Meta-Analysis Comparing the Risk of Myocardial Infarction Following Coronary Artery Bypass Grafting Versus Percutaneous Coronary Intervention in Patients With Multivessel or Left Main Coronary Artery Disease

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There is insufficient data regarding the comparative efficacy of coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI) regarding myocardial infarction (MI). Our systematic review included randomized controlled trials that compared CABG versus PCI with stents in patients with multivessel or left main coronary artery disease (CAD). Included trials should have had reported event number of MI and a clinical follow-up of one or more years. Data were pooled using a random-effects model. The primary end point was MI at the longest available follow-up in the intention-to-treat population. Fifteen trials with a total of 13,592 patients treated with either CABG (n = 6,596) or PCI (n = 6,996) were included. After a weighted follow-up of 4.5 years, patients treated with CABG had a significantly lower risk of MI than those treated with PCI (risk ratio [RR] 0.75, 95% confidence interval [CI] 0.58 to 0.96, p = 0.024). The lower risk of MI with CABG as compared with PCI was more evident during a longer duration of follow-up (≥3 years, RR 0.69, 95% CI 0.52 to 0.91, p = 0.008; ≥5 years, RR 0.64, 95% CI 0.48 to 0.86, p = 0.003) and in the diabetic population (RR 0.55, 95% CI 0.44 to 0.70, p <0.001). The magnitude of risk reduction was similar across patients with multivessel (RR 0.72, 95% CI 0.53 to 0.99) and left main CAD (RR 0.74, 95% CI 0.47 to 1.15). In conclusion, the present meta-analysis of studies involving patients with multivessel or left main CAD suggests a significant benefit of CABG over PCI concerning the risk of future MI. **(Am J Cardiol 2019;124:842−850)**

Myocardial revascularization with coronary bypass graft surgery (CABG) or percutaneous coronary intervention (PCI) is a well-established method to treat patients with severe coronary artery disease (CAD);[1,2] however, the choice of optimal revascularization strategy remains challenging. Numerous studies have compared the 2 revascularization strategies in various clinical settings and found that CABG, relative to PCI, reduces the rates of repeat revascularization in most patients with severe CAD and improves survival in certain subsets of patients.[3,4] However, it is less certain as to whether CABG is more effective than PCI in reducing myocardial infarction (MI).[5,6] Because MI results in a loss of functional myocardium and leads to a reduced quality of life, heart failure, and death in patients with established CAD,[7] the prevention of MI should be considered a high priority when selecting a revascularization strategy, nevertheless, individual randomized controlled trials (RCTs) comparing the 2 treatments have shown inconsistent results. Therefore, this investigation assesses the risk of MI after revascularization in a patient with severe CAD via a meta-analysis of RCTs to determine the potential benefits of CABG over PCI.

METHODS

The present study followed the guidelines for reports of meta-analyses of RCTs established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[8] The Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist is reported in the Supplemental Table 1. Electronic searches were performed through the EMBASE, Cochrane, and Pubmed databases to identify randomized trials that reported the clinical outcomes after CABG and PCI with stents. Searches were performed using a combination of keywords, including PCI, coronary stents, bare-metal, drug-eluting, revascularization, coronary artery bypass, CAD, MI, heart attack, and randomized. There was no language restriction for the search.

Studies were considered for inclusion if they met the flowing criteria: (1) randomized controlled study design, (2) comparison of CABG versus PCI with bare-metal or drug-eluting stents (DESs), (3) included a patient population with multivessel or left main CAD, (4) clinical follow-up of at

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least more than 1 year, (5) event number of MI available, and (6) fully published status. The most updated and inclusive data for each study were chosen for abstraction. Two investigators (PHL, HBP) independently reviewed the titles, abstracts, and studies to determine whether they met the inclusion criteria. When there was more than 1 publication from the same patient population, the study with the longest follow-up reporting the event number of MI was selected. Information was abstracted from the main text, tables, and supplemental material as cited. Data extracted from each RCT included baseline patient demographics, procedural variables, follow-up period, and outcome data. Eligible studies and extracted data were verified by the senior author (CWL) with conflicts resolved by consensus.

Internal validity of RCTs used in this meta-analysis was assessed using the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials.[9] The tool includes domains such as random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. Each domain was evaluated as low risk, unclear risk, or high risk of bias.

The present meta-analysis concentrated only on MI because metrics of patient mortality or clinical effectiveness have been thoroughly reported elsewhere.[1,10] The definitions for MI were identified for each of the studies by the type of biomarker assay used, the thresholds of biomarker elevation, changes on electrocardiogram, and the presence or absence of a symptom. The MI definitions as applied in each trial were incorporated in the analyses. The primary end point was MI with CABG versus PCI at the longest available follow-up in the intention-to-treat population. The secondary end point was the short-term risk of MI, which was analyzed by including trials that reported the rate of in-hospital, perioperative, or 30-day MI.

Within each trial, risk ratio (RR) as a measurement for the relative risk and 95% confidence interval (CI) for MI were calculated based on the reported events in the CABG and PCI groups. We used a random-effects model (DerSimonian and Laird method with Mantel-Haenszel procedure) to investigate the effect of CABG and PCI on MI across the trials and calculated pooled relative risks and 95% CI.[11] The Cochrane Q test and the I^2 statistic were used to examine heterogeneity. Heterogeneity was quantified as low with $I^2 < 25\%$, moderate with $I^2 \geq 25\%$ and $\leq 75\%$, and high with $I^2 > 75\%$. Publication bias was assessed by visual inspection of funnel plots and by Begg's test and the Egger's test for small-study effects.

A sensitivity analysis for the primary end point was performed after including trials with the higher precision of estimate (standard error $\leq$ 0.45) and longer ($\geq$3 years and $\geq$5 years) follow-up. To report summary estimates to account for conceptual and study design differences in different RCTs, we further conducted subgroup analyses according to the following subgroups: (1) trials that enrolled patients with diabetes mellitus, (2) trials that compared CABG with bare-metal stent versus first-generation DESs versus second-generation DESs, (3) trial subjects of multivessel or left main CAD. A multivariable random-effects meta-regression model, including variables such as age, gender, diabetes mellitus, publication year, follow-up duration, type of stent used, and type of CAD, was used to explore the source of potential heterogeneity of the primary result. Concerning the publication year, the year of the first report of each RCT was used to reflect changes in practice pattern or definition of MI over time. A 2-tailed p value of <0.05 was considered significant. The risk of bias graph was generated with Review Manager 5.3 (Cochrane Collaboration, Copenhagen, Denmark). The meta-analyses were performed using the "meta" and "metafor" package in R software (version 3.5.1, R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Of 864 potentially relevant articles initially screened, 15 trials randomizing 13,592 patients met the inclusion criteria, with 6,596 patients assigned to CABG and 6,996 assigned to PCI (Supplemental Figure 1). One underpowered RCT (VA CARDS) reporting the 2-year outcome in diabetic patients was excluded from the analysis because of the absence of precise information regarding MI.[12] Stent or Surgery trial reported an event number of MI only in the paper reporting 1-year outcome.[13,14] Overall, the quality of studies was high according to the Cochrane tool (Supplemental Figure 2). It must be stressed that none of the studies was blinded, but this was not considered a limitation because the blinding of participants (patients and clinicians) was not feasible due to the type of intervention.

Table 1 summarizes trial design and main characteristics of the patients. Five trials exclusively enrolled patients with left main CAD [5,6,15−17], the all-comers SYNTAX trial enrolled a mixed population of 3-vessel or left main CAD,[3] and others included multivessel CAD. Overall, the pooled mean age was 63.6 years, 10,206 (75.1%) were men and 5,924 (43.6%) had diabetes. In general, compared with earlier trials comparing CABG and bare-metal stents, more recent ones involved older patients and allowed the inclusion of higher risk patients with more complex CAD. The Supplemental Table 2 reports inclusion and exclusion criteria and definitions of MI in the individual RCT included in the meta-analysis.

As shown in Figure 1, pooled analysis of the 15 RCTs demonstrated that patients treated with CABG had a significantly lower risk of MI than those treated with PCI (RR 0.75, 95% CI 0.58 to 0.96, p = 0.024, $I^2 = 66\%$) during a weighted follow-up of 4.5 years. The test for potential publication bias was not significant (Supplemental Figure 3; no funnel plot asymmetry; p = 0.49 by Begg's test; p = 0.42 by small-study effects). Sensitivity analysis was conducted after excluding 5 trials with a standard error >0.45, demonstrating consistent results (RR 0.67, 95% CI 0.50 to 0.88, p = 0.004, $I^2 = 73\%$, p for Begg's test = 0.66). Considering the potential differences in performance between CABG and PCI over time, 11 trials with a follow-up of at least 3 years and 9 trials with a follow-up of at least 5 years were analyzed separately (Figure 2). Indeed, the lower risk of MI with CABG as compared with PCI was more evident during a longer duration of follow-up ($\geq$3 years, RR 0.69, 95% CI 0.52 to 0.91, p = 0.008, $I^2 = 67\%$, p for Begg's test = 0.64; $\geq$5 years, RR 0.64, 95% CI 0.48 to 0.86, p = 0.003,

Table 1
Characteristics of randomized trials of CABG versus PCI included in the meta-analysis

Study (publication year of longest FU)	Patients assigned to each arm, No.		FU, median, years	MVD	LMD	Primary end point				Age, mean, years	Men	DM	Type of stent used in PCI	ITA used in CABG
	CABG	PCI				Death	MI	Stroke	TVR or RR					
ARTS (2005)	605	600	5	+	○	+	+	+	+	61	76.5%	17.5%	BMS	93%
BARI-2D (2009)	378	798	5	+	○	+	○	○	○	62.3	70.4%	100%	BMS/ 1st-DES	94.2%
BEST (2015)	442	438	4.6	+	○	+	+	○	+	64.5	71.5%	34.4%	2nd-DES	99.3%
Boudriot (2011)	101	100	1	○	+	+	+	○	+	67.5	74.6%	36.3%	1st-DES	99%
CARDia (2010)	254	256	1	+	○	+	○	○	○	64	74.3%	100%	BMS/ 1st-DES	94%
Eefting (2003)	142	138	1	+	○	+	+	+	+	59.6	71%	11.4%	BMS	100%
ERACI II (2005)	225	225	5	+	○	+	+	+	+	62	79.4%	17.3%	BMS	94.7%
EXCEL (2016)	957	948	3	○	+	+	+	+	○	66	76.9%	29.1%	2nd-DES	98.4%
FREEDOM (2012)	947	953	5	+	○	+	+	+	○	63.2	71.4%	100%	1st-DES	94.4%
LE MANS (2016)	53	52	10	○	+	Change in LVEF				61	66.6%	18.1%	BMS/ 1st-DES	72%
MASS II (2010)	203	205	10	+	○	+	+	○	+	60	69.5%	26.0%	BMS	94.9%
NOBLE (2016)	592	592	5	○	+	+	+	+	+	66.2	78.7%	14.9%	2nd-DES	96.4%
PRECOMBAT (2015)	300	300	5	○	+	+	+	+	+	62.3	76.5%	32.0%	1st-DES	93.6%
SoS (2002)	500	488	1	+	○	○	○	○	+	61.5	79%	14.4%	BMS	92.8%
SYNTAX (2013)	897	903	5	+	+	+	+	+	+	65.1	77.6%	25.1%	1st-DES	96.8%

BMS = bare-metal stent; CABG = coronary artery bypass grafting; DES = drug-eluting stent; DM = diabetes mellitus; FU = follow-up; ITA = internal thoracic artery; LMD = left main disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MVD = multivessel disease; PCI = percutaneous coronary intervention; RR = repeat revascularization; TVR = target-vessel revascularization.

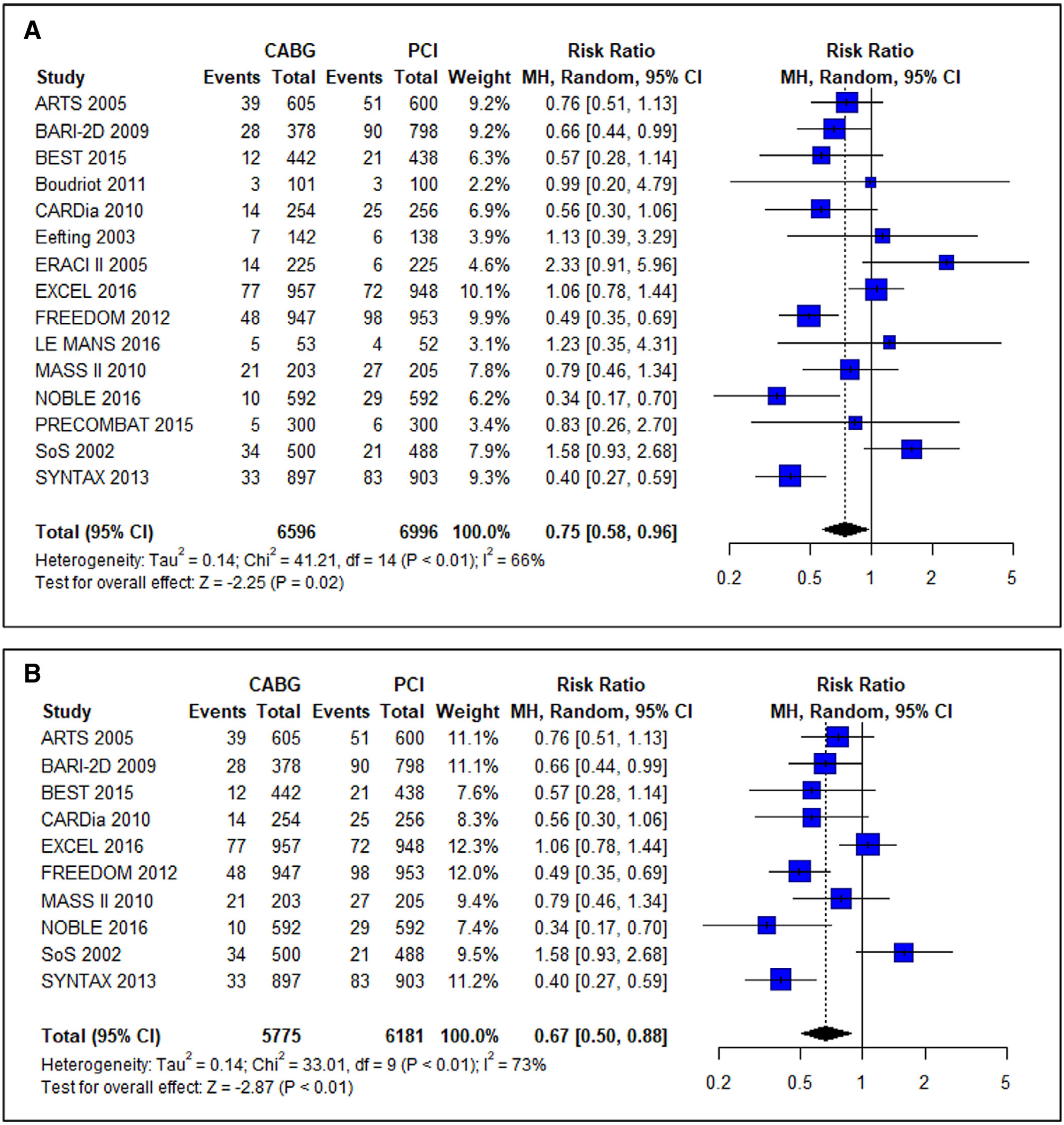

Figure 1. Forest plots comparing myocardial infarction events according to treatment arm. Forest plots in the overall trials (*A*) and that includes trials with a higher precision of estimate (standard error ≤ 0.45) (*B*). The black dotted line represents the random-effects generated overall estimate. CABG = coronary artery bypass grafting; CI = confidence intervals; MH = Mantel-Haenszel; PCI = percutaneous coronary intervention.

$I^2 = 60\%$, p for Begg's test = 0.25). Ten studies including a total of 8,743 patients contributed to an analysis of the short-term risk of MI (Supplemental Figure 4). Within 30 days there were 132 MIs in the 4,371 patients randomized to CABG and 95 MIs in the 4,372 patients randomized to PCI. Patients treated with CABG tended to have a higher short-term risk of MI than those treated with PCI (RR 1.33, 95% CI 1.02 to 1.75, p = 0.037, $I^2 = 2\%$, p for Begg's test = 0.72).

Considering that the practice patterns for both CABG and PCI have continuously changed over time, studies were classified according to the stent type used by the protocol (Figure 3). Five trials used bare-metal stents exclusively, 4 trials first-generation DESs, and 3 trials second-generation DESs. The remaining 3 trials included both bare-metal stents and first-generation DESs. We observed that the rate of MI reported in trials comparing CABG (115 MIs out of 1,675 cases, crude rate 6.9%) and bare-metal stents (111

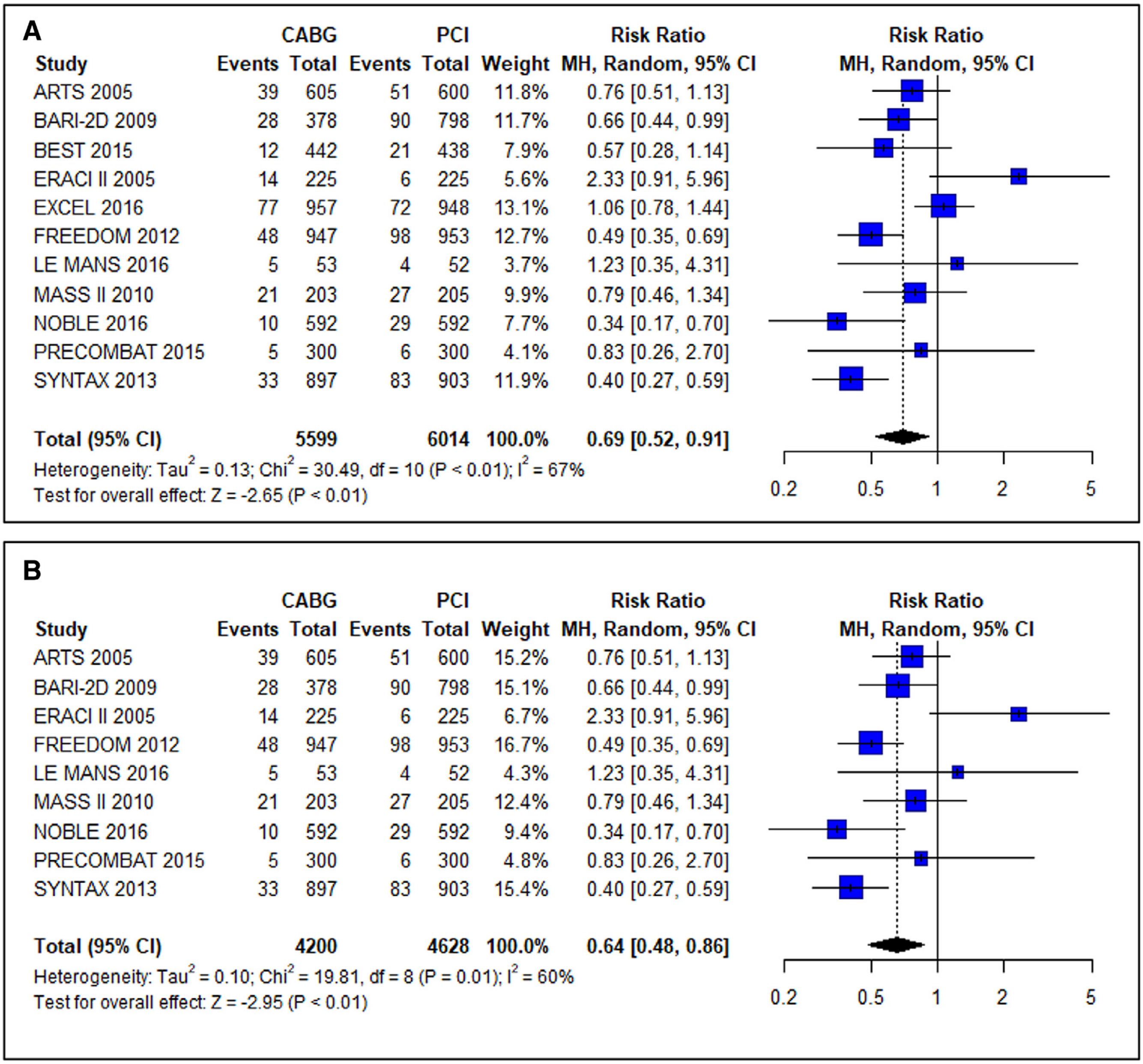

Figure 2. Risk ratios for myocardial infarction in trials with long-term follow-up. Forest plots that include trials with a follow-up of at least 3 years (*A*) and at least 5 years (*B*). The black dotted line represents the random effects-generated overall estimate. CABG = coronary artery bypass grafting; CI = confidence intervals; MH = Mantel-Haenszel; PCI = percutaneous coronary intervention.

MIs out of 1,656 cases, crude rate 6.7%) were similar, with a calculated pooled RR of 1.10 (95% CI 0.73 to 1.66). However, the pooled estimate for MI generally favored CABG in subgroup analyses that included trials involving DESs. Figure 4 shows analysis according to the type of CAD. There was a meaningful trend toward fewer MIs with CABG with a similar magnitude of risk reduction across patients with multivessel (RR 0.72, 95% CI 0.53 to 0.99) and left main CAD (RR 0.74, 95% CI 0.47 to 1.15). Three trials exclusively included diabetic patients by the protocol, whereas the other 3 trials separately reported the MI rates in a subgroup of diabetic patients (Supplementary Figure 5). The risk of MI was consistently lower after CABG than PCI in an analysis of 3 trials that were limited to patients with diabetes (RR 0.55, 95% CI 0.44 to 0.70, p <0.001, $I^2 = 0\%$) as well as in an analysis of all 6 trials (RR 0.64, 95% CI 0.50 to 0.82, p <0.001, $I^2 = 24\%$). The Supplemental Table 3 shows the results of multivariable random effects metaregression. We found no significant relation between the risk of MI and the clinical or study-level variables (test for moderators p = 0.66), with a moderate amount of residual statistical heterogeneity after adjustment (test for residual heterogeneity p = 0.02, $I^2 = 62\%$).

DISCUSSION

The primary findings of this systematic meta-analysis with a specific emphasis on the occurrence of MI are as

Study or Subgroup	CABG Events	CABG Total	PCI Events	PCI Total	Weight	Risk Ratio MH, Random, 95% CI
Subgroup = BMS						
ARTS 2005	39	605	51	600	9.2%	0.76 [0.51, 1.13]
ERACI II 2005	14	225	6	225	4.6%	2.33 [0.91, 5.96]
MASS II 2010	21	203	27	205	7.8%	0.79 [0.46, 1.34]
Eefting 2003	7	142	6	138	3.9%	1.13 [0.39, 3.29]
SoS 2002	34	500	21	488	7.9%	1.58 [0.93, 2.68]
Total (95% CI)		**1675**		**1656**	**33.4%**	**1.10 [0.73, 1.66]**
Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 8.67$, df = 4 (P = 0.07); $I^2 = 54\%$						
Test for overall effect: Z = 0.46 (P = 0.65)						
Subgroup = 1st DES						
Boudriot 2011	3	101	3	100	2.2%	0.99 [0.20, 4.79]
FREEDOM 2012	48	947	98	953	9.9%	0.49 [0.35, 0.69]
PRECOMBAT 2015	5	300	6	300	3.4%	0.83 [0.26, 2.70]
SYNTAX 2013	33	897	83	903	9.3%	0.40 [0.27, 0.59]
Total (95% CI)		**2245**		**2256**	**24.8%**	**0.47 [0.37, 0.60]**
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 2.49$, df = 3 (P = 0.48); $I^2 = 0\%$						
Test for overall effect: Z = -5.98 (P < 0.01)						
Subgroup = 2nd DES						
BEST 2015	12	442	21	438	6.3%	0.57 [0.28, 1.14]
EXCEL 2016	77	957	72	948	10.1%	1.06 [0.78, 1.44]
NOBLE 2016	10	592	29	592	6.2%	0.34 [0.17, 0.70]
Total (95% CI)		**1991**		**1978**	**22.7%**	**0.63 [0.31, 1.27]**
Heterogeneity: $Tau^2 = 0.31$; $Chi^2 = 9.5$, df = 2 (P < 0.01); $I^2 = 79\%$						
Test for overall effect: Z = -1.30 (P = 0.19)						
Subgroup = BMS+1st DES						
BARI-2D 2009	28	378	90	798	9.2%	0.66 [0.44, 0.99]
CARDia 2010	14	254	25	256	6.9%	0.56 [0.30, 1.06]
LE MANS 2016	5	53	4	52	3.1%	1.23 [0.35, 4.31]
Total (95% CI)		**685**		**1106**	**19.1%**	**0.66 [0.47, 0.91]**
Heterogeneity: $Tau^2 = 0$; $Chi^2 = 1.17$, df = 2 (P = 0.56); $I^2 = 0\%$						
Test for overall effect: Z = -2.49 (P = 0.01)						
Total (95% CI)		**6596**		**6996**	**100.0%**	**0.75 [0.58, 0.96]**
Heterogeneity: $Tau^2 = 0.14$; $Chi^2 = 41.21$, df = 14 (P < 0.01); $I^2 = 66\%$						
Test for overall effect: Z = -2.25 (P = 0.02)						
Test for subgroup differences: $Chi^2 = 12.28$, df = 3 (P < 0.01)						

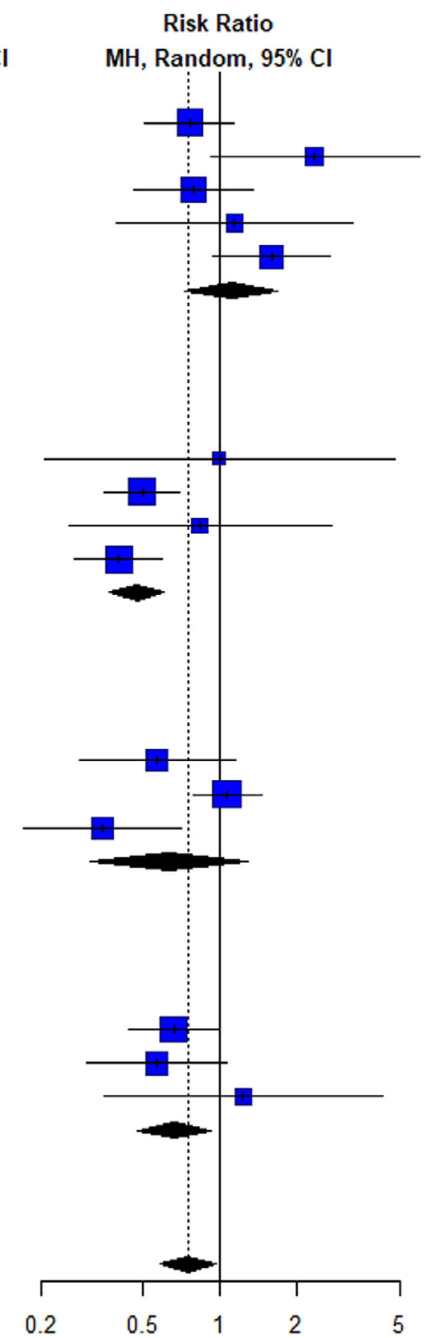

Figure 3. Risk ratios for myocardial infarction according to the type of stents. The black dotted line represents the random effects-generated overall estimate. BMS = bare-metal stent; CABG = coronary artery bypass grafting; CI = confidence intervals; DES= drug-eluting stent; MH = Mantel-Haenszel; PCI = percutaneous coronary intervention.

follows: (1) after a median follow-up of 4.5 years, the risk of MI was significantly lower with CABG than with PCI; (2) the risk reduction was more evident for patients with longer term follow-up, and in those with diabetes mellitus; and (3) the risk difference exists regardless of type of CAD and persist in the current second-generation DESs era. These findings support the notion that patients with severe CAD will benefit from CABG rather than PCI, and CABG is the preferred revascularization strategy in the prevention of future MIs.

The present meta-analysis shows that CABG appears to be associated with higher early risk of surgical complications, but the operative risk associated with CABG seems to be offset by a durable effect that translates into incremental benefits over time. These findings may be explained, at least in part, by the fundamental differences in the methodologies

Study or Subgroup	CABG Events	CABG Total	PCI Events	PCI Total	Weight	Risk Ratio MH, Random, 95% CI
Subgroup = Multivessel coronary artery disease						
ARTS 2005	39	605	51	600	8.7%	0.76 [0.51, 1.13]
BARI-2D 2009	28	378	90	798	8.6%	0.66 [0.44, 0.99]
BEST 2015	12	442	21	438	6.0%	0.57 [0.28, 1.14]
CARDia 2010	14	254	25	256	6.5%	0.56 [0.30, 1.06]
Eefting 2003	7	142	6	138	3.7%	1.13 [0.39, 3.29]
ERACI II 2005	14	225	6	225	4.4%	2.33 [0.91, 5.96]
FREEDOM 2012	48	947	98	953	9.3%	0.49 [0.35, 0.69]
MASS II 2010	21	203	27	205	7.4%	0.79 [0.46, 1.34]
SoS 2002	34	500	21	488	7.5%	1.58 [0.93, 2.68]
SYNTAX-MVD 2014	17	549	55	546	7.4%	0.31 [0.18, 0.52]
Total (95% CI)		**4245**		**4647**	**69.5%**	**0.72 [0.53, 0.99]**
Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 30.58$, df = 9 ($P < 0.01$); $I^2 = 71\%$						
Test for overall effect: Z = -2.00 (P = 0.05)						
Subgroup = Left main coronary artery disease						
Boudriot 2011	3	101	3	100	2.1%	0.99 [0.20, 4.79]
EXCEL 2016	77	957	72	948	9.5%	1.06 [0.78, 1.44]
LE MANS 2016	5	53	4	52	2.9%	1.23 [0.35, 4.31]
NOBLE 2016	10	592	29	592	5.9%	0.34 [0.17, 0.70]
PRECOMBAT 2015	5	300	6	300	3.2%	0.83 [0.26, 2.70]
SYNTAX-LM 2013	16	348	28	357	6.8%	0.59 [0.32, 1.06]
Total (95% CI)		**2351**		**2349**	**30.5%**	**0.74 [0.47, 1.15]**
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 10.06$, df = 5 ($P = 0.07$); $I^2 = 50\%$						
Test for overall effect: Z = -1.36 (P = 0.17)						
Total (95% CI)		**6596**		**6996**	**100.0%**	**0.73 [0.56, 0.93]**
Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 42.99$, df = 15 ($P < 0.01$); $I^2 = 65\%$						
Test for overall effect: Z = -2.51 (P = 0.01)						
Test for subgroup differences: $Chi^2 = 0.00$, df = 1 (P = 0.95)						

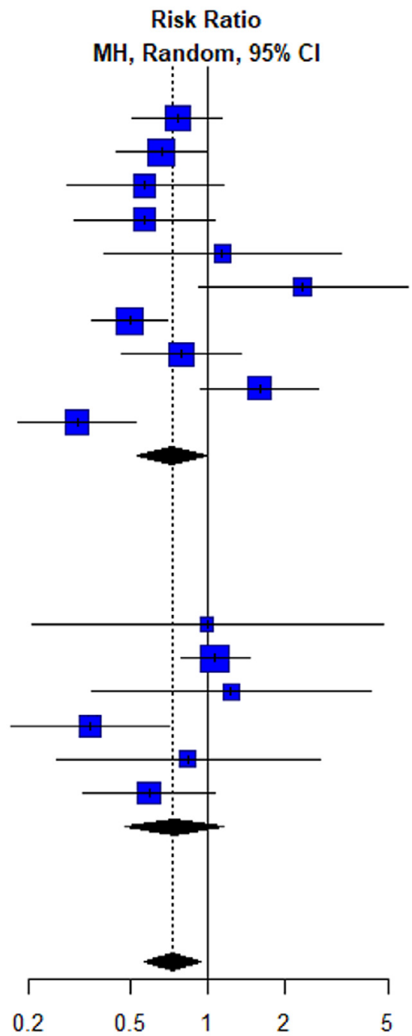

Figure 4. Risk ratios for myocardial infarction according to the type of coronary artery disease. The black dotted line represents the random effects-generated overall estimate. CABG = coronary artery bypass grafting; CI = confidence intervals; MH = Mantel-Haenszel; PCI = percutaneous coronary intervention.

of CABG and PCI. In contrast with PCI, which directly relieves the culprit lesion with stents, a graft in CABG is placed beyond the culprit lesion, which increases the probability to achieve complete revascularization (Supplemental Table 4) and may provide a protective role regarding future ischemic events arising from lesions at proximal segments, consequently, leading to a reduction in MI. Accordingly, although the introduction of DESs and improved interventional techniques have progressively enhanced the PCI outcomes, it does not seem to be sufficient to overcome the relative advantage of CABG arising from this methodologic difference. This has been supported by large real-world multivessel or left main registries comparing CABG and contemporary DESs.[18,19] The observation that the risk reduction of MI with CABG is more definite over time might be of clinical significance, especially for high-risk patients. Although MI is a well-established prognostic event, its negative impact may be more exacerbated in patients with previous MI, heart failure, or severe left ventricular dysfunction.[20,21] Because long-term prevention of additional myocardial damage is essential in these high-risk patients, who were largely underrepresented in clinical trials, our finding may be an important rationale to choose CABG when revascularization is considered, and presumably, an operative risk is acceptable. A further advance in myocardial protection, operative technique, and perioperative care will minimize the risk of postoperative MI, enhancing the long-term prognostic advantage of CABG over PCI.

One issue raised by our meta-analysis is the apparent heterogeneity in studies for MI, of which the reason could not be explained by a small-study effect or by important clinical and trial-level variables tested in the metaregression. However, this finding is consistent with the assessment of other previous meta-analyses[22,23] and should be understood by the relative MI outcomes of CABG versus PCI are determined by a complex interplay of patient co-morbidities, coronary anatomic complexity, procedural specifics, and other less tangible factors such as operator expertise and pharmacotherapy. For instance, improvements in stent design and PCI techniques have led to the inclusion of higher risk patients with more complex disease in randomized trials over time.[1] Thus, the similar risk of MI with CABG and bare-metal stents shown in our analysis would be most likely due to less complex CAD included in earlier trials. PCI was performed with different stents with varying efficacy and safety profiles,[24] and the recommendation or rates of intravascular ultrasound guidance, a practice that has been associated with higher event-free survivals with PCI,[25] was highly variable in trials. The use of off-pump CABG, a controversial technique that several studies showed less effective revascularization than the on-pump surgery,[26] ranged from 16% to 64% in trials. Moreover, the definition of MI was substantially different in studies not only for the early postoperative period but also for follow-up (Supplemental Table 2).[27–29] The presence of new Q wave or left bundle branch block was mandatory to adjudicate MI during follow-up in ERACI II and Stent or Surgery trial, whereas only a meaningful biomarker elevation was required for MI in LEMANS and Boudriot study. Further efforts may be needed to reach a reasonable consensus regarding the standard definition of procedure-related or nonprocedure-related MI.[30]

This study has several limitations. First, although the individual trials were randomized, the outcomes were analyzed from aggregate data, and we cannot exclude effects from differences in measured or unmeasured baseline characteristics. Second, the weighted follow-up period was 4.5 years, and a longer term outcome is required to determine whether the differences between CABG and PCI continue to accrue or are attenuated over time. Third, heterogeneity associated with pooled estimates in trials may have reduced evidence quality. Future RCTs comparing CABG and PCI should be designed with effort considering the factors discussed above to assure the quality of clinical trials for sensible interpretation.

In conclusion, the present meta-analysis of studies involving patients with multivessel or left main CAD supports a significant benefit of CABG over PCI concerning the rate of MI during a weighted follow-up of 4.5 years. Moderate interstudy heterogeneity was noted, likely because of differences in definitions of MI, the risk profile of enrolled patients, and procedural specifics.

Disclosures

The authors have no conflicts of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.06.009.

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