Meta-Analysis of Complete versus Culprit-Only Revascularization in Patients with ST-Segment Elevation Myocardial Infarction and Multivessel Coronary Disease

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Approximately half of patients with ST-segment elevation myocardial infarction (STEMI) present with noninfarct related multivessel coronary artery disease (CAD) during primary percutaneous coronary intervention (PCI). However, questions remain concerning whether patients with STEMI and multivessel CAD should routinely undergo complete revascularization. Our objective was to compare the risks of major cardiovascular outcomes and procedural complications in patients with STEMI and multivessel CAD randomized to complete revascularization versus culprit-only PCI. We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) comparing complete revascularization to culprit-only PCI. RCTs were identified via a systematic search of MEDLINE, Embase, and Cochrane CENTRAL. Count data were pooled using DerSimonian and Laird random-effects models with inverse variance weighting to obtain relative risks (RRs) and 95% confidence intervals (CIs). A total of 9 RCTs (n = 6,751) were included, with mean/median follow-up times ranging from 6 to 36 months. Compared with culprit-only PCI, complete revascularization was associated with a substantial reduction in major adverse cardiovascular events (13.1% vs 22.1%; RR: 0.54; 95%CI: 0.43 to 0.66), repeat myocardial infarction (4.9% vs 6.8%; RR: 0.64; 95%CI: 0.48 to 0.84), and repeat revascularization (3.7% vs 12.3%; RR: 0.33; 95%CI: 0.25 to 0.44). Complete revascularization may have beneficial effects on all-cause and cardiovascular mortality, but 95%CIs were wide. Findings for stroke, major bleeding, and contrast-induced acute kidney injury were inconclusive. In conclusion, complete coronary artery revascularization appears to confer benefit over culprit-only PCI in patients with STEMI and multivessel CAD, and should be considered a first-line strategy in these patients. **(Am J Cardiol 2020;135:40–49)**

The American College of Cardiology/American Heart Association (ACC/AHA) guidelines assign a class I recommendation for primary percutaneous coronary intervention (PCI) in patients with acute ST-segment elevation myocardial infarction (STEMI).[1] However, approximately half of these patients also present with noninfarct related multivessel coronary artery disease (CAD) at the time of primary PCI.[2] The ACC/AHA guidelines provide a class IIb recommendation for complete revascularization in STEMI patients who are hemodynamically stable, either at the time of primary PCI or in a staged procedure.[1] In contrast, the 2017 European Society of Cardiology (ESC) guidelines present a Class IIa recommendation.[3] With these inconsistent recommendations, questions remain concerning whether patients with STEMI and multivessel CAD should routinely receive complete revascularization. The recent publication of COMPLETE,[4] a large randomized controlled trial (RCT) comparing complete revascularization to culprit-only PCI for patients with STEMI and multivessel CAD, greatly contributes to the available data. However, individual trials were not powered to detect differences in the outcomes comprising their primary composite endpoints. Therefore, we performed a systematic review and meta-analysis to synthesize data across all available RCTs to compare major cardiovascular outcomes and procedural complications in patients with STEMI and multivessel CAD randomized to complete revascularization versus culprit-only PCI.

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Methods

Our systematic review and meta-analysis was conducted according to a prespecified protocol, with reporting as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[5]

We systematically searched MEDLINE via PubMed, Embase via Ovid, and the Cochrane CENTRAL databases from inception through October 10, 2019. Keywords (title/abstract) and Medical Subject Headings terms searched included those related to multivessel, STEMI, PCI, and RCT; the detailed search is reported in Supplemental Information A (Panels 1 to 3). The Cochrane Collaboration's search filter was used to restrict results to clinical trials in PubMed and Ovid.[6]

Two independent reviewers screened the titles and abstracts of identified publications using prespecified inclusion criteria. Citations considered potentially eligible were retrieved for full-text screening, with disagreements resolved by consensus or a third reviewer. Included articles were RCTs published in English or French which randomized patients with STEMI and multivessel CAD to complete revascularization or culprit-only PCI. Studies had to report at least one of the predefined primary outcomes (below) to be included. RCTs including more than 10% of patients in cardiogenic shock at the time of PCI were excluded, as were those whose maximum time from randomization to complete revascularization exceeded 45 days. Abstracts, editorials, and conference proceedings were also excluded. Data were extracted independently by 2 reviewers into a pilot-tested database, with disagreements resolved by consensus. Intention-to-treat analysis data were extracted for all outcomes. A complete list of the extracted data is found in Supplemental Information B.

The risk of bias for included RCTs was assessed independently by 2 reviewers using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials (RoB 2),[7] with disagreements resolved by consensus. All eligible RCTs were included in the meta-analysis irrespective of study quality. Pooled relative risks (RRs) and corresponding 95% confidence intervals (CIs) were calculated for primary and secondary outcomes reported by at least 3 RCTs using DerSimonian and Laird random-effects meta-analytic models with inverse variance weighting. Prespecified sensitivity analyses were performed which excluded any trial that differed significantly in baseline patient characteristics (e.g., conducted only in patients with diabetes). In post hoc sensitivity analyses, influence analyses were conducted to examine the impact of individual trials on study results. In addition, we conducted subgroup analyses in which we stratified by complete revascularization strategy (>80% of participants received fractional flow reserve [FFR]-guided complete revascularization versus angiography-guided). Heterogeneity was estimated using the I^2 statistic. Analyses were performed using the meta and metaphor packages in R version 3.5.2.

Results

The systematic search retrieved 913 citations, of which 723 remained after removing duplicates (Figure 1). Of the 26 full-text articles assessed for eligibility, 9 RCTs met our inclusion criteria (n = 6,751).[4,8-14]

Included RCTs were published between 2004 and 2019 (Table 1). Mean and/or median follow-up duration ranged between 6 to 36 months. For patients randomized to complete revascularization, 5 trials allowed for either immediate (during the primary PCI) or staged complete revascularization at the discretion of the treating cardiologist. In 2 trials, complete revascularization was performed during primary PCI only.[10,14] One trial had prespecified a staged complete revascularization, although no later than 3 weeks after the primary PCI.[15] Finally, 1 trial had 3 treatment arms: culprit-only PCI, immediate complete revascularization, or staged complete revascularization.[12] However, the staged arm was not included in this systematic review as it exceeded the prespecified maximum of 45 days from randomization to complete revascularization (mean of 56.8 ± 12.9 days from primary PCI). The majority of trials defined nonculprit lesions as being at least 50% to 70% in luminal diameter by angiographic visual estimation. Four trials also considered a FFR measurement of ≤0.75 to 0.80 as being diagnostic of a nonculprit lesion suitable for revascularization.[4,8,9,15] However, only the Compare-Acute, DANAMI-3-PRIMULTI, and Ghani trials had an FFR-guided complete revascularization approach that required both a visual estimation of ≥50% and an FFR of ≤0.75 to 0.80 for nonculprit lesion revascularization.[8,9,15] For patients randomized to culprit-only PCI, trial-specific criteria for repeat revascularization are summarized in Supplemental Information C. The majority of trials recommended contemporary guideline-based medical therapy postprocedure, and medical management was reported within trials to remain well-balanced between both treatment arms.

The majority of patients were males (77% to 87%) in their mid-50 to mid-60s (range of means: 54 to 66 years) (Table 2). Excluding the Hamza trial[13], which included only patients with diabetes, the prevalence of diabetes ranged between 6% and 20%. Hypertension was present in 31% to 55% of patients, and 31% to 75% of patients were current smokers. All patients presented with STEMI, and no trial included patients in cardiogenic shock. The proportion of patients with prior MI, PCI, or stroke was low (≤ 8%).

The overall RoB 2-defined risk of bias of included trials was low (Table 1, Supplemental Information D), however the Ghani trial (n = 119) had a high risk of bias due to deviations from the intended intervention.[15] A summary of the RoB 2 results stratified by risk domain can be found in Supplemental Information D.

Count data for major cardiovascular outcomes in each trial are reported in Table 3. In our pooled analyses, compared to culprit-only PCI, complete revascularization was associated with decreased risks of major adverse cardiovascular events (MACE) (13.1% vs 22.1%; RR: 0.54; 95%CI: 0.43 to 0.66; Figure 2), repeat myocardial infarction (MI) (4.9% vs 6.8%; RR: 0.64; 95%CI: 0.48 to 0.84; Figure 2), and repeat revascularization (3.7% vs 12.3%; RR: 0.33; 95%CI: 0.25 to 0.44; Figure 2). The results also suggested a trend favoring a reduction in all-cause mortality (4.4% vs 4.9%; RR: 0.87; 95%CI: 0.69 to 1.08; Figure 3) and cardiovascular mortality (2.5% vs 3.1%; RR: 0.78; 95%CI: 0.58

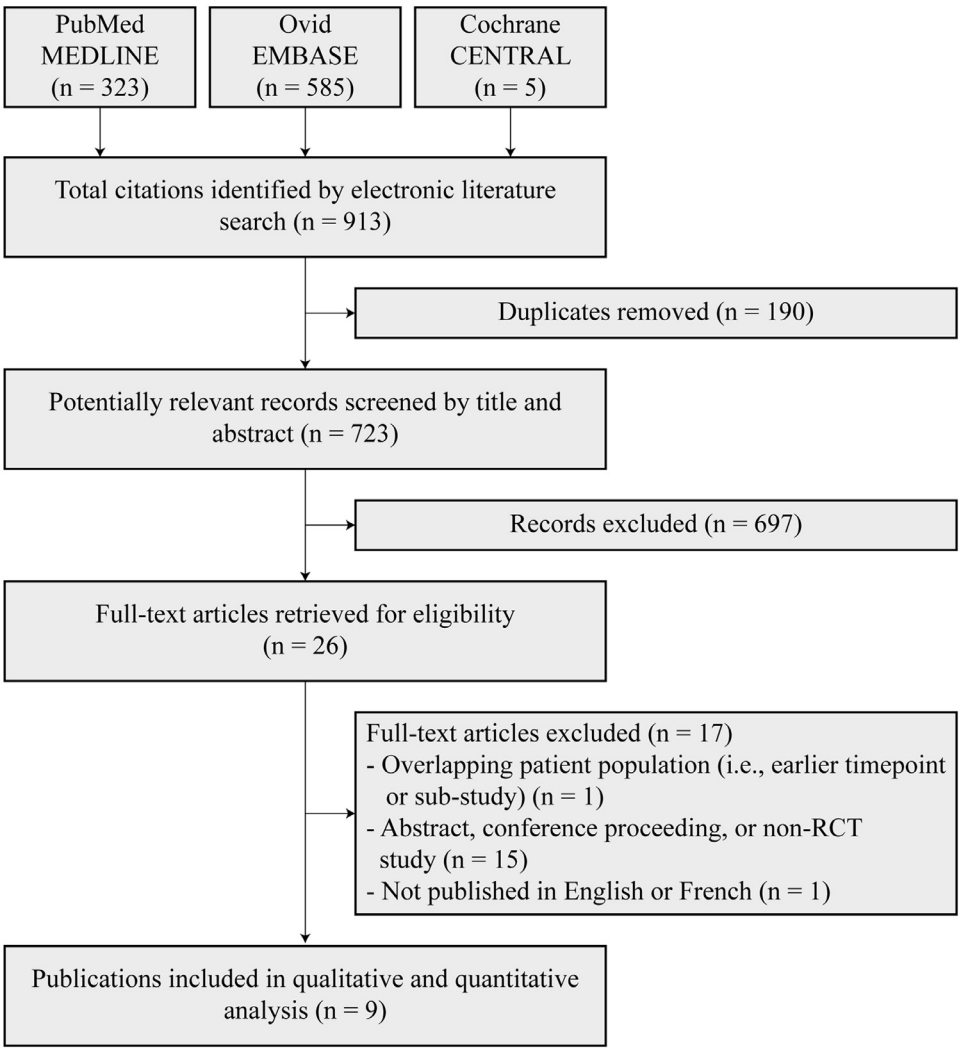

Figure 1. PRISMA flow diagram of study selection. PRISMA = preferred reporting items for systematic reviews and meta-analyses; RCT = randomized controlled trial.

to 1.04; Figure 3) with complete versus culprit-only PCI, although analyses were not conclusive as the confidence intervals included unity.

The incidence of unstable angina and heart failure were not pooled, as they were reported in only 2 trials. Complete revascularization reduced unstable angina in both the COMPLETE trial (n = 4,041) (3.5% vs 6.4%; hazard ratio (HR): 0.53; 95%CI: 0.40 to 0.71) and the PRAMI trial (n = 465) (5.1% vs 13.0%; HR: 0.35; 95%CI: 0.18 to 0.69).[4,10] Findings from the COMPLETE trial suggested no difference in the incidence of heart failure between complete revascularization and culprit-only PCI (2.9% vs 2.8%; HR: 1.04; 95%CI: 0.72 to 1.50), while results from the CvLPRIT trial (n = 296) (3.3% vs 6.9%; HR: 0.47; 95%CI: 0.16 to 1.38) were inconclusive.[4,11]

The incidence of adverse procedural outcomes was low across trials (Table 4). Pooled analyses of complete revascularization versus culprit-only PCI were inconclusive for stroke, major bleeding, and contrast-associated acute kidney injury (Figure 4). The incidence of stent thrombosis was not pooled, as it was reported in only 2 trials. The findings of both the COMPLETE trial (1.3% vs 0.9%; HR: 1.38; 95%CI: 0.76 to 2.49) and the Compare-Acute trial (0.7% vs 0.2%; HR: 0.58; 95%CI: 0.12 to 2.80) were inconclusive for stent thrombosis in patients randomized to complete revascularization compared to culprit-only PCI.[4,8]

In subgroup analyses stratified by complete revascularization strategy (FFR- or angiography-guided), point estimates for major cardiovascular and adverse procedural outcomes were inconclusive with corresponding wide 95% CIs given the limited amount of data available from trials that used a FFR-guided complete revascularization approach (Supplemental Information E). In post hoc influence analyses (Supplemental Information F, Panels 1 to 8), the omission of the COMPLETE trial[4] resulted in similar findings to the primary analysis, with the exception of cardiovascular mortality, where greater benefits were observed for complete versus culprit-only PCI (RR: 0.51; 95%CI: 0.29 to 0.88).

Discussion

In this meta-analysis of RCTs comparing complete versus culprit-only PCI in patients with STEMI and

Table 1
Study characteristics of complete versus culprit revascularization trials in patients with STEMI and multivessel coronary disease

	Sample size (n)	Countries of enrollment	Median follow-up (months)	Time from randomization to complete revascularization procedure (days)	Definition of nonculprit lesions	FFR-guided complete revascularization*	MACE definition	Overall risk of bias†
COMPLETE (2019)[4]	4,041	Multinational	36	1‡ (IQR: 1-3) 23§ (IQR: 12.5-33.5)	≥70% stenosis or 50-69% stenosis with FFR ≤0.80	No (<1%)	Cardiovascular death, MI, ischemia-driven revascularization, unstable angina, or NYHA class IV HF	Low
Compare-Acute (2017)[8]	885	Multinational	12	83% immediate	Angiographic stenosis of ≥50% and FFR ≤0.80	Yes (99%)	All-cause mortality, nonfatal MI, any revascularization, and cerebrovascular events	Low
DANAMI-3-PRIMULTI (2015)[9]	627	Denmark	27	2 (IQR: 2-4)	FFR ≤0.80 (with >50% by visual estimation) or >90% stenosis	Yes (94%)	All-cause mortality, recurrent MI, or ischemia-driven (subjective or objective) revascularization of lesions in noninfarct related arteries	Low
PRAMI (2013)[10]	465	UK	23¶	Immediate	≥50% stenosis deemed treatable by PCI	No	Cardiovascular death, nonfatal MI, or refractory angina	Low
CvLPRIT (2015)[11]	296	UK	12	64% immediate#	≥70% stenosis in single projection	No	All-cause mortality, recurrent MI, HF, and ischemic-driven revascularization by PCI/CABG	Low
Politi (2009)[12]	149	Italy	30¶	Immediate	>70% stenosis	No	All-cause mortality, re-infarction, re-hospitalization for acute coronary syndrome and repeat coronary revascularization (PCI/CABG)	Some concerns
Ghani (2012)[15]	119	Netherlands	36	7.5 (IQR: 5-20)	FFR <0.75 (with >50% by visual estimation or QCA) or >90% stenosis	Yes (81%)	All-cause mortality, nonfatal MI, and additional, revascularization procedures	High
Hamza (2016)[13]	100	NR	6	Immediate or <3 days	≥80% stenosis	No	All-cause mortality, recurrent MI, and ischemia-driven revascularization (PCI/CABG)	Some concerns
HELP AMI (2004)[14]	69	Italy	12	Immediate	NR	No	NR	Some concerns

CABG = coronary artery bypass grafting; FFR = fractional flow reserve; HF = heart failure; IQR = interquartile range; MACE = major adverse cardiovascular events; MI = myocardial infarction; NR = not reported; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; QCA = quantitative coronary angiography; STEMI = ST-segment elevation myocardial infarction; UK = United Kingdom.

* Considered as "yes" if >80% of patients in the complete revascularization arm underwent FFR-guided complete revascularization.

† Evaluated in duplicate using the revised Cochrane Collaboration's tool for assessing risk of bias in randomized trials (RoB 2 tool).

‡ For patients randomized to complete revascularization among whom the intended timing of nonculprit lesion PCI was during index hospitalization (n = 1,285).

§ For patients randomized to complete revascularization among whom the intended timing of nonculprit lesion PCI was after hospital discharge (n = 596).

¶ Reported as mean follow-up time.

Complete revascularization was recommended at the time of primary PCI if there were no contraindications. Alternatively, nonculprit lesions were required to be treated during the index admission. 64% of the complete revascularization group received complete revascularization at the same procedural session as culprit PCI based on operator judgment.

Table 2
Baseline demographic and clinical characteristics of complete versus culprit-only revascularization trials in patients with STEMI and multivessel coronary disease

	Age (mean)	Male sex	Diabetes mellitus	Systemic hypertension	Current smoker	Prior		
						MI	PCI	Stroke
COMPLETE (2019)[4]	62.0	79.8%	19.5%	49.7%	39.7%	7.5%	7.0%	3.1%
Compare-Acute (2017)[8]	61.3	77.2%	15.5%	47.2%	46.1%	7.9%	7.8%	4.1%
DANAMI-3-PRIMULTI (2015)[9]	63.5	80.7%	11.3%	44.0%	49.6%	7.0%	NR	NR
PRAMI (2013)[10]	62.0	78.1%	17.8%	40.2%	47.5%	7.5%	NR	4.3%
CvLPRIT (2015)[11]	64.9	81.1%	13.6%	36.6%	30.6%	4.2%	3.1%	NR
Politi (2009)[12]	65.6	76.5%	19.5%	55.0%	NR	NR	NR	NR
Ghani (2012)[15]	61.7	80.2%	5.9%	31.8%	45.3%	5.8%	3.3%	0.8%
Hamza (2016)[13]	54.3	84.0%	100.0%	31.0%	75.0%	8.0%	7.0%	NR
HELP AMI (2004)[14]	63.9	87.3%	18.8%	42.0%	70.1%	NR	NR*	NR

MI = myocardial infarction; NR = not reported; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.
* Reported as 0% in the complete revascularization arm (n = 52) and 2% in the culprit-only revascularization arm (n = 17); however, given the sample size, the number of individuals with prior PCI would be <1.

Table 3
Major cardiovascular outcomes at maximum follow-up of complete versus culprit-only revascularization trials in patients with STEMI and multivessel coronary disease

	Sample size (n)		All-cause mortality		Cardiovascular mortality		MACE		Repeat myocardial infarction		Ischemia-driven revascularization	
	Complete	Culprit	Complete	Culprit	Complete	Culprit	Complete	Culprit	Complete	Culprit	Complete	Culprit
COMPLETE (2019)[4]	2,016	2,025	96 (4.8%)	106 (5.2%)	59 (2.9%)	64 (3.2%)	272 (13.5%)	426 (21.0%)	109 (5.4%)	160 (7.9%)	29 (1.4%)	160 (7.9%)
Compare-Acute (2017)[8]	295	590	4 (1.4%)	10 (1.7%)	3 (1.0%)	6 (1.0%)	23 (7.8%)	121 (20.5%)	7 (2.4%)	28 (4.7%)	18 (6.1%)	103 (17.5%)
DANAMI-3-PRIMULTI (2015)[9]	314	313	15 (4.8%)	11 (3.5%)	5 (1.6%)	9 (2.9%)	40 (12.7%)	68 (21.7%)	15 (4.8%)	16 (5.1%)	17 (5.4%)	52 (16.6%)
PRAMI (2013)[10]	234	231	12 (5.1%)	16 (6.9%)	4 (1.7%)	10 (4.3%)	21 (9.0%)	53 (22.9%)	7 (3.0%)	20 (8.7%)	16 (6.8%)	46 (19.9%)
CvLPRIT (2015)[11]	150	146	4 (2.7%)	10 (6.8%)	2 (1.3%)	7 (4.8%)	15 (10.0%)	31 (21.2%)	2 (1.3%)	4 (2.7%)	8 (5.3%)	16 (11.0%)
Politi (2009)[12]	65	84	6 (9.2%)	13 (15.5%)	4 (6.2%)	10 (11.9%)	15 (23.1%)	42 (50.0%)	2 (3.1%)	7 (8.3%)	6 (9.2%)	28 (33.3%)
Ghani (2012)[15]	79	40	4 (5.1%)	0	NR	NR	28 (35.4%)	14 (35.0%)	14 (17.7%)	0	15 (19.0%)	13 (32.5%)
Hamza (2016)[13]	50	50	1 (2.0%)	4 (8.0%)	NR	NR	3 (6.0%)	12 (24.0%)	1 (2.0%)	2 (4.0%)	1 (2.0%)	6 (12.0%)
HELP AMI (2004)[14]	52	17	1 (1.9%)	0	NR	NR	11 (21.2%)	6 (35.3%)	1 (1.9%)	1 (5.9%)	9 (17.3%)	6 (35.3%)

MACE = major adverse cardiovascular events; NR = not reported; STEMI = ST-segment elevation myocardial infarction.

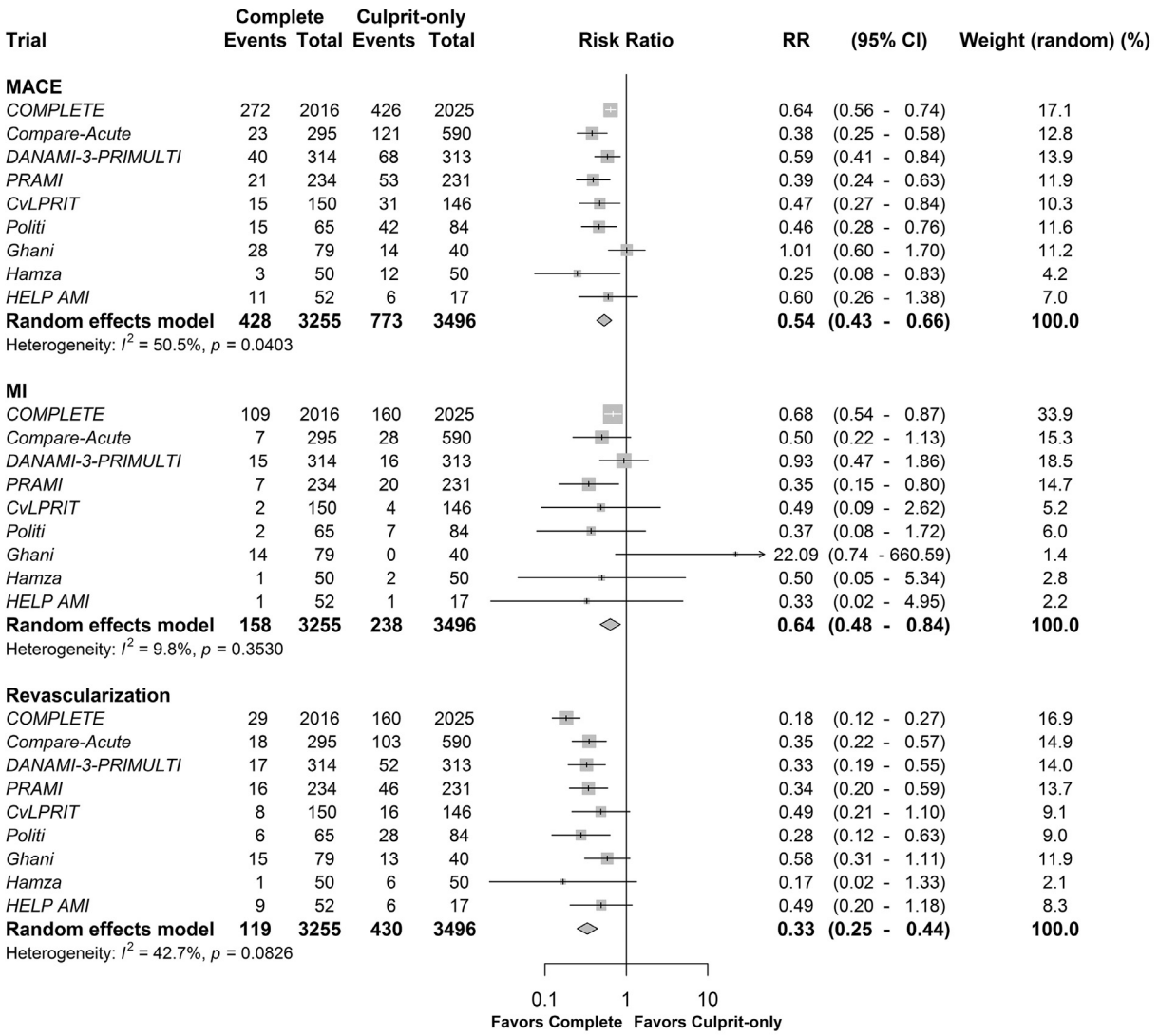

Figure 2. Forest plot of the relative risks of major cardiovascular outcomes in STEMI patients with multivessel coronary disease randomized to complete revascularization compared to culprit-only PCI. CI = confidence interval; MACE = major adverse cardiovascular events; MI = myocardial infarction; PCI = percutaneous coronary intervention; RR = relative risk; STEMI = ST-segment elevation myocardial infarction.

multivessel CAD, complete revascularization was associated with a lower risk of MACE, repeat MI, and repeat revascularization. There was also a trend towards reduced incidence of all-cause mortality and cardiovascular mortality, however these findings were not definitive. The absolute number of adverse procedural outcomes was low across trials; differences between complete versus culprit-only PCI for stroke, major bleeding, and contrast-associated acute kidney injury were inconclusive. Our meta-analysis, which included the recent COMPLETE trial,[4] increased the precision of treatment estimates for the reductions in MACE, MI, and repeat revascularization, and lends further support to the efficacy and safety of complete revascularization for patients with STEMI and multivessel CAD.

For many years, the routine practice of complete revascularization was not recommended by either the ACC/AHA or ESC guidelines.[16,17] Prior to the publication of RCTs, meta-analyses of observational studies suggested an increased risk of long-term mortality associated with complete revascularization.[18,19] Retrospective studies and subanalyses from trials that did not randomize to complete or culprit-only revascularization are at risk for confounding by indication (or contraindication), particularly for patients with acute coronary syndromes, who initially present with varying levels of stability.[20,21] Despite propensity-matching patients with similar baseline characteristics, residual bias is likely given the presence of unmeasured confounders that may influence a provider's choice of culprit-only PCI versus complete revascularization.[22] However, based on the publication of pivotal RCTs randomizing patients to complete versus culprit-only PCI, complete revascularization for STEMI now has a Class IIa recommendation in the 2017 ESC guidelines and a Class IIb recommendation in the 2015 ACC/AHA guidelines.[1,3] The COMPLETE trial adds 4,041 additional patients and 698 additional MACE, more than doubling the available evidence and substantially

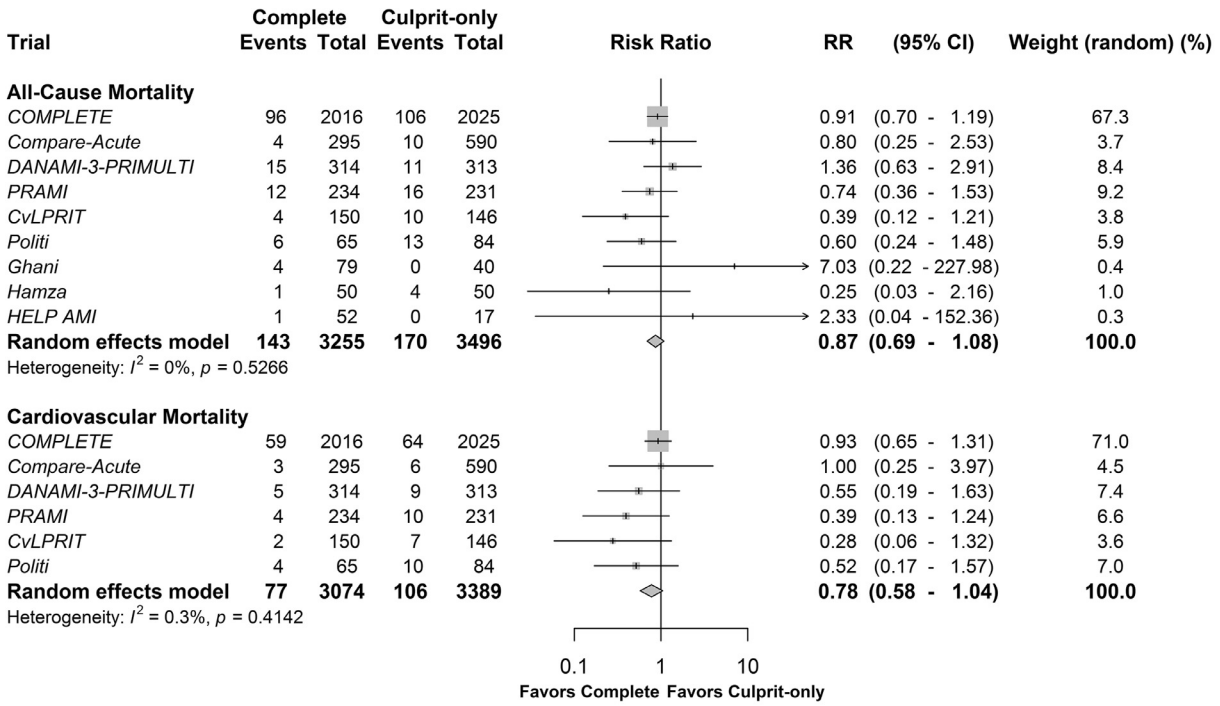

Figure 3. Forest plot of the relative risks of all-cause and cardiovascular mortality in STEMI patients with multivessel coronary disease randomized to complete revascularization compared to culprit-only PCI. CI = confidence interval; PCI = percutaneous coronary intervention; RR = relative risk; STEMI = ST-segment elevation myocardial infarction.

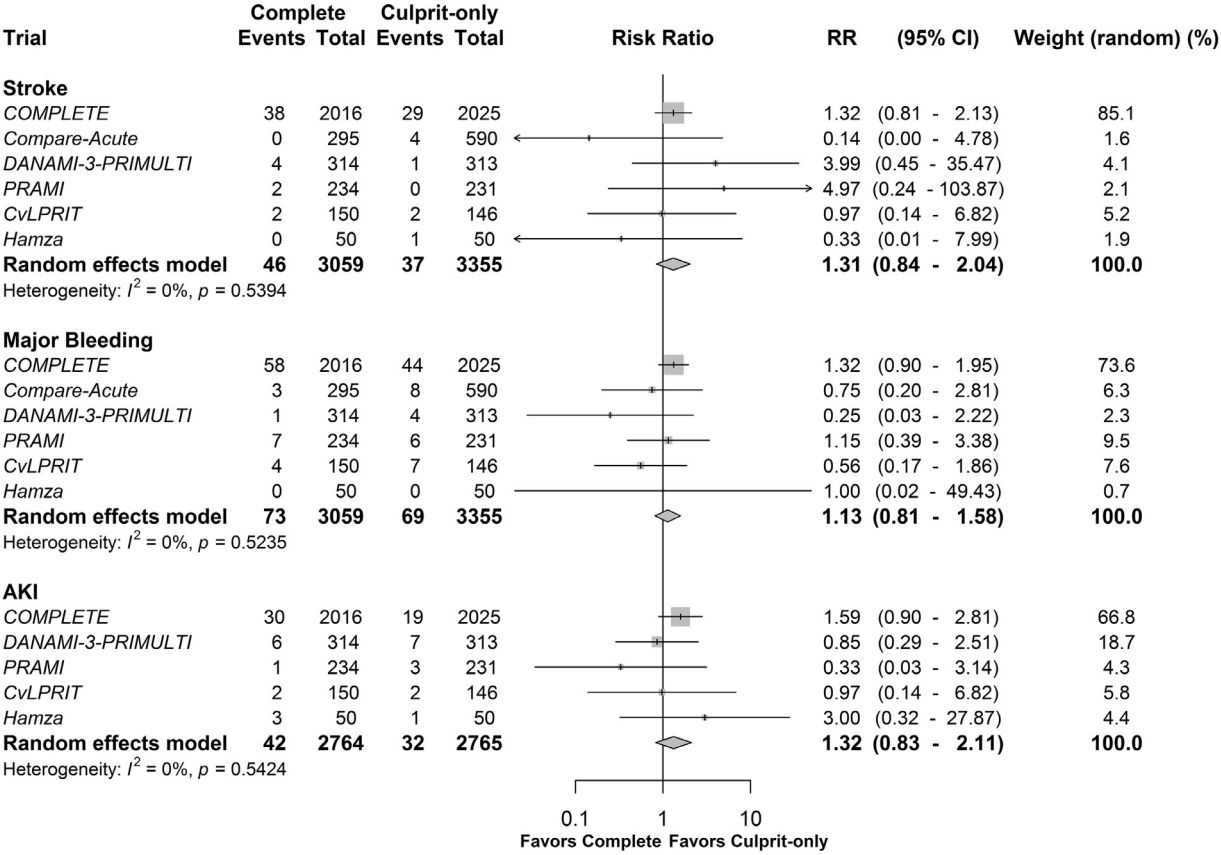

Figure 4. Forest plot of the relative risks of procedural outcomes in STEMI patients with multivessel coronary disease randomized to complete revascularization compared to culprit-only PCI. AKI = acute kidney injury; CI = confidence interval; PCI = percutaenous coronary intervention; RR = relative risk; STEMI = ST-segment elevation myocardial infarction.

Table 4
Procedural outcomes at maximum follow-up of complete versus culprit-only revascularization in patients with STEMI and multivessel coronary disease

	Sample size (n)		Stroke		Major bleeding		Contrast-associated acute kidney injury		Stent thrombosis	
	Complete	Culprit	Complete	Culprit	Complete	Culprit	Complete	Culprit	Complete	Culprit
COMPLETE (2019)[4]	2,016	2,025	38 (1.9%)	29 (1.4%)	58 (2.9%)	44 (2.2%)	30 (1.5%)	19 (0.9%)	26 (1.3%)	19 (0.9%)
Compare-Acute (2017)[8]	295	590	0	4 (0.7%)	3 (1.0%)	8 (1.4%)	NR	NR	2 (0.7%)	1 (0.2%)
DANAMI-3-PRIMULTI (2015)[9]	314	313	4 (1.3%)	1 (0.3%)	1 (0.3%)*	4 (1.3%)*	6 (1.9%)†	7 (2.2%)†	NR	NR
PRAMI (2013)[10]	234	231	2 (0.9%)	0	7 (3.0%)*	6 (2.6%)*	1 (0.4%)‡	3 (1.3%)‡	NR	NR
CvLPRIT (2015)[11]	150	146	2 (1.3%)	2 (1.4%)	4 (2.7%)	7 (4.8%)	2 (1.3%)	2 (1.4%)	NR	NR
Politi (2009)[12]	65	84	NR	NR	NR	NR	NR	NR	NR	NR
Ghani (2012)[15]	79	40	NR	NR	NR	NR	NR	NR	NR	NR
Hamza (2016)[13]	50	50	0	1 (2.0%)	0	0	3 (6.0%)	1 (2.0%)	NR	NR
HELP AMI (2004)[14]	52	17	NR	NR	NR	NR	NR	NR	NR	NR

NR = not reported; STEMI = ST-segment elevation myocardial infarction.
* Defined as bleeding requiring transfusion or surgery.
† Defined as contrast-induced nephropathy (>50% rise in plasma creatinine).
‡ Defined as contrast-induced nephropathy requiring dialysis.

increasing the precision of estimated treatment effects for major cardiovascular outcomes compared to previous meta-analyses.

While our data suggest that complete revascularization confers benefit over culprit-only PCI, the optimal method of selecting nonculprit lesions for complete revascularization remains unclear. Physiological guidance of revascularization, via routine FFR or instantaneous wave-free ratio measurement, has been demonstrated as a valuable tool for quantifying the lesion-specific need for revascularization compared to visual estimation.[22] These measurements provide an estimate of physiological flow limitation, allowing for an objective determination of the ischemic severity of a given stenosis. In the context of staged complete revascularization of patients with stable CAD, FFR-guided revascularization has improved composite outcomes of all-cause mortality, MI, or revascularization, compared to angiography-guided complete revascularization, as well as standard medical therapy.[22,23] While several of the trials included in this meta-analysis used FFR-guided complete revascularization, no study has compared FFR-guided complete revascularization to angiography-guided complete revascularization only in patients with STEMI.[8,9] Although the gold-standard for determining physiological stenosis severity, FFR is subject to additional risks, including interpretational complications (especially in multivessel CAD), additional time for assessment, and financial constraints for every pressure wire used.[24-26] A FFR-guided complete revascularization sensitivity analysis of our included trials was inconclusive given the limited amount of data available from trials using an FFR-guided approach. It therefore remains to be determined whether, in the context of an acute STEMI, FFR-guided complete revascularization confers benefit over angiography-guided complete revascularization of multivessel CAD.

Our meta-analysis has several potential limitations. First, the follow-up duration of the largest included trial was 3 years.[4] While this is reflective of the time period for real-world adverse events to occur, longer term data may contribute further to our understanding of complete revascularization's effects on major cardiovascular outcomes. Second, no trial randomized patients according to the timing of complete revascularization, making it difficult to recommend an immediate versus index hospitalization or staged PCI approach. Third, there was between-trial variability in the prespecified management strategy of patients randomized to nonculprit PCI who developed refractory symptoms. While influence analyses mitigate several of the potential effects of this limitation, a patient-level analysis would be helpful to further assess this issue. Fourth, our meta-analysis may also be affected by publication bias, an inherent limitation to most knowledge syntheses. Lastly, while this meta-analysis suggests complete revascularization is likely to reduce all-cause and cardiovascular mortality, we were underpowered to detect differences between groups for these endpoints. Likewise, the incidence of procedural complications was low in both groups, and these comparisons were inconclusive.

Our study was designed to compare the risks of major cardiovascular and procedural outcomes of complete versus culprit-only PCI in patients with STEMI and multivessel CAD. Complete revascularization was associated with decreased MACE, repeat MI, and repeat revascularization. Findings were inconclusive for all-cause mortality, cardiovascular mortality, and procedural complications. Overall, these data suggest that complete coronary artery revascularization confers benefit over culprit-only PCI in patients with STEMI and multivessel CAD and should be considered a first-line revascularization strategy in these patients.

Author Contributions

Jeremy Y. Levett: Conceptualization, Methodology, Investigation, Writing – Original Draft; Sarah B. Windle:

Methodology, Project Administration, Writing − Review & Editing; Kristian B. Filion: Methodology, Supervision; Josselin Cabaussel: Software, Formal Analysis, Data Curation; Mark J. Eisenberg: Conceptualization, Supervision, Writing − Review & Editing.

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Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.08.030.

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