93	Single center, retrospective	Additional >70% diameter stenosis in ≥1 major non-IRA or in the LM	SBP <90 mmHg for >30 min, use catecholamine or intra-aortic baloon support to maintain SBP ≥90 mmHg, end-organ hypoperfusion (cold or diaphoretic extremities, altered mental status or anuria)	Admission >24 h from symptom onset without ongoing ischemia, hemodynamic stability, suboptimal or failed PCI, thrombolysis before PCI, stenosis <70% in IRA, single vessel coronary artery disease	2-year all-cause death	2 years
Thiele (2,9); 2018	2013–2018	344	313	Multicenter, randomized, open-label	Stenosis >70% in ≥2 major vessels (≥2 mm in diameter)	SBP <90 mmHg for >30 min, use catecholamine therapy to maintain SBP ≥90 mmHg, pulmonary congestion, and impaired organ perfusion with ≥1 the following criteria: oliguria with urine output <30 mL/hr, arterial lactate level >2.0 mmol/L, altered mental status, cold and clammy skin and limbs	Resuscitation >30 min, no intrinsic heart action, indication for primary CABG, severe deficit in cerebral function, shock with a noncardiogenic cause, shock >12 hr before randomization, life expectancy <6 months, age >90 years, pulmonary embolism, renal insufficiency	A composite of death from any cause or severe renal failure leading to renal-replacement therapy within 30 days after randomization	1 year

CABG, coronary artery bypass grafting; CAD, coronary artery disease; CI, cardiac index; CO-PCI, culprit-only percutaneous coronary intervention; IABP, intra-aortic balloon pump; IRA, infarct related artery; LM, left main coronary artery; MACE, major adverse cardiovascular events; MACCE, major adverse cardiac and cerebrovascular events; MI, myocardial infarction; MVD, multivessel coronary artery disease; MV-PCI, multivessel percutaneous coronary intervention; NA, not available; NSTEMI, non-ST-segment elevation myocardial infarction; RCT, randomized controlled trial; SBP, systolic blood pressure; SVD, single-vessel disease.

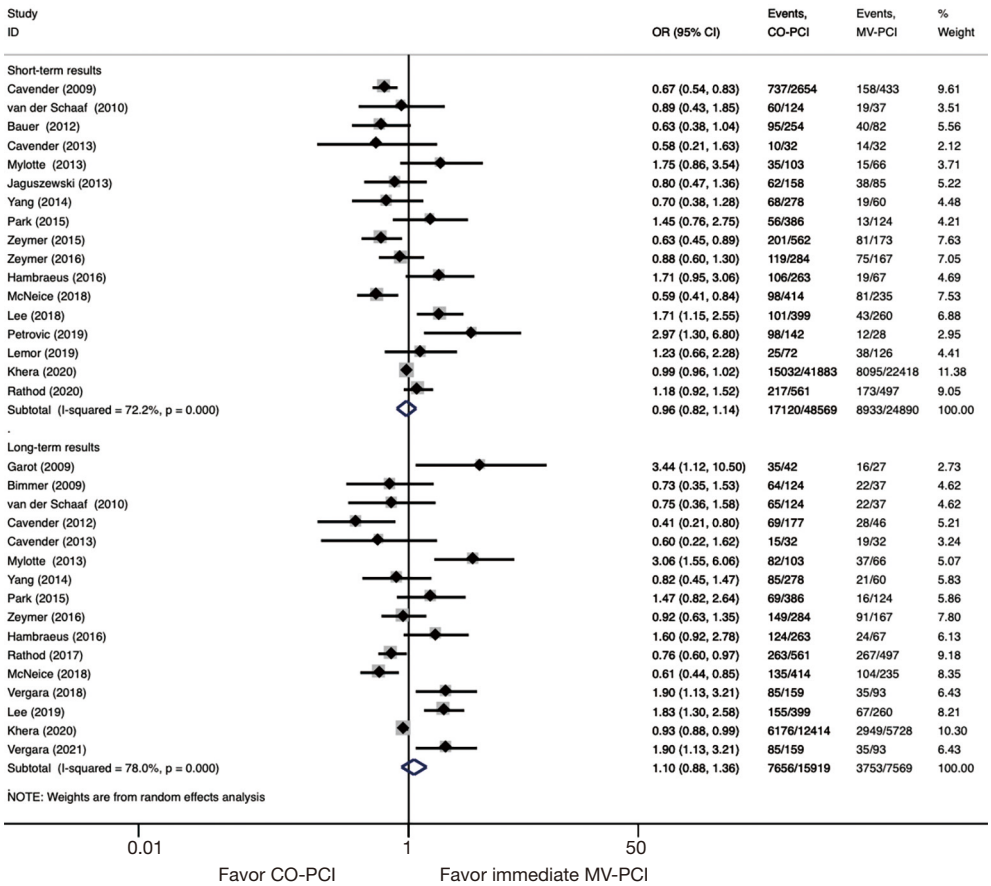

Figure 2 Forest plot of all-cause mortality.

highly prothrombotic and inflammatory milieu, increased procedural time, more contrast use (34), and potential periprocedural complications in the non-IRA. These potential harm may result in higher risks of myocardial infarction and stent thrombosis, even increase the risk of all-cause mortality.

Currently, a large amount of large-scale randomized clinical trials including PRAMI (35), CvLPRIT (36), DANAMI-3-PRIMULTI (37), COMPARE-ACUTE (38), COMPLETE (39) trials, together with meta-analyses (40,41) all suggested that MV-PCI performed in an immediate or staged manner was better than CO-PCI in decreasing the risks of MACE, cardiovascular death, myocardial infarction, and revascularization. However, the problem is that patients with cardiogenic shock were excluded from these randomized trials. Therefore, physicians are supposed to arise awareness about the potential harms associated with MV-PCI when extrapolating these evidence to unstudied populations with cardiogenic shock.

In the largest randomized CULPRIT-SHOCK trial conducted in 83 European centers (2,9), 706 patients with cardiogenic shock were randomly assigned to CO-PCI group (n=351) or immediate MV-PCI group (n=355). During 30-days follow up, the primary outcome defined as the composite of death and renal-replacement therapy was lower with the CO-PCI arm when compared with the immediate MV-PCI arm (45.9% *vs.* 55.4%; RR: 0.83; 95% CI: 0.71 to 0.96; P=0.01). In addition, the incidences of death (43.3% *vs.* 51.6%; RR: 0.84; 95% CI: 0.72 to 0.98; P=0.03) was also lower with CO-PCI arm, without significant difference in renal-replacement therapy (11.6% *vs.* 16.4%; RR: 0.71; 95% CI: 0.49 to 1.03; P=0.07). Concordant with the CULPRIT-SHOCK trial, the CathPCI Registry including 64,301 patients also suggested that in-hospital complications (OR: 1.18; 95% CI: 1.14 to 1.23) was also higher in MV-PCI group when compared with CO-PCI group (29). It is postulated that

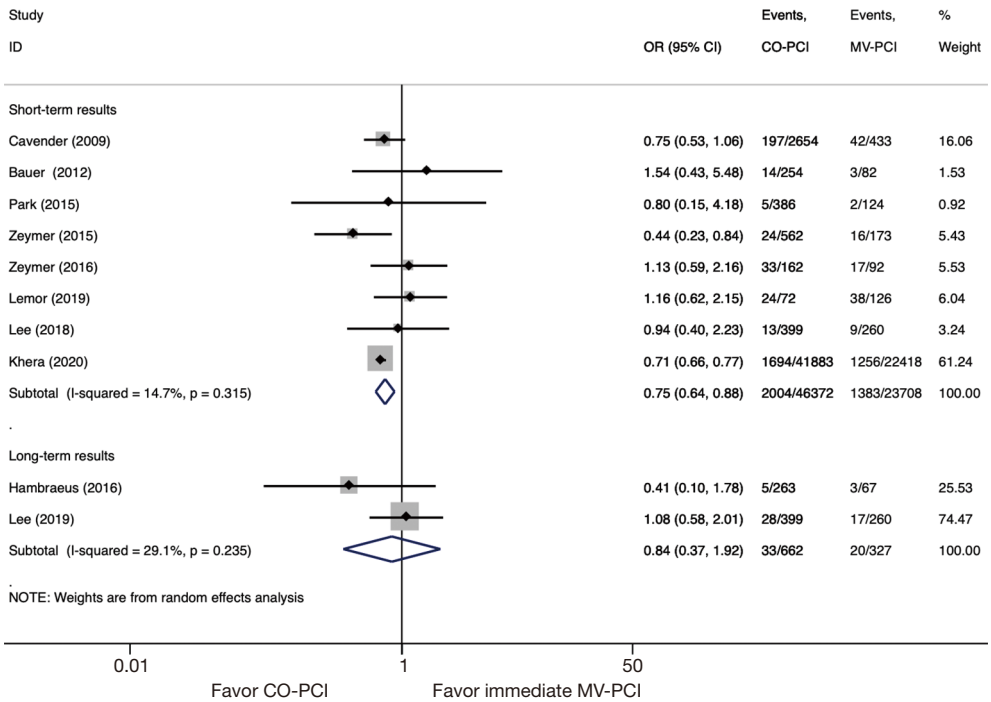

Figure 3 Forest plot of renal failure.

prolonged procedures in MV-PCI group are associated with more blood loss and higher load of iodinated contrast, especially for these patients who already have hemodynamic derangements. Moreover, performing non-IRA PCI may lead to potential procedure-related complications or myocardial injury, these complications or myocardial injury may offset the short-term benefit associated with additional revascularization. At one year, however, the CULPRIT-SHOCK trial indicated that the rate of death (50.0% *vs.* 56.9%; RR: 0.88; 95% CI: 0.76 to 1.01) and renal-replacement therapy (11.6% *vs.* 16.4%; RR: 0.71; 95% CI: 0.49 to 1.03) were similar between CO-PCI versus immediate MV-PCI arms, yet rehospitalization due to heart failure (5.2% *vs.* 1.2%; RR: 4.46; 95% CI: 1.53 to 13.04) and revascularization (32.3% *vs.* 9.4%; RR: 3.44; 95% CI, 2.39 to 4.95) occurred more frequently with CO-PCI arm. Therefore, in the high-risk STEMI patients with MVD and complicated by cardiogenic shock, it is not suggested to perform immediate MV-PCI due to higher incidence of 30-day all-cause mortality. However, just performing CO-PCI may increase the long-term risks of rehospitalization for heart failure and revascularization. In that case, staged MV-PCI, which perform CO-PCI in the early stage and revascularize non-IRA at a later time, maybe the optimal option. An international survey including a total of 143 participants suggested that confronted with STEMI patients with MVD complicated by cardiogenic shock, 55.2% of participants chose to revascularize IRA with staged PCI of non-IRA (staged MV-PCI). CO-PCI (28.0%), immediate MV-PCI (11.9%), and CABG (4.9%) were standard approaches at some centers (42). In our meta-analysis based on real-world analyses, the short-term myocardial infarction was increased in CO-PCI group, which indicated that after CO-PCI, staged PCI of non-IRA are supposed to be performed to reduce the risk of myocardial infarction. However, the potential role of staged PCI has not yet been established in a cardiogenic shock population, which should be evaluated in further studies. Moreover, although CO-PCI could reduce the risk of stroke relative to immediate MV-PCI, yet the reduced risk was mainly confined to retrospective studies without significant differences in prospective studies. Therefore, further studies are needed to confirm the influence of immediate MV-PCI on stroke.

Limitations

First, the 18 included observational studies had limitations

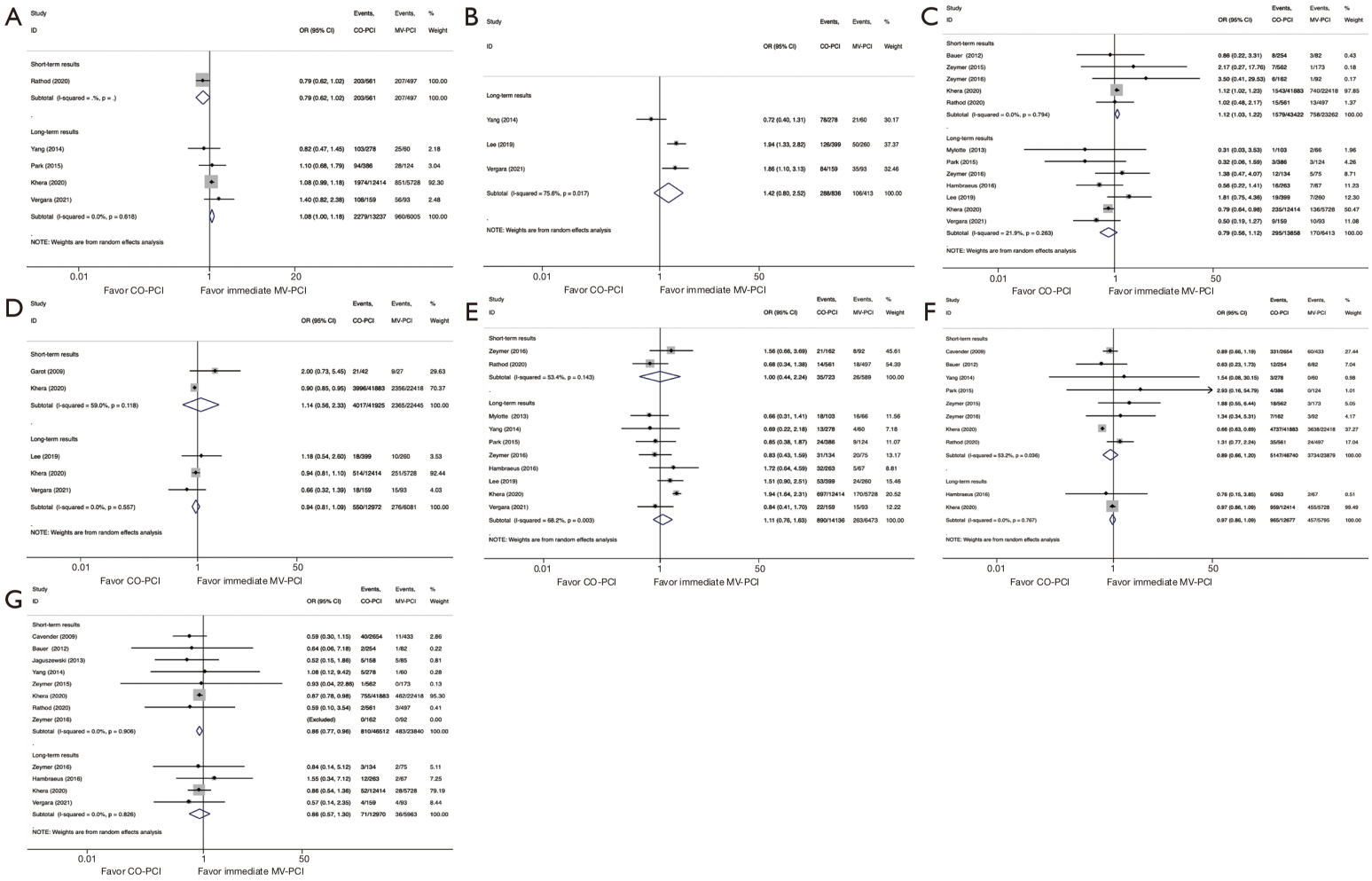

Figure 4 Forest plot of secondary outcomes defined as MACE (A), cardiac death (B), myocardial infarction (C), heart failure (D), revascularization (E), major bleeding (F), and stroke (G). MACE, major adverse cardiovascular events.

inherent to observational studies such as selection bias and unmeasured confounding. However, these data reflected the real-world scenario in clinical practice. Second, the differences in study period, design, sample size, definition of MVD, exclusion criteria, and follow-up time may increase study heterogeneity and limit the generalization of our conclusions. As shown in the short- (I^2=72.2%) and long-term (I^2=78.0%) all-cause mortality, the heterogeneity was high. We tried to mitigate the heterogeneity by using a random effects model. Meanwhile, subgroup analysis was performed according to follow up time and study type. Third, the study carried out by Khera *et al.* (29) contained the largest number of patients (64,301, 87.5%), which may lead to bias for the results of our meta-analysis. However, after excluding the largest study, similar results were still observed. Fourth, data about the severity of shock or hemodynamic parameters were not systematically reported, and records about revascularization success were deficient, which restrained us to complete confounding factors evaluation and draw solid conclusions. Therefore, further studies, especially randomized trials are needed to confirm or refute our conclusions.

Conclusions

Our meta-analysis shows that in STEMI patients with MVD complicated by cardiogenic shock, CO-PCI could reduce the risks of renal failure and stroke, but increase the risk of myocardial infarction compared with immediate MV-PCI. Similarly, the results in randomized trial also indicated that CO-PCI decreased the short-term composite primary endpoint of death or renal-replacement therapy, yet increased long-term risk of rehospitalization for heart failure and revascularization. Based on these results, CO-PCI should be considered at the time of primary PCI in STEMI patients with MVD complicated by cardiogenic shock, and if feasible in clinical practice, MV-PCI in a staged procedure can be considered to decrease long-term risks of myocardial infarction, heart failure and revascularization.

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Footnote

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Supplementary

Table S1 Baseline characteristics of included patients

First Author; Year	Group	Age (years)	Male (%)	Hypertension (%)	Hyperlipidemia (%)	Diabetes (%)	Smoking (%)	Heart rate (beats/min)	SBP (mm Hg)	LVEF	Three vessel disease (%)
Cavender (15), 2009	CO-PCI; MV-PCI	66.312.8; 66.413.0	64.7; 64.2	63.4; 59.8	50.7; 50.6	27.3; 30.5	62.1; 56.1	NA	NA	NA	NA
van der Schaaf (16), 2010	CO-PCI; MV-PCI	67.411.4; 6713.3	67.7; 81.1	25.8; 29.7	24.2; 24.3	21.8; 24.3	29.8; 29.7	NA	NA	NA	53.2; 62.2
Bauer (17), 2012	CO-PCI; MV-PCI	65.412.2; 67.212.2	68; 71	67; 60	55; 47	35; 40	54; 55	NA	NA	NA	46; 51
Cavender (18), 2013	CO-PCI; MV-PCI	6613; 6314	62; 72	79; 72	24; 16	31; 35	71; 67	8521; 9427	10726; 10623	3214; 249	52; 51
Mylotte (19), 2013	CO-PCI; MV-PCI	68.511.8; 6512.4	71.9; 75.8	48.5; 53	40.8; 45.5	25.2; 25.8	31.1; 34.8	9821.2; 9520	8321.2; 8215.7	30.39; 319.6	47.6; 51.5
Jaguszewski (20), 2013	CO-PCI; MV-PCI	6511.2; 64.711.7	74.7; 77.6	61.1; 56.5	57.9; 39.7	25; 26.1	54.5; 57.1	NA	NA	NA	NA
Yang (21), 2014	CO-PCI; MV-PCI	70; 57	57.9; 63.3	57.9; 50	23.4; 21.7	16.5; 21.7	35.6; 40	66.532.7; 71.835.2	8339; 87.633.8	45.913.9; 48.515.3	44.2; 46.7
Zeymer (22), 2015	CO-PCI; MV-PCI	70; 68	71; 72	78; 81	69; 69	35; 39	39; 32	NA	NA	NA	62; 70
Park (23), 2015	CO-PCI; MV-PCI	68; 65.5	65.8; 71	54.5; 53.7	9.7; 9.8	23.3; 25.6	46.6; 47.6	62; 66	80; 80	50.311.1; 49.815.3	39.9; 46
Hambraeus (24), 2016	CO-PCI; MV-PCI	71.310.9; 68.211.8	65.4; 67.2	39.5; 38.8	16.7; 22.4	23.6; 26.9	41.9; 49.3	NA	NA	NA	51.3; 25.4
Zeymer (25), 2017	CO-PCI; MV-PCI	6812; 6912	29.9; 26.3	75.1; 67.5	39.9; 42.2	32.4; 40.1	36.2; 28.3	9026; 9627	9223; 9722	3514.8; 34.613.7	62; 72.5
McNeice (26), 2018	CO-PCI; MV-PCI	NA	75.4; 75.3	58.6; 59.5	41.6; 46.5	29.9; 34.6	27.4; 19.1	NA	NA	29.3; 30.9	NA
Lee (12), 2019	CO-PCI; MV-PCI	67.312.8; 66.212.4	74.9; 73.5	54.6; 52.3	46.6; 46.9	40.9; 41.2	36.3; 40.4	NA	NA	4712.7; 44.313.2	33.3; 33.8
Petrovic (27), 2019	CO-PCI; MV-PCI	64.5; 70.0	89.3; 52.1	50.0; 60.6	32.1; 19.7	28.6; 30.3	21.4; 34.5	NA	NA	35.0; 35.0	NA
Lemor (28), 2020	CO-PCI; MV-PCI	63.311.6; 64.811.8	76.4; 81.8	NA	NA	55.1; 55.4	NA	95; 99	98; 95	NA	50.7; 49.2
Khera (29), 2020	CO-PCI; MV-PCI	66.6; 65.9	68.2; 68.5	71.4; 71.9	58.0; 59.8	31.7; 35.0	34.5; 31.4	NA	NA	NA	NA
Rathod (30), 2020	CO-PCI; MV-PCI	68.112.9; 66.513.2	76.6; 82.7	48.7; 41.6	3.7; 34.0	20.7; 19.5	37.1; 35.2	NA	NA	NA	45.0; 43.3
Vergara (31), 2021	CO-PCI; MV-PCI	70.512.7; 69.712.4	68.6; 66.7	45.3; 39.8	27.7; 30.1	23.3; 29.0	30.8; 28.0	NA	NA	29.59.6; 29.68.2	49.7; 62.4
Thiele (2,9), 2018	CO-PCI; MV-PCI	70; 70	74.9; 78.1	59; 61.5	33.1; 34.8	30.3; 34.6	25.4; 27.4	90; 91	85-130; 83-120	33; 30	63.6; 63.2

CO-PCI, culprit-only percutaneous coronary intervention; LVEF, left ventricular ejection fraction; MV-PCI, multivessel percutaneous coronary intervention; NA, not available; SBP, systolic blood pressure.

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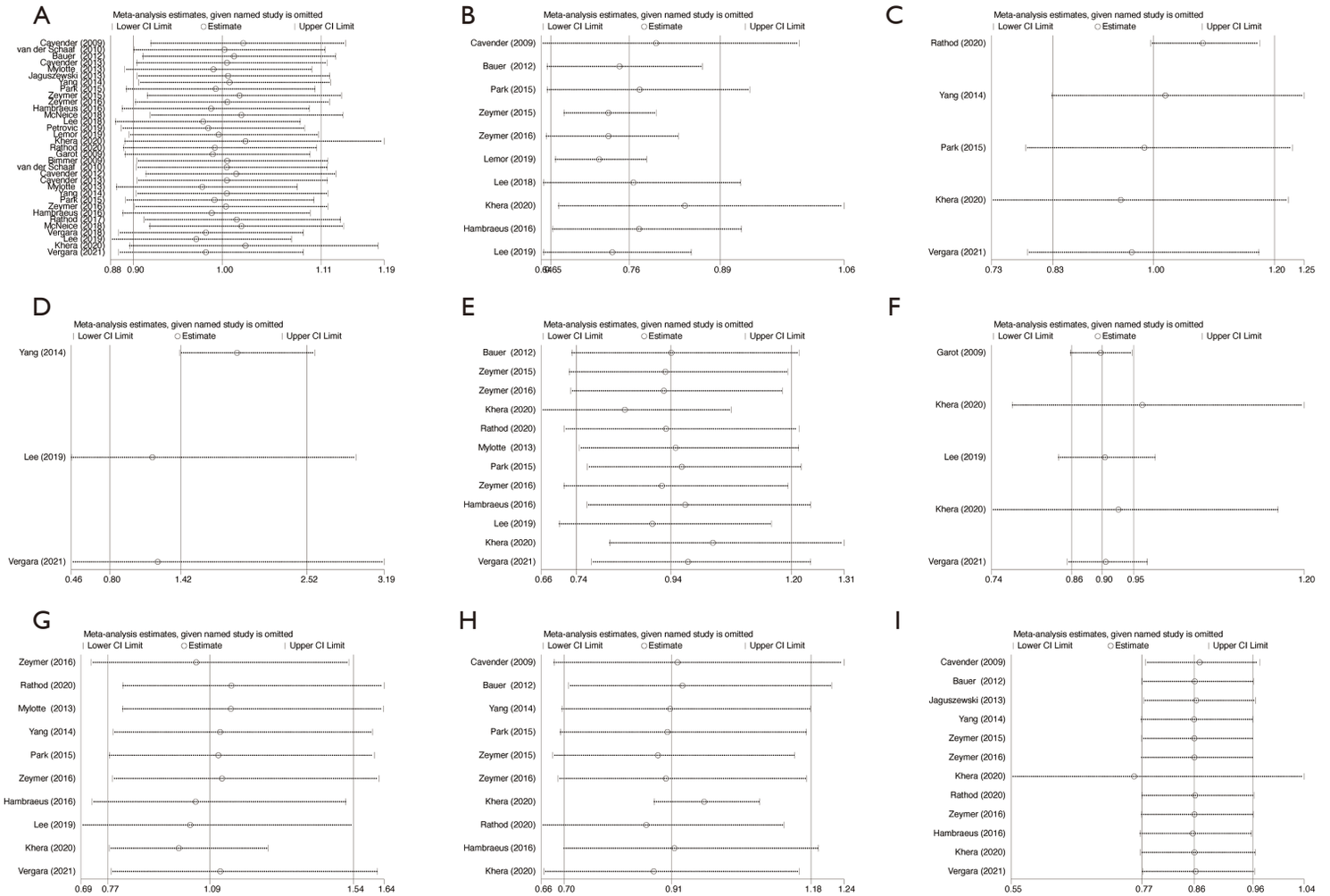

Figure S1 Sensitivity analyses of all-cause mortality (A), renal failure (B), major adverse cardiovascular events (C), cardiac death (D), myocardial infarction (E), heart failure (F), revascularization (G), bleeding (H), and stroke (I).

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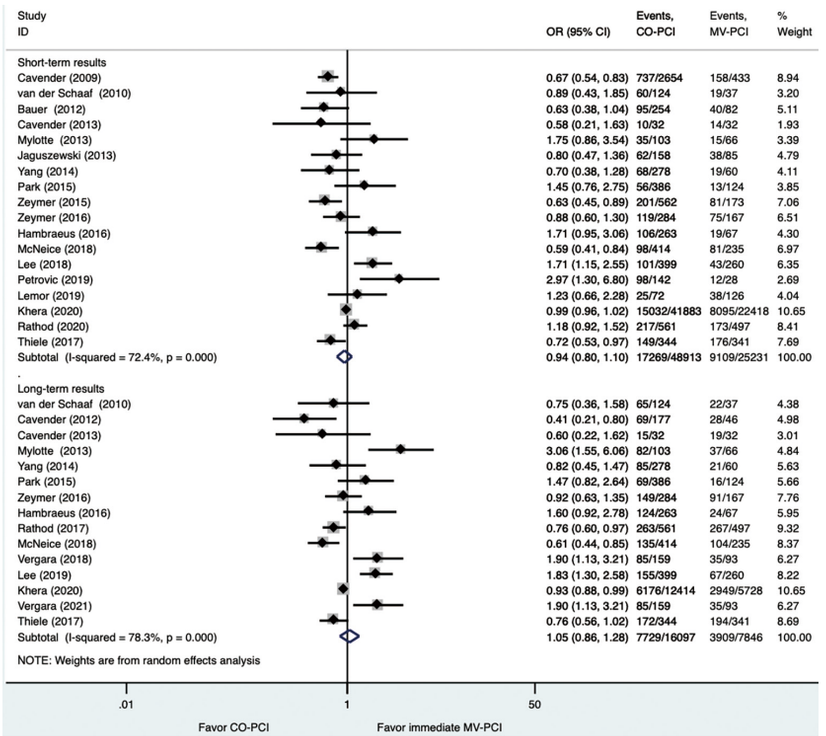

Figure S2 Analysis of all-cause mortality after adding randomized trial.

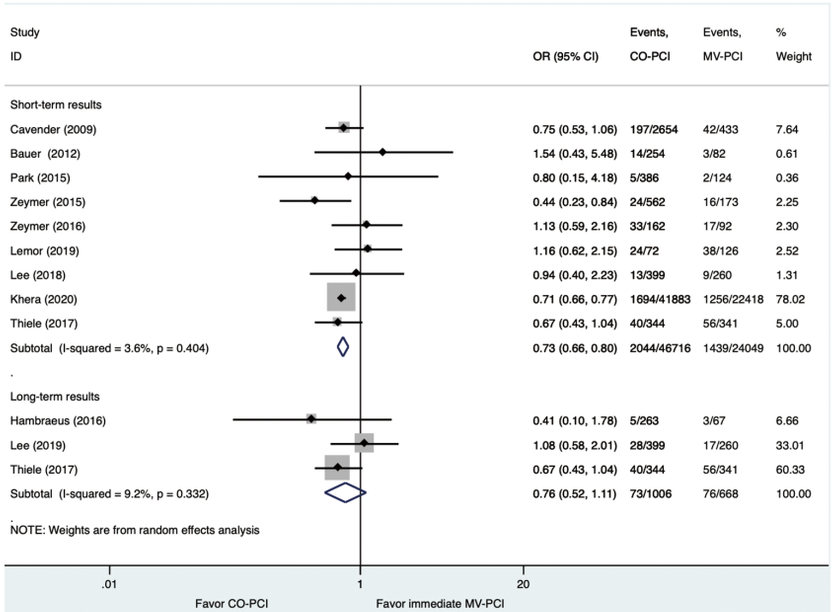

Figure S3 Analysis of renal failure after adding randomized trial.

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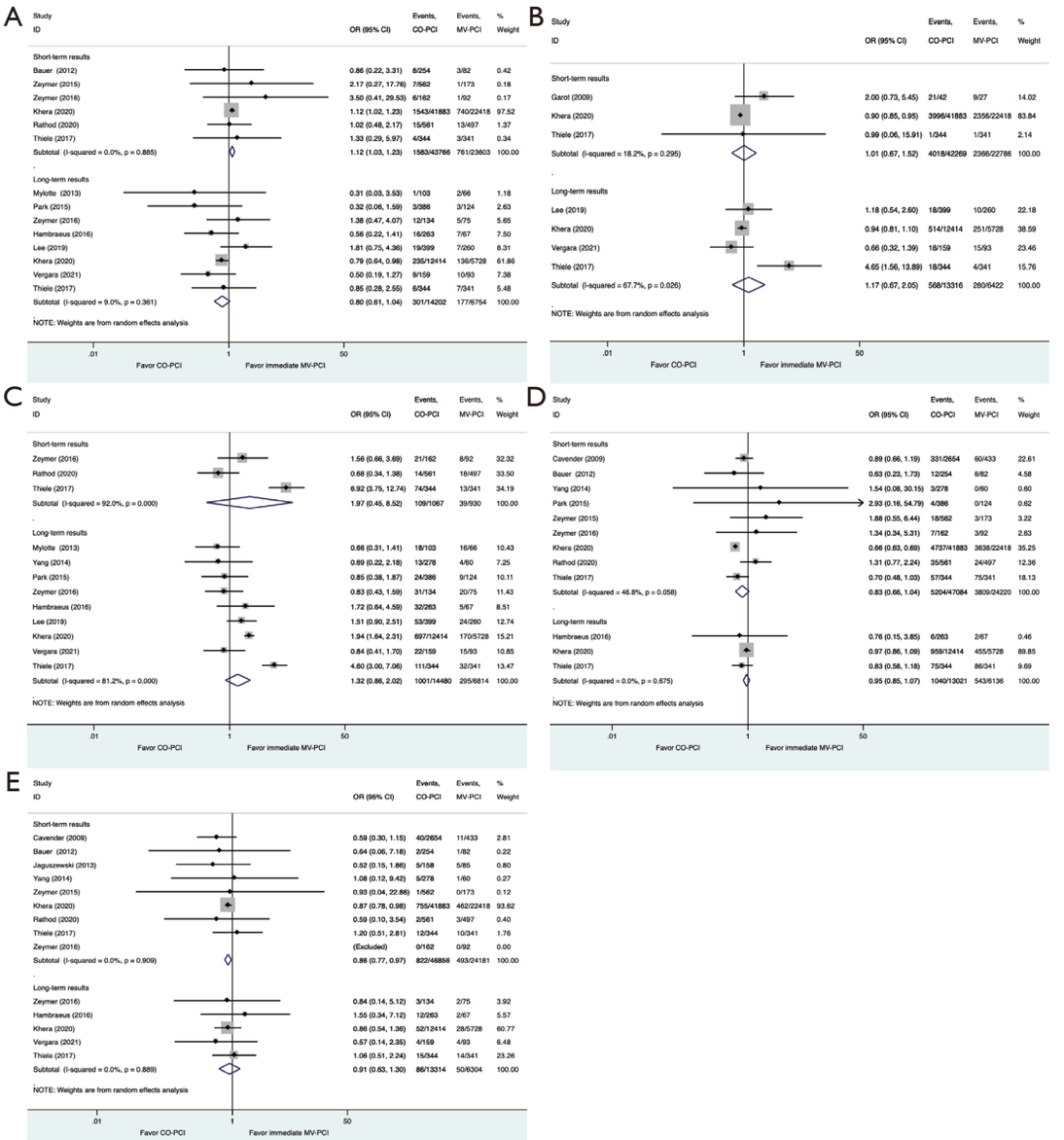

Figure S4 Analysis of myocardial infarction (A), heart failure (B), revascularization (C), bleeding (D), and stroke (E) after adding randomized trial.

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Figure S5 Subgroups analyses of all-cause death (A), myocardial infarction (B), stroke (C), revascularization (D), renal failure (E), bleeding (F), heart failure (G), cardiac death (H), and major adverse cardiovascular events (I) based on prospective versus retrospective, single center versus multicenter studies.

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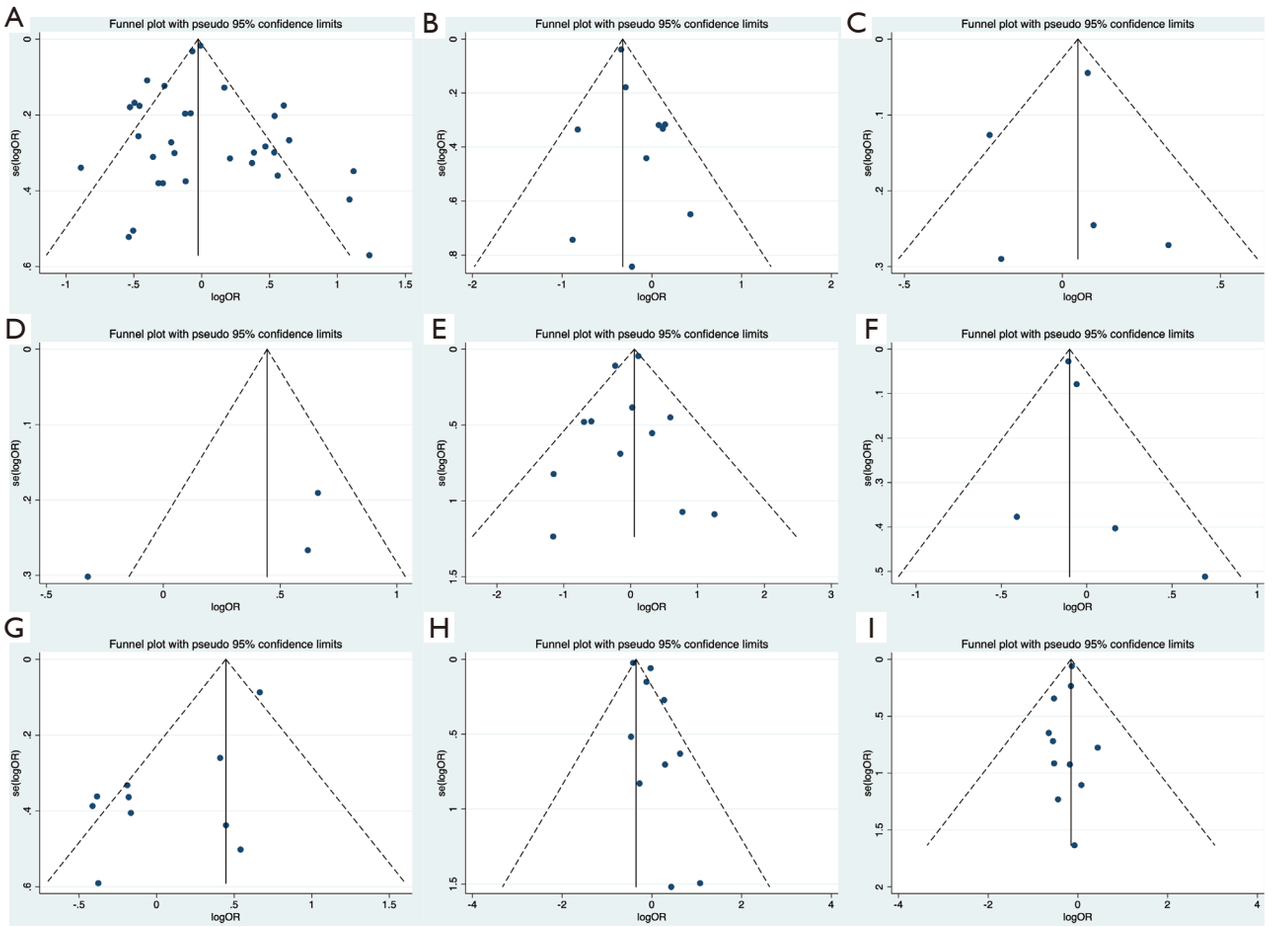

Figure S6 Funnel plot of all-cause mortality (A), renal failure (B), major adverse cardiovascular events (C), cardiac death (D), myocardial infarction (E), heart failure (F), revascularization (G), bleeding (H), and stroke (I).

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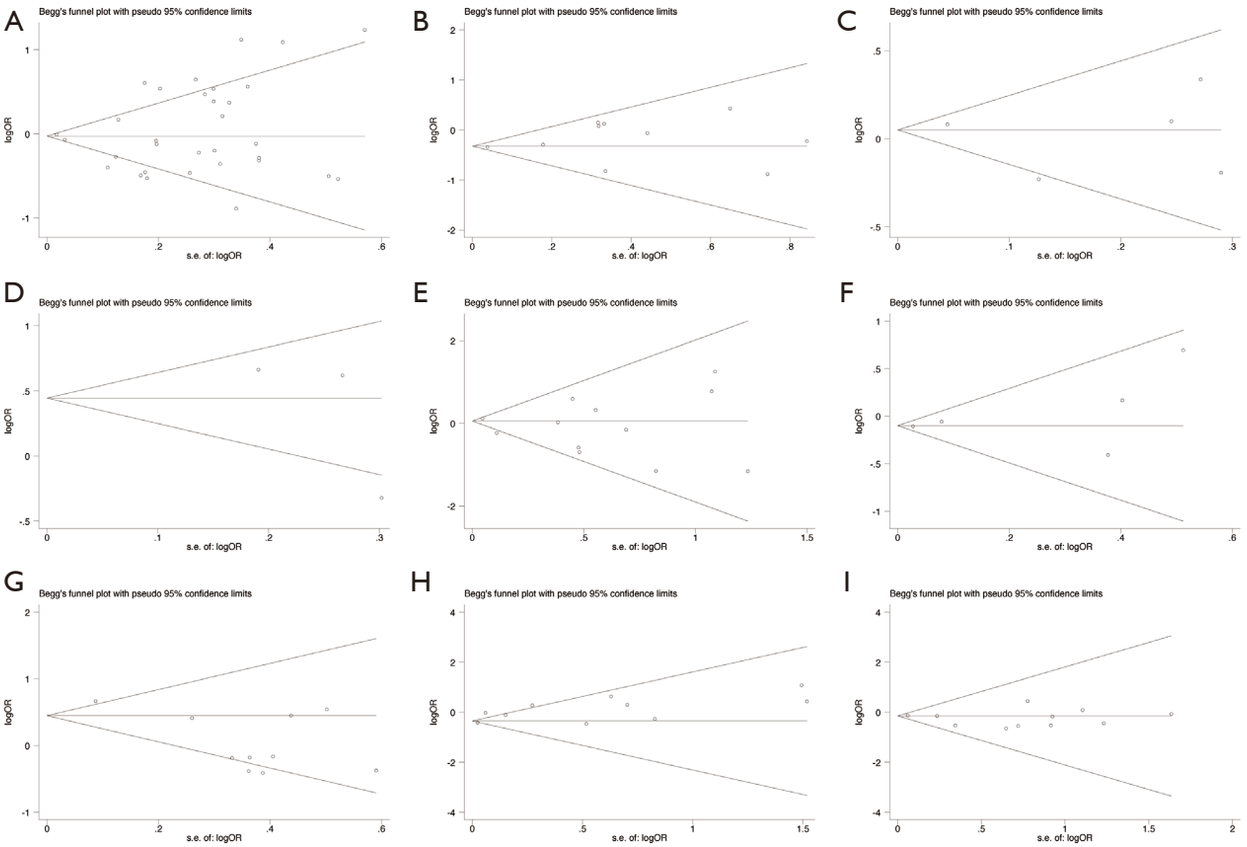

Figure S7 Begg's test of all-cause mortality (A), renal failure (B), major adverse cardiovascular events (C), cardiac death (D), myocardial infarction (E), heart failure (F), revascularization (G), bleeding (H), and stroke (I).

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