Meta-analysis Comparing Culprit Vessel Only Versus Multivessel Percutaneous Coronary Intervention in Patients With Acute Myocardial Infarction and Cardiogenic Shock

Muhammad Shahzeb Khan, MD[a], Tariq Jamal Siddiqi, MBBS[b], Muhammad Shariq Usman, MBBS[b], Haris Riaz, MD[c], Abdur Rahman Khan, MD[d], M. Hassan Murad, MD[e], Ankur Kalra, MD[f], Vincent M. Figueredo, MD[g,h], and Deepak L. Bhatt, MD, MPH[i,*]

Cardiogenic shock (CS) after a myocardial infarction continues to be associated with high mortality. Whether percutaneous coronary intervention (PCI) of noninfarct coronary arteries (multivessel intervention [MVI]) improves outcomes in CS after acute myocardial infarction (AMI) remains controversial. MEDLINE, Cochrane CENTRAL, and Scopus databases were searched for original studies comparing MVI with culprit-vessel intervention (CVI) in AMI patients with multivessel disease and CS. Risk ratios (RRs) and 95% confidence intervals were calculated and pooled using a random effects model. Thirteen studies, consisting of 7,906 patients ($n_{MVI} = 1,937$; $n_{CVI} = 5,969$), were included in this meta-analysis. Overall, the MVI and CVI groups did not differ significantly in the risk of short-term mortality (RR: 1.06 [0.91, 1.23]; p = 0.45; $I^2 = 75.82\%$), long-term mortality (RR: 0.93 [0.78, 1.11]; p = 0.37; $I^2 = 67.92\%$), reinfarction (RR: 1.16 [0.75, 1.79]; p = 0.50; $I^2 = 0\%$), revascularization (RR: 0.84 [0.48, 1.47]; p = 0.54; $I^2 = 83.01\%$), bleeding (RR: 1.15 [0.96, 1.38]; p = 0.09, $I^2 = 0\%$), or stroke (RR: 1.29 [0.86, 1.94]; p = 0.80, $I^2 = 0\%$). However, significantly increased risk of renal failure was seen in the MVI group (RR: 1.35 [1.10, 1.66]; p = 0.004; $I^2 = 0\%$). On subgroup analysis, it was seen that results from retrospective studies showed higher short-term mortality in the MVI group in comparison with prospective studies (p = 0.003). The certainty in estimates is low due to the largely observational nature of the evidence. In conclusion, MVI provides no additional reduction in short- or long-term mortality in AMI patients with multivessel disease and CS. Additionally, the risk of renal failure may be higher with the use of MVI. **(Am J Cardiol 2019;123:218−226)**

Cardiogenic shock (CS) is the leading cause of death in patients presenting with acute myocardial infarction (AMI).[1] In AMI patients without shock, multivessel intervention (MVI) appears to reduce the need for future revascularization.[2−4] It is debated whether AMI patients with multivessel disease (MVD) and CS should be treated with immediate percutaneous coronary intervention (PCI) of the culprit-vessel exclusively, or of all coronary arteries with clinically important stenoses. American College of Cardiology and/or American Heart Association guidelines recommend MVI in all hemodynamically unstable MVD patients.[5] However, this recommendation is based on conflicting results from observational studies.[6−16] Two previous meta-analyses have also shown varying results[17,18]; however, these were conducted before the publication of a recent large scale observational study (Lee, 2018), which favored MVI.[19] In contrast, the recent "Culprit Lesion Only PCI versus Multivessel PCI in Cardiogenic Shock (CULPRIT-SHOCK)" trial showed significantly lower mortality with culprit-vessel intervention (CVI) versus MVI.[20] In an attempt to resolve the inconsistencies, we pooled data from all available studies to date to compare the safety and efficacy of MVI versus CVI in patients with AMI, MVD, and CS.

Methods

This meta-analysis was reported in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analyses and the American Heart Association

[a]Department of Internal Medicine, John H. Stroger Jr. Hospital of Cook County, Chicago, Illinois; [b]Department of Internal Medicine, Dow University of Health Sciences, Karachi, Pakistan; [c]Department of Cardiology, Cleveland Clinic, Cleveland, Ohio; [d]Department of Cardiology, University of Louisville, Louisville, Kentucky; [e]Evidence-Based Practice Center, Mayo Clinic, Rochester, New York; [f]Harrington Heart & Vascular Institute, University Hospitals Cleveland Medical Center, Division of Cardiovascular Medicine, Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio; [g]Department of Cardiology, Institute for Heart & Vascular Health, Einstein Medical Center, Philadelphia, Pennsylvania; [h]Department of Medicine, Sidney Kimmel College of Medicine, Thomas Jefferson University, Philadelphia, Pennsylvania; and [i]Department of Cardiology, Brigham and Women's Hospital Heart & Vascular Center, Harvard Medical School, Boston, Massachusetts. Manuscript received August 3, 2018; revised manuscript received and accepted September 25, 2018.

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*Corresponding author: Deepak L. Bhatt, MD, MPH. Brigham and Women's Hospital Heart & Vascular Center, Harvard Medical School 75 Francis Street, Boston, MA 02115 Phone: 1-857-307-1992, Fax: 1-857-307-1955

E-mail addresses: dlbhattmd@post.harvard.edu; shahzebkhan@gmail.com (D.L. Bhatt).

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guidelines for systematic reviews.[21,22] Two reviewers (TJS and MSU) independently searched MEDLINE, Cochrane CENTRAL, and Scopus databases in April 2018. No time or language restrictions were set. The detailed search strategies are provided in the Supplementary Table S1. To cast a broad net, the "title, abstract and keywords" filter was used. Other data sources included bibliographies of relevant reviews, editorials from major medical journals, websites of major journals, conference proceedings for indexed abstracts, and databases of grey and/or unpublished literature.

All studies retrieved from the search were transferred to endnote and duplicates were identified and removed. The remaining studies were then screened by 2 reviewers (TJS and MSU) on the basis of title and abstract. Finally, full texts were read to assess relevance. A third reviewer (MSK) was consulted to resolve discrepancies. Studies were selected based on the following eligibility criteria: (1) the study was an observational study or a randomized control trial (RCT); (2) the study included patients presenting with AMI, MVD, and CS; (3) all patients underwent either MVI or CVI; and (4) at least one of the outcomes being studied was reported.

Study data were sought from the full texts of the included studies as well as previous reviewer studies or meta-analyses on the topic. The main outcomes of interest were short- and long-term mortality. Short-term mortality was defined as in-hospital or 30-day death. Long-term mortality was defined as death over a period of ≥6 months. The following other outcomes were included: reinfarction and revascularization. Safety end points included renal impairment (defined as need for renal replacement therapy or renal function tests indicating renal failure), bleeding (defined as Valve Academic Research Consortium [VARC] ≥2 or Thrombolysis in Myocardial Infarction [TIMI] major bleeding), and stroke. Apart from mortality, all other outcomes were reported over the entire study period.

Risk of bias was carried out by 2 independent reviewers (TJS and MSU), and a third (MSK) was consulted to solve discrepancies. Cochrane Collaboration's risk of bias tool was used to investigate the risk of bias of the RCTs, and Newcastle-Ottawa scale (NOS)was used to assess the risk of bias of observational studies. We did not derive quantitative global judgments about risk of bias; rather we determined risk of bias in RCTs based on adequacy of allocation concealment and the likelihood of bias due to attrition. We determined risk of bias in observational studies based on adequacy of cohort selection and outcome ascertainment. The overall quality of evidence (i.e., certainty in the estimates) was evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[23,24]

Open Meta-Analyst was used to perform the meta-analysis.[25] Risk ratios (RRs) and 95% confidence intervals were calculated using raw, unadjusted data from each included study. The RRs were pooled using a random effects model because of anticipated heterogeneity in study settings and populations. Forest plots were created to visually assess the results of pooling. Subgroups were created based on type of study (retrospective or prospective); and subgroup differences were tested using the chi-square test. Multivariate meta-regression was carried out to study whether any of the following covariates independently correlated to the effect size: average age, percentage of females, and percentage of patients with dyslipidemia, hypertension, diabetes, and previous MI. Leave-one-out sensitivity analysis was conducted to assess if any single study disproportionately influenced the results. Furthermore, we carried out cumulative meta-analysis to study temporal trends.[26] This chronological meta-analysis reveals if there is a consistency in the results of consecutive studies, and indicates the point at which no further studies are necessary because the results continually favor 1 procedure. Subgroup analysis, meta-regression, sensitivity analysis, and cumulative meta-analysis were carried out for the following outcomes: short-term mortality, long-term mortality, and renal failure. Heterogeneity across studies was evaluated using the I^2 index, and a value of $I^2 = 25\%$ to 50% was considered mild, 50% to 75% as moderate, and >75% as severe.[27] Visual inspection of the funnel plot and Egger's regression test was used to assess for publication bias. A p value of <0.05 was considered significant in all cases.

Results

The initial search revealed 959 potentially relevant studies. After exclusions, 13 studies were included in the meta-analysis (6 retrospective,[12–16,21] 5 prospective,[17–19,22,25] 1 RCT,[26] and 1 post- hoc analysis of a RCT[20]). The Preferred Reporting Items for Systematic Review and Meta-Analyses flow chart outlining the literature search is shown in Figure 1. Eleven of the studies had a multicenter design, and 2 had a single-center design. The 13 studies comprised 7,906 patients ($n_{MVI} = 1{,}937$; $n_{CVI} = 5{,}969$). Individual study and baseline patient characteristics are outlined in Tables 1 and 2, respectively.

The summarized results of our meta-analysis are shown in Figure 2.

Overall, there was no significant difference in the risk of short-term mortality between the MVI and CVI groups (patients: 7,906; RR: 1.06 [0.91, 1.23]; $p = 0.45$; $I^2 = 75.82\%$; Supplementary Figure S1.0). Subgroup analysis showed that retrospective studies showed significantly higher mortality in the MVI group (RR: 1.296 [1.181, 1.422]; $p < 0.001$; $I^2 = 0\%$), whereas prospective studies showed no significant difference (RR: 0.88 [0.69, 1.11]; $p = 0.28$; $I^2 = 78.28\%$). The difference between subgroups was significant ($p = 0.003$). Upon multivariate meta-regression (Table 3), RR was significantly positively associated with the percentage of patients with history of hypertension ($p < 0.001$); RRs for short-term mortality were not significantly associated with any other covariate being evaluated. Cumulative meta-analysis revealed a trend toward lower RRs (increasingly favoring MVI) with time. The results do not appear to have reached consistency (Supplementary Figure S1.1). Leave-one-out sensitivity analysis did not identify any single study that disproportionately influenced the results (Supplementary Figure S1.2). Of note, results remained nonsignificant upon removal of Thiele (new RR: 1.04 [0.88, 1.24]; $p > 0.05$) and Lee studies (new RR: 1.11 [0.96, 1.27]; $p > 0.05$).

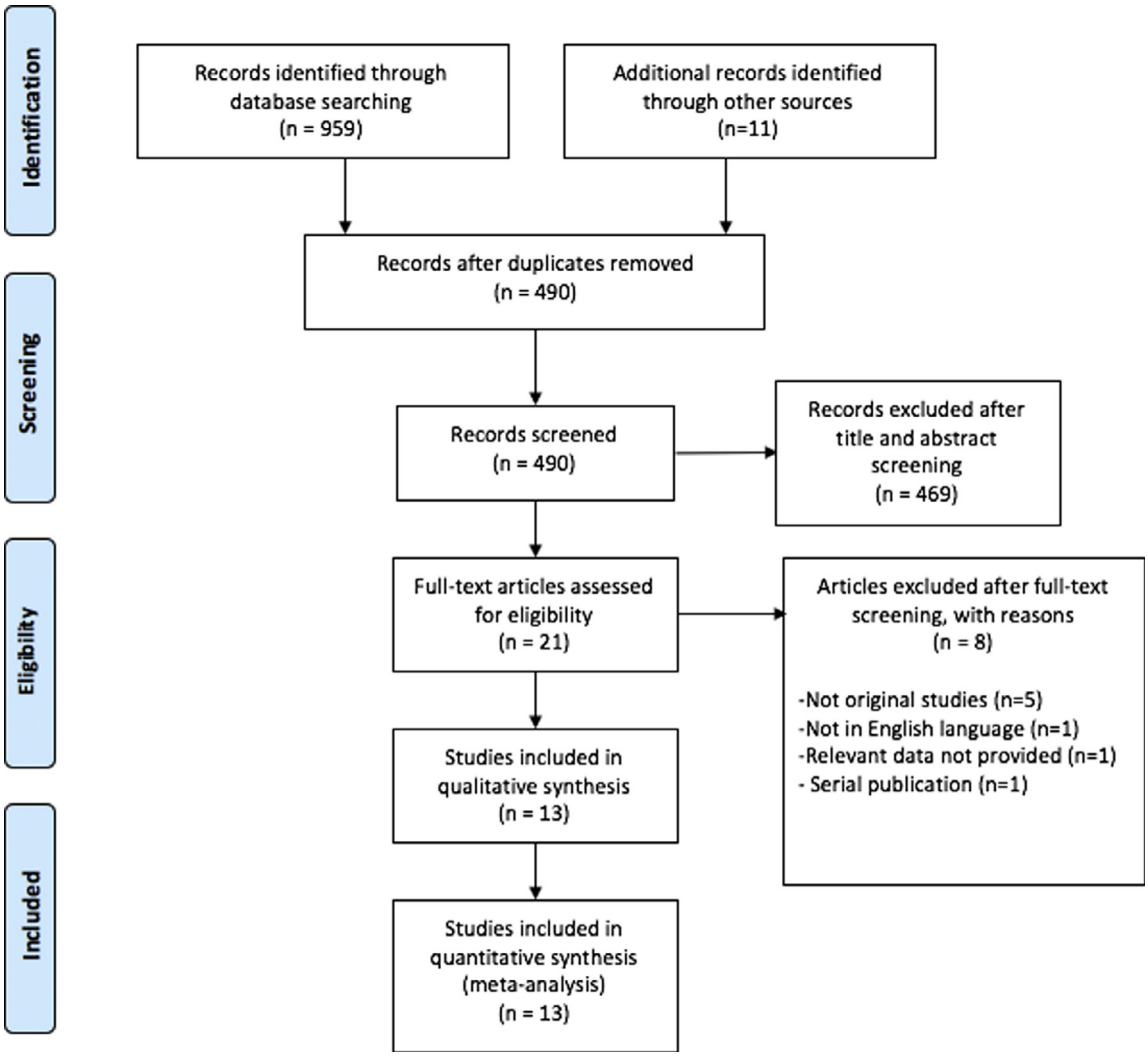

Figure 1. PRISMA flow chart, outlining the literature search. Thirteen trials were selected from the initial 490 potential studies.

Overall, there was no significant difference in the risk of long-term mortality between the MVI and CVI groups (patients: 3,527; RR: 0.93 [0.78, 1.11]; $p = 0.370$; $I^2 = 67.92\%$; Supplementary Figure S2.0). However, upon subgroup analysis, a significant difference ($p = 0.02$) was noted between results from retrospective (RR: 1.14 [0.96, 1.36]; $p = 0.13$; $I^2 = 0\%$) and prospective (RR: 0.82 [0.67, 1.03]; $p = 0.06$; $I^2 = 64.65\%$) studies, with retrospective studies showing increased mortality with MVI relative to prospective studies, similar was observed with short-term mortality. Upon multivariate meta-regression, RRs for long-term mortality were not significantly associated with any of the covariates being evaluated. Chronological cumulative meta-analysis revealed a trend toward lower RRs (lesser long-term mortality with MVI). The results did not appear to have reached consistency (Supplementary Figure S2.1). Leave-one-out sensitivity analysis did not reveal any disproportionately influential studies (Supplementary Figure S2.2). In particular, results remained nonsignificant upon removal of Lee (new RR: 0.93 [0.80, 1.01]; $p > 0.05$) and Thiele studies (new RR: 0.90 [0.76, 1.07]; $p > 0.05$).

No significant difference was noted between the MVI and CVI groups in the risk of reinfarction (patients: 3,780; RR: 1.16 [0.75, 1.79]; $p = 0.50$; $I^2 = 0\%$; Supplementary Figure S3.0), or the need for revascularization after PCI (patients: 2,709; RR: 0.84 [0.48, 1.47]; $p = 0.54$; $I^2 = 83.01\%$; Supplementary Figure S4.0). Furthermore, the MVI and CVI groups did not differ significantly in the risk of bleeding (patients: 5,833; RR: 1.15 [0.96, 1.38]; $p = 0.09$, $I^2 = 0\%$; Supplementary Figure S6.0) or stroke (patients: 5,549; RR: 1.29 [0.86, 1.94]; $p = 0.80$, $I^2 = 0\%$; Supplementary Figure S7.0).

The incidence of renal failure was significantly higher in the group receiving MVI (patients: 6,154; RR: 1.35 [1.10, 1.66]; $p = 0.004$; $I^2 = 0\%$; Supplementary Figure S5.0). There was no significant difference in results ($p = 0.71$) derived from retrospective (RR: 1.42 [0.89, 2.27]; $p = 0.14$; $I^2 = 43.9\%$) versus prospective (RR: 1.28 [0.94, 1.74]; $p = 0.11$; $I^2 = 0\%$) studies. Upon multivariate meta-regression, it was seen that RRs for renal failure were not significantly associated with any of the study-level covariates being evaluated. Chronological cumulative meta-analysis did not show temporal trends in any direction, and results

Table 1
Study characteristics

Study	Year	Data Source	Study period	Sample size (MVI/CVI)	Study design	Definition of MVD	Definition of CS	Follow-up (days)
Cavender	2009	NCDR	2004-2007	3090 (432/2658)	Multicenter; retrospective	CAD in >1 major artery	SBP <80 mmHg and/or a CI <1.8 l/min/m^2 despite maximal treatment or requiring intravenous inotropes and/or an IABP to maintain SBP at >80 mmHg and/or the CI >1.8 l/min/m^2	In-hospital
Schaaf	2010	-	1997-2005	161 (37/124)	Single center; retrospective;	≥1 stenosis >50% of the coronary lumen diameter in ≥1 of the non-IRA major arteries or left main stenosis ≥50%	SBP ≤90 mm Hg for ≥30 min or vasopressors required to maintain SBP >90 mm Hg, evidence of end-organ hypo perfusion, and evidence of elevated filling pressures.	365
Bauer	2012	EHS-PCI	2005-2008	336 (82/254)	Multicenter; retrospective	≥70% stenosis in ≥2 major coronary arteries	SBP ≤90 mmHg for ≥30 min or inotropes needed to maintain a SBP >90 mmHg, end-organ hypo perfusion and increased filling pressures	In-hospital
Cavender	2013	-	2002-2010	199 (43/156)	Single center; retrospective; propensity matched	≥50% stenosis in ≥2 major coronary arteries	SBP <90 mmHg, and/or CI <2.2 l/min/m^2, and/or parenteral inotropic or vasopressor agents or mechanical support needed to maintain a SBP >90 mmHg	1,825
Jaguszewski/Jeger	2013	AMIS Plus	2005-2012	243 (85/158)	Multicenter; retrospective	≥50% in ≥2 major coronary arteries and involving the left main lesions	Killip class 4	In-hospital (70 patients had 1-year mortality data)
Mylotte	2013	-	1998-2010	169 (66/103)	Multicenter; prospective	≥70% stenosis in a major (≥2.5-mm diameter) non-IRA, distal left main lesion with significant stenosis of the Ostia of both distal arteries	SBP <90 mmHg for >30 min or need for supportive measures to maintain a SBP ≥90 mmHg, and end-organ hypo perfusion after survived out-of-hospital cardiac arrest	180
Yang	2014	KWGMI + KAMIR	2005-2010	138 (60/78)	Multicenter; prospective	≥50% stenosis in ≥1 major non-IRA	SBP <90 mm Hg or vasopressors required to maintain a SBP >90 mm Hg; signs of hypo perfusion; and clinical evidence of elevated left ventricular filling pressure	Median 224 (IQR = 46-383)
Park	2015	KAMIR	2006-2012	510 (124/386)				Median 194 (IQR = 14-374)

(*continued on next page*)

Table 1 (***Continued***)

Study	Year	Data Source	Study period	Sample size (MVI/CVI)	Study design	Definition of MVD	Definition of CS	Follow-up (days)
					Multicenter; prospective	≥50% stenosis in ≥2 major coronary arteries	SBP <90 mm Hg for >30 min or need for supportive management to maintain SBP ≥ 90mmHg and end organ hypo fusion	
Zeymer	2015	ALKK-PCI	2008-2011	735 (173/562)	Multicenter; retrospective	≥50% stenosis in ≥2 coronary arteries	SBP <90 mm Hg, heart rate >100 bpm and end-organ hypo perfusion,	In-hospital
Hambraeus	2016	SCARR	2006-2012	330 (67/263)	Multicenter; prospective	-	-	365
Zeymer	2016	IABP-SHOCK II	2009-2012	451 (167/284)	Multicenter; post hoc analysis of RCT	≥50% stenosis in ≥2 coronary arteries	SBP <90 mmHg for >30 min or need for catecholamine to maintain a SBP >90 mmHg + clinical signs of pulmonary congestion, and impaired end-organ perfusion	365
Thiele	2017	-	2013-2017	685 (341/344)	Multicenter; randomized control trial	>70% stenosis in ≥ 2 major vessels	SBP <90 mmHg for >30 min or need for catecholamine to maintain a SBP >90 mmHg + clinical signs of pulmonary congestion, and impaired end-organ perfusion	30
Lee	2018	KAMIR-NIH	2011-2015	659 (260/399)	Multicenter; prospective	≥50% in ≥1 major non-IRA or in left main	SBP <90 mm Hg for >30 min or need for supportive management to maintain SBP ≥90 mmHg and pulmonary congestion + impaired end organ perfusion	365

ALKK-PCI = Arbeitsgemeinschaft Leitende Kardiologische Krankenhausärzte-PCI registry; AMIS Plus = acute myocardial infarction in Switzerland Plus Registry; CAD = coronary artery disease; CI = cardiac index; CS = cardiogenic shock; EHS-PCI = Euro Heart Survey PCI Registry; IABP = Intra-aortic balloon pump; IQR = interquartile range; IRA = infarct-related artery; KAMIR = Korean Acute Myocardial Infarction Registry; KWGMI = Korea Working Group on Myocardial Infarction Registry; MI = myocardial infarction; MVD = multivessel disease; MV-PCI = multivessel PCI; NA = not available or not specified; NCDR = National Cardiovascular Data Registry; PCI = percutaneous coronary intervention; SBP = systolic blood pressure; SCAAR = Swedish Coronary Angiography and Angioplasty Registry.

Table 2
Baseline characteristics of patients in the included studies

Study	Year	Age, average			Females (%)			BMI (kg/m^2), average			Dyslipidemia (%)			Hypertension (%)			Diabetes mellitus (%)			Prior myocardial infarction (%)			Heart failure (%)			Chronic kidney disease (%)		
		Total	MVI	CVI	Total	MVI	CVI	Total	MVI	CVI	Total	MVI	CVI	Total	MVI	CVI	Total	MVI	CVI	Total	MVI	CVI	Total	MVI	CVI	Total	MVI	CVI
Cavender	2009	66	64	66	35	36	35	27	28	27	50	50	50	63	60	63	27	30	27	23	22	23	32	41	31	8	8	8
Schaaf	2010	67	67	67	29	19	32	-	-	-	24	24	24	26	28	26	22	24	22	-	-	-	-	-	-	-	-	-
Bauer	2012	65	67	65	31	29	32	28	27	28	53	47	55	65	60	67	36	40	35	35	32	36	11	9	11	7	9	6
Cavender	2013	65	63	66	36	28	38	28	29	28	22	16	24	77	72	79	32	35	31	34	44	31	-	-	-	12	19	10
Jaguszewski /Jeger	2013	65	65	65	24	22	25	-	-	-	52	40	58	59	56	61	25	26	25	-	-	-	7	3	9	7	9	6
Mylotte	2013	67	65	69	30	34	28	26	25	26	43	46	41	50	53	48	25	26	25	26	21	30	-	-	-	-	-	-
Yang	2014	69	67	70	39	37	40	-	-	-	23	22	23	57	50	58	18	22	17	6	8	5	-	-	-	-	-	-
Park	2015	68	66	68	33	29	34	23	24	23	10	10	10	55	54	55	24	26	23	-	-	-	-	-	-	-	-	-
Zeymer	2015	70	68	70	29	28	29	-	-	-	69	69	69	79	81	78	36	39	35	43	33	46	-	-	-	43	51	40
Hambraeus	2016	70	68	71	35	33	35	-	-	-	18	22	17	40	39	40	25	27	24	11	9	11	5	6	5	3	2	3
Zeymer	2016	68	69	68	29	26	30	-	-	-	41	42	40	72	68	75	35	40	32	25	18	29	-	-	-	23	20	24
Thiele	2017	70	70	70	24	22	25	27	27	27	34	35	33	60	62	59	32	35	30	17	16	18	-	-	-	-	-	-
Lee	2018	67	66	67	25	26	25	23	24	23	47	47	47	54	52	55	41	41	41	8	7	9	-	-	-	38	34	40

CVI = culprit vessel intervention; MVI = multivessel intervention.

appeared to be consistent (Supplementary Figure S5.1). Leave-one-out sensitivity analysis revealed that results became nonsignificant upon removal of either Cavender (new RR: 1.36 [0.99, 1.87]; $p > 0.05$) or Thiele study (new RR: 1.32 [0.98, 1.78]; $p > 0.05$; Supplementary Figure S5.2). Removal of Lee study did not alter the overall results significantly (new RR: 1.347 [1.141, 1.764]; $p < 0.05$).

Included nonrandomized studies were of low risk of bias, with the majority having adequate cohort selection methods and outcome ascertainment (Supplementary Table S2). The single RCT included in this meta-analysis was of overall low risk of bias (Supplementary Table S3). Visual inspection of the funnel plot (Figure 3) suggested publication bias, which was confirmed using Egger's regression test ($p < 0.001$). The overall quality of the body of evidence (certainty in the estimates) was low, mainly due to the observational nature of most of the studies. The large sample size likely makes the estimates precise, and suggests a true nonsignificant association.

Discussion

This systematic review and meta-analysis of 7,906 AMI patients with MVD and CS found no significant difference between MVI and CVI for short- and long-term mortality. There were also no differences in subsequent reinfarction or need for revascularization. However, patients who underwent MVI may have higher risk of developing renal failure. These findings should be interpreted cautiously because they were mainly derived from nonrandomized studies. However, these studies were judged to have low risk of bias and adequate power to study these associations.

The non-significant results of short- and long-term mortality were robust, with sensitivity analysis revealing no single study with a disproportionate effect on the results. In contrast, the first meta-analysis in this area[23] demonstrated significantly increased short-term mortality with MVI (RR: 1.26 [1.12, 1.41]; $p = 0.001$). This study was updated by Kolte et al[24] with the addition of 1 observational study, upon which the short-term mortality results became nonsignificant (odds ratio: 1.08 [0.81, 1.43]; $p = 0.61$). Our meta-analysis builds upon evidence from these previous analyses, with the addition of 2 major studies (Lee, 2018 and Thiele, 2018) consisting of 1,344 patients.[25,26] In contrast to our results, as well as the results from KAMIR-NIH registry (Lee, 2018), the CULPRIT-SHOCK trial (Thiele, 2018) showed significantly increased 30-day mortality with MVI.[26] This is the only RCT comparing MVI and CVI in AMI patients presenting with MVD and CS. Several methodologic factors could have played a role in this finding. Although observational studies such as the one by Lee et al. are unable to control for confounders to the same extent as a clinical trial, trials have preset protocols that may differ from real-world practice. For example, 82 patients (24% of the sample size) in the CULPRIT-SHOCK trial underwent immediate PCI for chronic total occlusions, which is unlikely in real-world scenarios. Future trials must account for methodologic factors likely to influence results.

An interesting finding in our study was the significant difference in results derived from prospective and retrospective

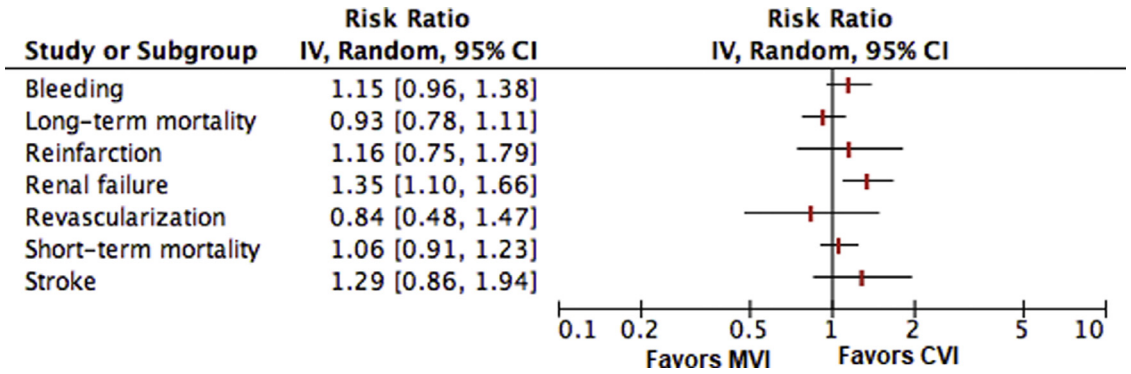

Figure 2. Summarized results of meta-analysis. The MVI and CVI groups did not differ significantly in the risk of short-term mortality, long-term mortality, reinfarction, revascularization, bleeding, or stroke. However, significantly increased risk of renal failure was seen in the MVI group. CVI = culprit-vessel intervention; MVI = multivessel intervention.

studies. In both the short- and long-term mortality outcomes, retrospective studies relatively favored CVI over MVI. The results from prospective studies should be given more consideration as they are better able to control for confounding factors. The prospective studies included in this meta-analysis had a lower risk of bias (mean NOS scores: prospective = 8; retrospective = 7). Upon isolated analysis of prospective studies, no significant difference was seen between MVI and CVI in short- or long-term mortality, which is consistent with our overall results. Furthermore, all prospective studies were conducted more recently (2013 to 2018) in comparison with the retrospective ones (2009 to 2015). This could explain the temporal shift toward lower mortality with MVI seen upon cumulative meta-analysis. Visual inspection of the cumulative meta-analysis forest plot suggests an ongoing trend, with lack of consistency in recent results, suggesting that the current evidence is not reliable and further studies are required.

There are several arguments in favor of MVI in AMI patients with MVD. Noninfarct-related artery revascularization has been shown to improve LV function by restoring blood flow to hibernating myocardium and may promote myocardial salvage by increasing blood flow to the watershed areas.[28] In contrast, PCI of additional nonculprit lesions may increase the risk of periprocedural MI and contrast-induced renal failure.[29] Although our meta-analysis of CS patients shows a temporal shift of results in support of MVI to decrease mortality, the results are still nonsignificant, indicating that currently available data do not show any additional benefit in survival with MVI in AMI patients complicated by CS.

The increase in the risk of renal failure with MVI seen in our study was not surprising given the increased use of contrast dye in patients who underwent this procedure. AMI patients complicated with CS are generally older (average age 65 to 70 years in our study), and hence are at a higher risk of developing contrast- induced nephropathy.[30] The CULPRIT-SHOCK trial showed a nonsignificant trend toward increased risk of renal failure in the MVI group.[26] It must be noted that in this trial, 12.5% of the patients in the CVI group were actually treated with immediate MVI, due to a range of clinical factors. This could have confounded the results, preventing the increased risk of renal failure with MVI from being fully apparent.

Consistent with previous meta-analyses, we noted no significant difference between the 2 treatment strategies regarding subsequent reinfarction, bleeding, or stroke. We also found no significant difference in the rate of repeat revascularization in each group with our meta-analysis, despite the high rate of repeat revascularization rate in the CVI group in the CULPRIT-SHOCK trial.

There are some limitations to this meta-analysis. First, our results are primarily derived from observational studies, which are unable to account fully for confounding factors and selection bias. Second, there was slight variation in the definition of end-points such as myocardial reinfarction, acute renal failure, bleeding, and stroke. Third, significant publication bias and heterogeneity were of concern. Lastly, study-level meta-regression is susceptible to ecological bias, and its results should only be considered exploratory.

In conclusion, MVI is not associated with better survival versus CVI in AMI patients with MVD and CS. MVI may

Table 3
Results of multivariate meta-regression

Covariate	Short-term mortality		Long-term mortality		Renal failure	
	Coefficient	p value	Coefficient	p value	Coefficient	p value
Age	−0.018	0.638	−0.021	0.754	0.211	0.063
Percentage of females	0.001	0.967	−0.022	0.050	0.017	0.855
Percentage of patients with dyslipidemia	−0.003	0.574	−0.010	0.463	0.029	0.511
Percentage of patients with hypertension	0.030	<0.001	0.011	0.585	−0.027	0.591
Percentage of patients with diabetes	−0.018	0.323	−.018	0.402	−0.040	0.633
Percentage of patients with previous myocardial infarction	−0.004	0.656	n/a*	n/a*	n/a*	n/a*

* Not enough studies for meta-regression.

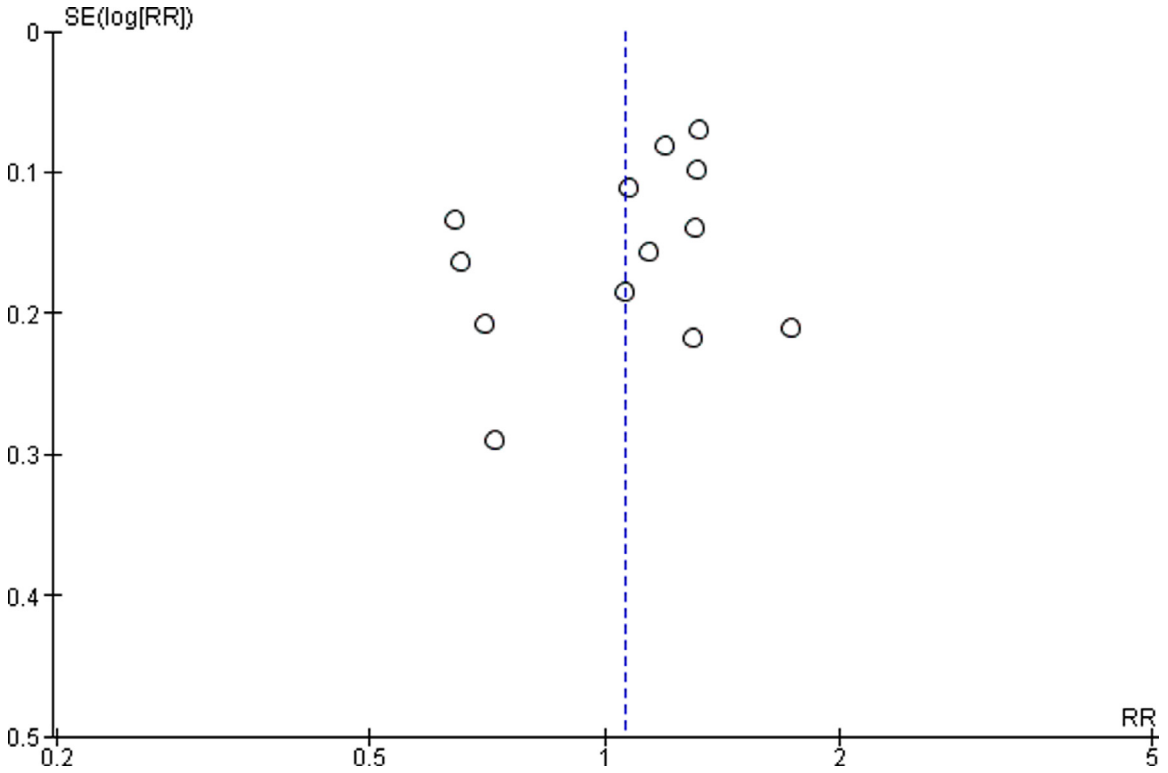

Figure 3. Funnel plot. Visual inspection of the funnel plot suggested publication bias. RR = risk ratios.

increase the risk of renal failure in these patients, hence, CVI currently appears to be the better option. Future trials should attempt to reduce confounding between the 2 experimental groups, and simulate real-life situations to a greater extent.

Disclosures

Dr. Deepak L. Bhatt discloses the following relationships: Advisory Board: Cardax, Elsevier Practice Update Cardiology, Medscape Cardiology, Regado Biosciences; Board of Directors: Boston VA Research Institute, Society of Cardiovascular Patient Care, TobeSoft; Chair: American Heart Association Quality Oversight Committee; Data Monitoring Committees: Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute, for the PORTICO trial, funded by St. Jude Medical, now Abbott), Cleveland Clinic, Duke Clinical Research Institute, Mayo Clinic, Mount Sinai School of Medicine, Population Health Research Institute (including for the COMPLETE trial); Honoraria: American College of Cardiology (Senior Associate Editor, Clinical Trials and News, ACC.org; Vice-Chair, ACC Accreditation Committee), Baim Institute for Clinical Research (formerly Harvard Clinical Research Institute; RE-DUAL PCI clinical trial steering committee funded by Boehringer Ingelheim), Belvoir Publications (Editor in Chief, Harvard Heart Letter), Duke Clinical Research Institute (clinical trial steering committees), HMP Global (Editor in Chief, Journal of Invasive Cardiology), Journal of the American College of Cardiology (Guest Editor; Associate Editor), Population Health Research Institute (for the COMPASS operations committee, publications committee, steering committee, and USA national co-leader, funded by Bayer), Slack Publications (Chief Medical Editor, Cardiology Today's Intervention), Society of Cardiovascular Patient Care (Secretary/Treasurer), WebMD (CME steering committees); other: Clinical Cardiology (Deputy Editor), NCDR-ACTION Registry Steering Committee (Chair), VA CART Research and Publications Committee (Chair); Research Funding: Abbott, Amarin, Amgen, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Chiesi, Eisai, Ethicon, Forest Laboratories, Idorsia, Ironwood, Ischemix, Lilly, Medtronic, PhaseBio, Pfizer, Regeneron, Roche, Sanofi Aventis, Synaptic, The Medicines Company; Royalties: Elsevier (Editor, Cardiovascular Intervention: A Companion to Braunwald's Heart Disease); Site Coinvestigator: Biotronik, Boston Scientific, St. Jude Medical (now Abbott), Svelte; Trustee: American College of Cardiology; Unfunded Research: FlowCo, Merck, Novo Nordisk, PLx Pharma, Takeda. The other authors have no disclosures. Dr. Ankur Kalra discloses the following relationships: Consultant: Medtronic and Philips.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.amjcard.2018.09.039.

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