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CME

# Outcomes After Complete Versus Incomplete Revascularization of Patients With Multivessel Coronary Artery Disease

## A Meta-Analysis of 89,883 Patients Enrolled in Randomized Clinical Trials and Observational Studies

Santiago Garcia, MD,*† Yader Sandoval, MD,‡ Henri Roukoz, MD, MS,† Selcuk Adabag, MD, MS,*† Mariana Canoniero, MD,§ Demetris Yannopoulos, MD,† Emmanouil S. Brilakis, MD, PhD||¶

*Minneapolis, Minnesota; and Dallas, Texas*

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**CME Objective for This Article:** At the conclusion of this activity, the learner should be able to compare CR versus IR in patients with multivessel CAD.

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From the *Division of Cardiology, Department of Medicine, Minneapolis Veterans Affairs Healthcare System, Minneapolis, Minnesota; †Department of Medicine, University of Minnesota Medical School, Minneapolis, Minnesota; ‡Department of Medicine, Hennepin County Medical Center, Minneapolis, Minnesota; §Department of Medicine, Division of Cardiology, Park Nicollet Clinic Heart and Vascular Center, St. Louis Park, Minnesota; ||Department of Medicine, Division of Cardiology, VA North Texas Healthcare System, Dallas, Texas; and the ¶University of Texas Southwestern Medical School, Dallas, Texas. The contents of this paper do not represent the views of the Department of Veterans Affairs or the U.S. government.

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# Outcomes After Complete Versus Incomplete Revascularization of Patients With Multivessel Coronary Artery Disease

## A Meta-Analysis of 89,883 Patients Enrolled in Randomized Clinical Trials and Observational Studies

**Objectives** This study sought to perform a systematic review and meta-analysis of studies comparing complete revascularization (CR) versus incomplete revascularization (IR) in patients with multivessel coronary artery disease.

**Background** There are conflicting data regarding the benefits of CR in patients with multivessel coronary artery disease.

**Methods** We identified observational studies and subgroup analysis of randomized clinical trials (RCT) published in PubMed from 1970 through September 2012 using the following keywords: "percutaneous coronary intervention" (PCI); "coronary artery bypass graft" (CABG); "complete revascularization"; and "incomplete revascularization." Main outcome measures were total mortality, myocardial infarction, and repeat revascularization procedures.

**Results** We identified 35 studies including 89,883 patients, of whom 45,417 (50.5%) received CR and 44,466 (49.5%) received IR. IR was more common after PCI than after CABG (56% vs. 25%; $p < 0.001$). Relative to IR, CR was associated with lower long-term mortality (risk ratio [RR]: 0.71, 95% confidence interval [CI]: 0.65 to 0.77; $p < 0.001$), myocardial infarction (RR: 0.78, 95% CI: 0.68 to 0.90; $p = 0.001$), and repeat coronary revascularization (RR: 0.74, 95% CI: 0.65 to 0.83; $p < 0.001$). The mortality benefit associated with CR was consistent across studies irrespective of revascularization modality (CABG: RR: 0.70, 95% CI: 0.61 to 0.80; $p < 0.001$; and PCI: RR: 0.72, 95% CI: 0.64 to 0.81; $p < 0.001$) and definition of CR (anatomic definition: RR: 0.73, 95% CI: 0.67 to 0.79; $p < 0.001$; and nonanatomic definition: RR: 0.57, 95% CI: 0.36 to 0.89; $p = 0.014$).

**Conclusions** CR is achieved more commonly with CABG than with PCI. Among patients with multivessel coronary artery disease, CR may be the optimal revascularization strategy. (J Am Coll Cardiol 2013;62:1421–31) © 2013 by the American College of Cardiology Foundation

Over 1,000,000 coronary revascularization procedures are performed every year in the United States for the treatment of coronary artery disease (CAD) (1). Coronary revascularization improves symptoms and, in select groups, reduces myocardial infarction and long-term mortality (2–5).

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Achieving complete revascularization (CR) has long been a goal of coronary artery bypass graft (CABG) surgery (6,7). A seminal observation from the CASS (Coronary Artery Surgery Study) registry showed that patients with multivessel CAD and severe angina that received 3 or more grafts had better survival relative to patients who received 1 or 2 grafts (8). By extension, the concept of CR has also been advocated in percutaneous coronary intervention (PCI) (9,10). Despite this long-held belief, observational studies have yielded conflicting results (10–12) and no large multicenter randomized clinical trial (RCT) has ever tested whether CR is superior to incomplete revascularization (IR). CR is infrequent in clinical practice (10,13), and guidelines do not formally address the issue of CR in detail (14,15). Thus, the purpose of the present investigation was to perform a systematic review and meta-analysis of RCTs and observational studies to determine if CR is associated with improved clinical outcomes compared with outcomes of IR.

## Methods

We identified observational studies and RCTs published in PubMed from 1970 through September 2012 using the following keywords: "percutaneous coronary intervention"; "coronary artery bypass graft"; "complete revascularization"; and "incomplete revascularization." We limited our search criteria to include studies published in the English language and those involving humans. We identified additional studies by searching Clinicaltrials.gov and by hand-searching references cited in relevant publications. This methodological approach has been previously validated (16). "RCT," as used throughout this paper, refers to the design of the study from which the data was obtained. It does not imply that the randomization variable was completeness of revascularization.

**Data sources and study search strategy.** We included observational studies and RCTs that: 1) enrolled patients with multivessel CAD referred for coronary revascularization with CABG or PCI; 2) compared the outcomes of CR versus IR using any of the definitions listed in Online Table 1 (14); and 3) reported long-term mortality rates.

We excluded: 1) studies assessing the role of PCI on the nonculprit vessel for the treatment of ST-segment elevation myocardial infarction; 2) studies comparing outcomes of PCI for chronic total occlusion (CTO) (success vs. failure) unless the degree of completeness of revascularization was also reported; 3) studies that focused on patients with redo-CABG; and 4) single-center studies with small sample size (≤100 patients in each treatment arm).

**Study selection.** Our initial search yielded 6,668 citations (Fig. 1). Of these, 6,134 (92%) were excluded by title search because of irrelevant content, animal subjects, or publication in a language other than English. The abstracts of the remaining 534 studies were reviewed. Of these, 109 abstracts were deemed eligible for full-text manuscript review, and 425 (79.5%) were excluded for various reasons (Fig. 1). Of the 109 full-text manuscripts reviewed for eligibility, 24 met the inclusion criteria. An additional 11 manuscripts were identified through hand-searching leading to a total of 35 studies included in this meta-analysis.

**Data extraction.** Data were abstracted by 2 reviewers (S.G. and Y.S.) using standardized data extraction forms. Discrepancies were resolved by consensus. Abstracted information included study design, time frame, key patient and procedural characteristics, and relevant outcomes. For RCTs that reported outcomes for CABG and PCI separately, we made 2 entries, 1 for each revascularization modality. When outcomes were not reported separately, we included the study in the main analysis but not in the subgroup analysis of revascularization modalities.

**Outcomes.** The primary outcome for this systematic review was all-cause mortality. Secondary outcomes were myocardial infarction (MI) and repeat revascularization.

**Methodological quality.** Study selection, data collection, analysis, and reporting of the results were performed using the recommendations of the MOOSE (Meta-analysis Of Observational Studies in Epidemiology) Group (17). Heterogeneity across trials was assessed using the Cochrane Q-statistic ($p < 0.1$ was considered significant) and $I^2$-statistic (18). $I^2$ describes the percentage of total variation across studies that is due to heterogeneity rather than chance (18). A value of 0% indicates no heterogeneity, and larger values indicate increased heterogeneity. Publication bias was visually estimated by assessing funnel plots.

We calculated weighted risk ratios (RR) and 95% confidence intervals (CIs) for categorical variables. Each RR was calculated according to the DerSimonian-Laird random effects model. Automatic "zero cell" correction was used for studies with no events for a particular outcome. All analyses were performed using STATA software (version 10.1, StataCorp, College Station, Texas).

## Results

**Study and patient characteristics.** The characteristics of the 35 studies that met eligibility criteria are displayed in Table 1 and Online Appendix 1. A full listing of all 35 papers is provided in Online Appendix 2. Of these, 28 were observational studies, 5 were subgroup analysis of RCTs, 1 was a subgroup analysis of a non-RCT, and 1 was a single-center RCT comparing CR versus IR. Four of the 35 studies reported outcomes for PCI and CABG separately, resulting in 39 entries (Table 1). Of the 39 study entries, 34 (87%) used an anatomic definition of CR, 2 (5%) a functional definition, 2 (5%) a numerical definition, and 1 (2.5%) multiple definitions of CR. The funnel plots were not suggestive of a publication bias (Online Figs. 1 to 3). Online Appendix 3 contains the definition of MI used in each study.

The present analysis includes 89,883 patients, of which 45,417 (50.5%) received CR and 44,466 (49.5%) received IR. The revascularization modality was CABG for 25,938 patients (29%) and PCI for the remaining 63,945 patients (71%).

Mean age of the study participants was 63 ± 7 years, 74% were male, 25% had diabetes mellitus, and 43% had a previous MI. The mean follow-up time was 4.6 ± 4 years.

**Abbreviations and Acronyms**

**CABG** = coronary artery bypass graft

**CAD** = coronary artery disease

**CI** = confidence interval

**CR** = complete revascularization

**CTO** = chronic total occlusion

**FFR** = fractional-flow reserve

**IR** = incomplete revascularization

**MI** = myocardial infarction

**OR** = odds ratio

**PCI** = percutaneous coronary intervention

**RCT** = randomized clinical trial

**RR** = risk ratio

**Mortality.** Of the 89,883 patients included in this meta-analysis, 12,259 (13%) died during follow-up. CR was associated with reduced long-term mortality relative to IR (RR: 0.71; 95% CI: 0.65 to 0.77; $p < 0.001$, $I^2 = 71\%$) (Fig. 2, Online Table 2). The mortality benefit was observed in patients treated with CABG and PCI (CABG: RR: 0.70, 95% CI: 0.61 to 0.80; $p < 0.001$; $I^2 = 80\%$; and PCI: RR: 0.72, 95% CI: 0.64 to 0.81; $p < 0.001$; $I^2 = 62\%$) (Figs. 3 and 4). Likewise, the mortality benefit associated with CR was seen in RCTs (RR: 0.76, 95% CI: 0.62 to 0.92; $p = 0.006$; $I^2 = 0\%$) and observational studies (RR: 0.70, 95% CI: 0.64 to 0.77; $p < 0.001$, $I^2 = 78\%$) and did not vary substantially with the definition of CR (anatomic RR: 0.73, 95% CI: 0.67 to 0.79; $p < 0.001$; $I^2 = 65\%$; and nonanatomic RR: 0.54; 95% CI: 0.36 to 0.89; $p = 0.01$; $I^2 = 88\%$).

**Myocardial infarction.** Eighteen of 35 studies reported 1,509 MI during follow-up. Compared with IR, CR was associated with lower risk of MI (RR: 0.78, 95% CI: 0.68 to 0.90; $p = 0.001$; $I^2 = 19\%$). A reduction in MI was observed among PCI-treated patients (PCI: RR: 0.80, 95% CI: 0.71 to 0.91; $p = 0.001$; $I^2 = 0\%$) but not among CABG-treated patients (CABG: RR: 0.69, 95% CI: 0.44 to 1.10; $p = 0.12$; $I^2 = 62\%$). The lower risk of MI was seen in RCTs (RR: 0.72, 95% CI: 0.61 to 0.86; $p < 0.001$; $I^2 = 0\%$), observational studies (RR: 0.78, 95% CI: 0.61 to 1.00; $p = 0.05$; $I^2 = 44\%$), and studies that used an anatomic definition of CR (RR: 0.72, 95% CI: 0.63 to 0.83; $p < 0.001$; $I^2 = 0.3\%$). Only 1 study reported MI rates using a nonanatomic definition of CR (RR: 0.99, 95% CI: 0.74 to 1.25; $p = 0.79$).

**Repeat coronary revascularization.** Twenty of 35 studies reported 5,756 repeat revascularization procedures during follow-up. Compared with IR, CR was associated with lower

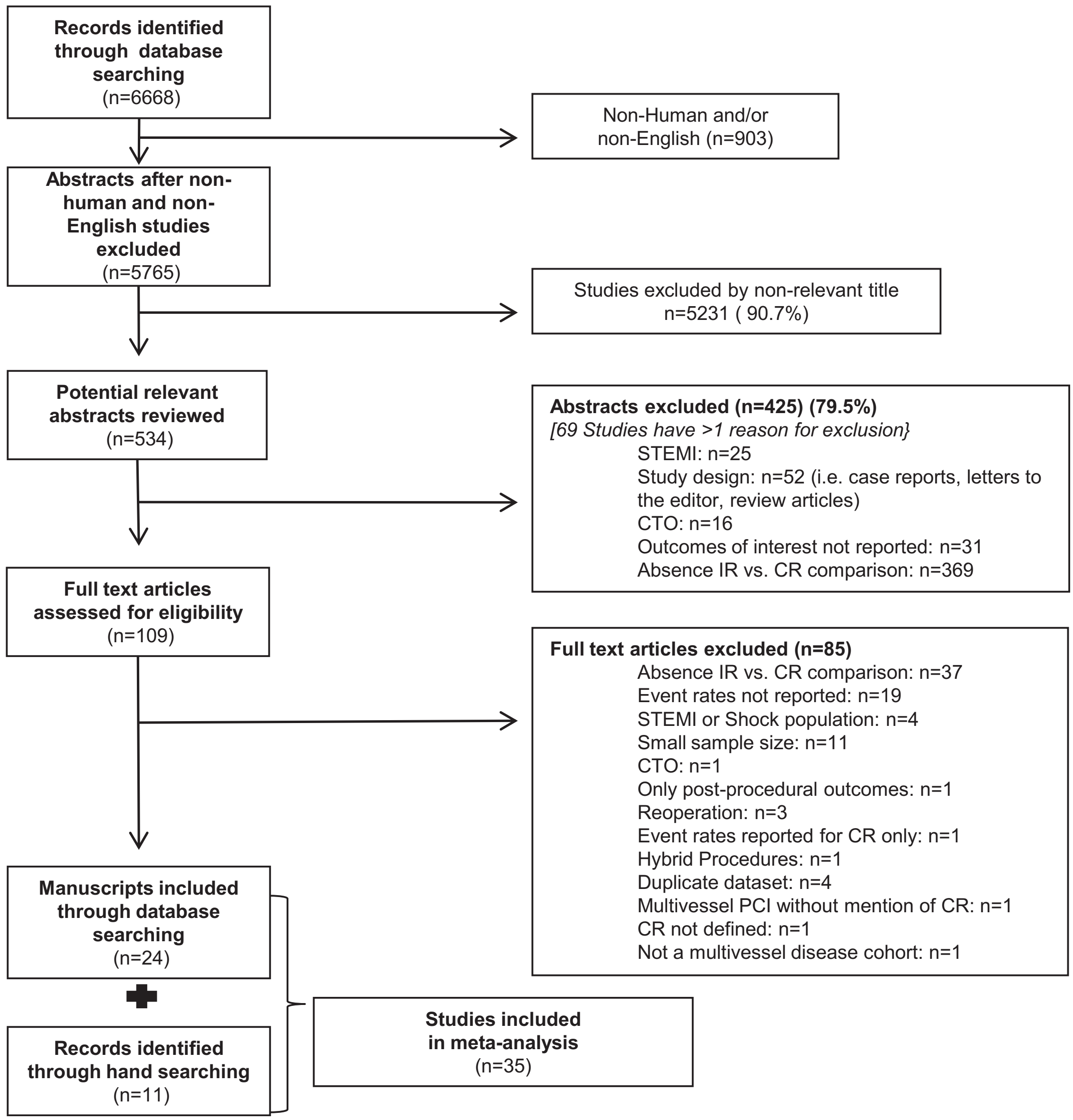


**Figure 1** **Flow Diagram of the Literature Search and Study Selection**

A total of 6,668 citations were identified through database searching and 109 full text manuscripts were reviewed for eligibility, of which 24 met the inclusion criteria. Eleven manuscripts were identified through hand searching, leading to a total of 35 studies included in this meta-analysis. CR = complete revascularization; CTO = chronic total occlusions; IR = incomplete revascularization; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

risk of repeat revascularization procedures (RR: 0.74, 95% CI: 0.65 to 0.83; $p < 0.001$; $I^2 = 65\%$). CR was associated with fewer repeat revascularization procedures among PCI-treated patients (RR: 0.72, 95% CI: 0.63 to 0.81; $p < 0.001$; $I^2 = 70\%$) but not among CABG-treated patients (RR: 0.92, 95% CI: 0.67 to 1.28; $p = 0.64$; $I^2 = 22\%$). The benefit of CR in reducing repeat revascularization procedures was seen in RCTs (RR: 0.67, 95% CI: 0.60 to 0.75; $p < 0.001$; $I^2 = 0\%$) and observational studies (RR: 0.79, 95% CI: 0.66 to 0.95; $p = 0.01$; $I^2 = 76\%$). CR was associated with a reduced need for repeat coronary revascularization in studies that used an anatomic definition of CR (RR: 0.74, 95% CI: 0.66 to 0.83; $p < 0.001$; $I^2 = 54\%$). Only 1 study reported repeat revascularization rates using a nonanatomic definition of CR (RR: 0.55, 95% CI: 0.44 to 0.67; $p < 0.001$).

## Discussion

The results of this systematic review and meta-analysis of CR versus IR in patients with multivessel CAD show that CR is more often achieved with CABG than with PCI and is associated with a 30% reduction in long-term mortality, a 22% reduction in MI, and a 26% reduction in repeat coronary revascularization procedures. The lower mortality associated with CR was seen in both PCI- and CABG-treated patients and was independent of the study design and definition of CR.

The association between CR and lower risk for subsequent cardiovascular events may be causal. CR may improve clinical outcomes by reducing or eliminating myocardial ischemia, which has been linked to worse prognosis, especially when large (19). CR may improve exercise capacity, reduce the risk of arrhythmic events, and improve tolerance to future acute coronary ischemic events (20). Alternatively, IR may be a surrogate marker for higher baseline ischemic burden and more advanced CAD that is less amenable to revascularization by either PCI or CABG.

The findings of this study have several practical implications for cardiologists and surgeons alike. First, given the strong clinical benefit in patients with multivessel disease, CR may be the optimal revascularization strategy. The likelihood of achieving CR with either revascularization modality, ideally estimated by a heart team approach, should influence the decision to proceed with CABG or PCI. With this approach in the SYNTAX (Synergy Between PCI With Taxus and Cardiac Surgery) trial (21), the rates of IR were 43.3% for PCI and 36.8% for CABG, which compares favorably with historical cohorts (13), while still highlighting the procedural complexity of achieving CR. The most common reasons for not achieving CR with PCI in SYNTAX were the presence of CTO (odds ratio [OR]: 2.46, 95% CI: 1.81 to 3.39; $p < 0.01$), bifurcation disease (OR: 1.44, 95% CI: 1.09 to 1.89; $p = 0.01$), and diffuse disease or small vessels (<2 mm) (OR: 1.53, 95% CI: 1.12 to 2.10, $p < 0.008$) (22). Overall, the SYNTAX score, a surrogate marker for disease complexity, was higher in IR than in CR patients (31.4 $\pm$ 11 vs. 26.2 $\pm$ 10; $p < 0.01$) (22). Many of the barriers for achieving CR with PCI are no longer insurmountable (23). For example, CTO-PCI has evolved dramatically over the last decade with experienced operators reporting recanalization rates of 80% to 90% with advanced CTO techniques such as dual injections, antegrade dissection re-entry, and retrograde wiring (24–26). The most common reasons for not achieving CR with CABG were unstable angina presentation (OR: 1.37, 95% CI: 1.01 to 1.85; $p = 0.04$), diffuse disease or small vessels (OR: 2.10, 95% CI: 1.51 to 2.93; $p < 0.001$), and number of lesions (OR: 1.71, 95% CI: 1.55 to 1.90; $p < 0.001$) (20). Some of those barriers may be hard to overcome; bypassing small vessels is associated with higher rates of saphenous vein graft failure, and some patients may not have enough saphenous vein conduits to allow revascularization of all potential coronary targets. Based on data from the BARI (Bypass Angioplasty Revascularization Investigation) trial and others (27) showing no survival disadvantage when non–left anterior descending artery territories were left ungrafted, many surgeons have advocated the concept of incomplete "reasonable" revascularization mainly as an attempt to limit aortic cross-clamp time (28–31). Our study cannot address this issue, yet it would suggest that leaving potentially viable and graftable target coronary arteries unrevascularized is not prudent.

Second, the mortality benefit seen in this meta-analysis with CR was of about the same magnitude ($\sim$30%) in patients receiving CABG or PCI, which suggests that the revascularization modality may not be as important as the objective of achieving CR is. For example, in the SYNTAX trial for patients in the lowest tercile of the SYNTAX score ($\leq$22), IR rates between PCI and CABG were not dissimilar (31% vs. 27%) and no statistical difference in major adverse cardiac or cerebrovascular events was seen between PCI (13.6%) and CABG (14.7%) at 1-year ($p = 0.71$) (21). In contrast, for patients in the highest tertile of the SYNTAX score ($\geq$33) as the rates of incomplete revascularization increased disproportionately for PCI patients (57%) so did major adverse cardiac or cerebrovascular events rates, which were 23.4% for PCI and 10.9% for CABG ($p < 0.001$) at 1 year and 34% and 19% at 3 years ($p < 0.001$), respectively (30). Our study extends this observation by demonstrating that CR may provide similar relative reduction in the risk of major adverse cardiovascular events in patients treated with either PCI or CABG.

Third, although the majority of studies (87%) included in this meta-analysis used an anatomic definition of CR, the results did not change significantly for the hard endpoint of long-term mortality when a nonanatomic definition of CR was used. For the outcomes of MI and repeat revascularization, only 1 study reported event rates using a nonanatomic definition.

The current data lacks a standardized, universal definition of what constitutes an IR procedure (14,29). Gössl et al. (31) recently proposed a universal definition of IR using coronary angiography and fractional-flow reserve (FFR) data. The proposed definition of incomplete anatomic and functional revascularization is based on the inability to treat: 1) all coronary segments that have a $\geq$50% to 70% diameter stenosis and an FFR $\leq$0.80; or 2) >70% stenosis without FFR that supply a significant degree of viable myocardium. Based on the previous work by Piljs et al. (32) regarding the excellent long-term outcomes of patients with intermediate stenosis and insignificant FFR and the observation that FFR-guided PCI in patients with multivessel CAD is superior to angiography-guided PCI (33), a definition of IR that includes anatomy and physiology seems intuitive, although it requires prospective validation.

Finally, the finding that in patients treated with CABG CR was not associated with a reduction in MI or repeat revascularization procedures may be due to the small number of studies that reported those outcomes. Alternatively, the degree of completeness of revascularization may not be as important in reducing MI or repeat procedures in CABG as long as the 3 major epicardial vessels are grafted (27).

**Study limitations.** First, observational studies and post hoc analysis of randomized clinical trials were included in

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**Table 1** Summary of Key Demographic Characteristics of Observational Studies and Randomized Clinical Trials Included in the Meta-Analysis

| Study Name/First Author | Revascularization Modality | Study Period | Study Design | Definition of CR Used | Follow-Up, yrs | ACS, %* | Prevalence of IR, % | Male Sex, % | Mean Age, yrs | Previous MI, % | Diabetes, % |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ARTS I CABG/van der Brand | CABG | 1997–1998 | Post-hoc analysis of RCT CABG vs. PCI | Anatomic | 1 | 36–39 | 16 | 69 | 61 | 36–43 | 15–23 |
| ARTS I PCI/van der Brand | PCI | 1997–1999 | Post-hoc analysis of RCT CABG vs. PCI | Anatomic | 1 | 36–40 | 30 | 79 | 61–62 | 43–44 | 17–19 |
| ARTS II PCI/Sarno | PCI | 2003–2004 | Post-hoc analysis of non-RCT | Anatomic | 5 | 41–49 | 39 | 77 | 62–63 | 32–36 | 25–26 |
| Asian Medical Center/Kim CABG cohort | CABG | 2003–2005 | Observational cohort study CABG vs. PCI | Anatomic | 5 | 61 | 33 | 72 | 61–62 | 22–27 | 38–44 |
| Asian Medial Center/Kim PCI cohort (1) | PCI | 2003–2005 | Observational cohort study CABG vs. PCI | Anatomic | 5 | 42 | 59 | 71 | 60–62 | 10 | 30–32 |
| SYNTAX CABG/Head | CABG | 2005–2007 | Post-hoc analysis of RCT CABG vs. PCI | Anatomic | 3 | 26–32 | 37 | 79 | 64–65 | 31–37 | 22–25 |
| SYNTAX PCI/Head | PCI | 2005–2007 | Post-hoc analysis of RCT CABG vs. PCI | Anatomic | 3 | 27–30 | 43 | 79 | 65 | 32 | 22–30 |
| MASS II CABG/D'Oliveira Vieira | CABG | 1995–2001 | Post-hoc analysis of RCT CABG vs. PCI | Anatomic | 10 | 0 | 36 | 72 | 62 | 55 | 41 |
| MASS II PCI/D'Oliveira Vieira | PCI | 1995–2001 | Post-hoc analysis of RCT CABG vs. PCI | Anatomic | 10 | 0 | 64 | 67 | 59 | 57 | 34 |
| Emory/Jones | CABG | 1978–1981 | Observational cohort CABG study | Anatomic | 5 | 63 | 27 | 84 | 54 | 55 | NR |
| Cleveland/Scott | CABG | 1971–1997 | Observational cohort CABG study | Anatomic | 20 | NR | 38 | 81 | 54 | 41 | 8 |
| BARI/Van der Salm | CABG | 1988–1991 | Post-hoc analysis of RCT CABG vs. PCI and observational cohort CABG study | Multiple definitions | 7 | 65 | 17 | 74 | 62 | 53 | 19 |
| Cedars Sinai/Kleisli | CABG | 1998–2000 | Observational cohort CABG study | Functional | 5 | NR | 9 | 63 | 71 | 18–33 | 31–45 |
| Leipzig/Rastan | CABG | 2000–2007 | Observational cohort CABG study | Anatomic | 5 | NR | 10 | 77 | 67 | 47 | 31–38 |
| Wash U/Kozower (2) | CABG | 1986–2003 | Observational cohort CABG study | Anatomic | 8 | 30–34 | 20 | 52 | 83 | NR | 27–36 |
| Bristol Heart Institute/Caputo (3) | CABG | 1996–2002 | Observational cohort CABG study | Numerical | 2 | NR | 16 | 75 | NR | NR | 18–20 |
| University of Heidelberg/Osswald (2) | CABG | 1988–1999 | Observational cohort CABG study | Anatomic | 0.5 | NR | 16 | 65 | 77 | NR | NR |
| Quebec Heart and Lung University Institute/Mohammadi (2) | CABG | 1992–2008 | Observational cohort CABG study | Anatomic | 8 | 33–40 | 18 | 59 | 82 | 57–70 | 20–27 |
| BARI trial and registry/Kip (4) | PCI | 1988–1991 | Post-hoc analysis of RCT CABG vs. PCI plus registry | Anatomic | 5 | NR | 41 | NR | 61 | 50–56 | 15–20 |
| BARI/Bourassa | PCI | 1988–1991 | Post-hoc analysis of RCT CABG vs. PCI | Anatomic | 5 | 63 | 36 | 77 | 62 | 51–59 | 17–23 |

*Continued on the next page*

**Table 1 Continued**

| Study Name/First Author | Revascularization Modality | Study Period | Study Design | Definition of CR Used | Follow-Up, yrs | ACS, %* | Prevalence of IR, % | Male Sex, % | Mean Age, yrs | Previous MI, % | Diabetes, % |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Erasmus University/Ijsselmuiden | PCI | 1995–1998 | Single-center RCT | Anatomic | 5 | 37 | 50 (randomized) | 74 | 62 | 42 | 14 |
| New York State registry/Hannan (5) | PCI | 1997–2000 | Observational cohort PCI study | Anatomic | 3 | NR | 69 | 69 | NR | 32 | 71† |
| New York State registry/Hannan (5) | PCI | 2003–2004 | Observational cohort PCI study | Anatomic | 1.5 | 37 | 69 | 67 | NR | 30–38 | 28–34 |
| Careggi Hospital/Valenti (6) | PCI | 2003–2006 | Observational cohort PCI study | Anatomic | 2 | 32–39 | 38 | 83 | 67–69 | 45–54 | 21–24 |
| ACUITY/Genereux (7) | PCI | 2003–2005 | Observational cohort PCI study | Score-based | 1 | 100 | 60 | 68 | 59–63 | 25–34 | 25–34 |
| ACUITY/Rosner (8) | PCI | 2003–2005 | Observational cohort PCI study | Anatomic | 1 | 100 | 37 | 69 | 59–61 | 28–31 | 28–31 |
| Nikolsky (9) | PCI | 1992–1999 | Observational cohort PCI study | Anatomic | 3 | 22 | 73 | 73 | 61 | 27–37 | 100 |
| University of Catania/Tamburino | PCI | 2002–2005 | Observational cohort PCI study | Anatomic | 3 | 45–55 | 58 | 79 | 61–63 | 23–33 | 32–35 |
| Legnano Italy/Mariani | PCI | 1997–1998 | Observational cohort PCI study | Anatomic | 1 | 100 | 76 | 83 | 63 | 41 | 17 |
| NHLBI dynamic registry/Srinivas (10) | PCI | 1997–2004 | Observational cohort PCI study | Anatomic | 1 | 34–39 | 78 | 67 | 61–63 | 20–30 | 29–32 |
| Basel University Hospital/Kloeter | PCI | 1993–1997 | Observational cohort PCI study | Anatomic | 2.5 | NR | 40 | 82 | 59 | 60 | 15 |
| CABRI/Breeman (11) | PCI | 1990–1994 | Post-hoc analysis of RCT | Anatomic | 1 | 25 | 72 | 81 | 61 | 40–53 | 9–17 |
| Emory/Jones | CABG | 1978–1981 | Observational cohort CABG study | Anatomic | 11 | 52–56 | 28 | 84 | 57 | 55–63 | NR |
| New York State registry/Wu (12) | PCI | 1999–2000 | Observational cohort PCI study | Anatomic | 8 | NR | 70 | 69 | NR | 55 | 27 |
| Henan Province/Yang | PCI | 2003–2006 | Observational cohort PCI study | Anatomic | 1.5 | 92 | 78 | 78 | 61 | 35 | 19 |
| Duke/McNeer | CABG | 1969–1973 | Observational cohort CABG study | Numeric | 2 | NR | 52 | NR | NR | 43–58 | 9 |
| Warsaw Institute of Cardiology/Norwa-Otto | PCI | 1988–1997 | Observational cohort PCI study | Functional | 11 | 30–36 | 69 | 82 | 52 | 58–65 | 7 |
| University of Toronto/Appleby | PCI | 2000–2007 | Observational cohort PCI study | Anatomic | 3.7 | 53 | 65 | 72 | 63 | 32 | 27 |
| Saint Louis University/Tyras | CABG | 1970–1977 | Observational cohort CABG study | Anatomic | 4 | 10 | 29 | 85 | 52 | 48 | 16 |
| Saint Louis University/Deligonul | PCI | 1983–1986 | Observational PCI cohort study | Anatomic | 2 | 49 | 31 | 76 | NR | 45 | NR |

Please see Online Appendix 1 for the notes on this table.

ACS = acute coronary syndrome; ACUITY = Acute Catheterization and Urgent Intervention Triage Strategy; ARTS = Arterial Revascularization Therapies Study; BARI = Bypass Angioplasty Revascularization Investigation; CABG = coronary artery bypass graft; CABRI = Coronary Angioplasty versus Bypass Revascularization Investigation; MASS II = Second Medicine, Angioplasty or Surgery Study; MI = myocardial infarction; NHLBI = National Heart, Lung, and Blood Institute; NR = not reported; PCI = percutaneous coronary intervention; RCT = randomized clinical trial; SYNTAX = Synergy Between PCI with Taxus and Cardiac Surgery.

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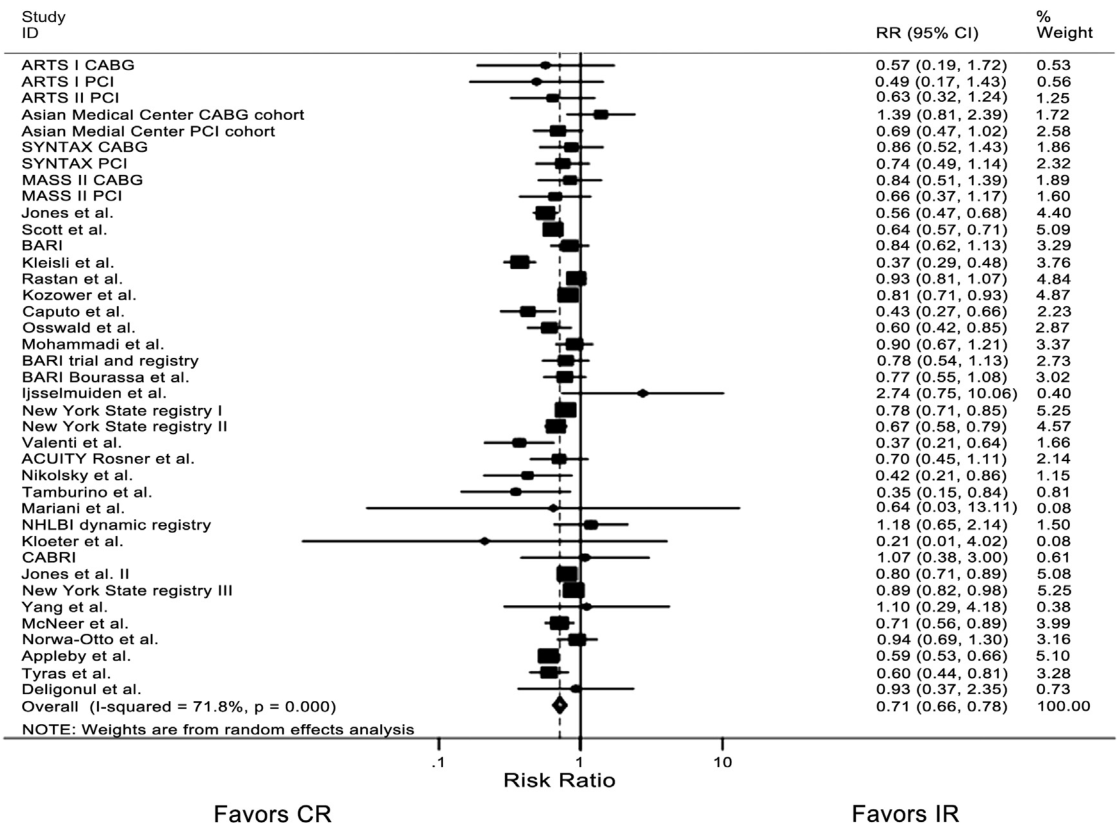


**Figure 2** Pooled Analysis With RR and 95% CI for the Occurrence of Total Mortality

**Boxes** are the relative risk estimates from each study; the **horizontal bars** are 95% confidence intervals (CI). The size of the **box** is proportional to the weight of the study in the pooled analysis. ACUITY = Acute Catheterization and Urgent Intervention Triage Strategy; ARTS = Arterial Revascularization Therapies Study; BARI = Bypass Angioplasty Revascularization Investigation; CABG = coronary artery bypass graft; CABRI = Coronary Angioplasty Versus Bypass Revascularization Investigation; NHLBI = National Heart, Lung, and Blood Institute; RR = risk ratio(s); SYNTAX = Synergy Between PCI With Taxus and Cardiac Surgery; other abbreviations as in Figure 1.

this meta-analysis. Many of these studies had different entry criteria, study populations, and follow-up time. This is a source of increased heterogeneity that may limit the generalizability of our conclusions to the broader multivessel CAD population (18). However, the beneficial effects of CR in terms of reducing mortality, MI, and repeat revascularization procedures persisted when the analysis was restricted to RCTs with similar entry criteria and low heterogeneity ($I^2 < 25\%$). Second, it is plausible that IR could be a surrogate marker for residual CAD or other important comorbidities that, though not amenable to revascularization, would place patients at risk of adverse clinical events (CTO, small vessel disease, etc). It should be emphasized that only 1 RCT included in this meta-analysis randomized patients to IR versus CR. The remainder are direct comparisons of CABG versus PCI in which the decision to perform IR or CR was not randomized and, therefore, was subject to potential bias. Only an RCT directly comparing CR versus IR can answer this question. The finding that CR was superior to IR even in RCTs that required equivalent complete anatomic revascularization prior to patient enrollment suggests that selection bias alone is unlikely to explain our findings. Third, caution is advised when extrapolating our findings to patients with multivessel CAD undergoing primary PCI for ST-segment elevation myocardial infarction as these patients were not included in our study. Fourth, the extent of IR could not be quantified. It is possible that IR of a small myocardial territory would carry less risk than IR of a large or multiple myocardial segments would. Fifth, for PCI-treated patients, the outcome of repeat coronary revascularization should be interpreted with caution, as it is likely that in some of the studies included in this meta-analysis staged PCI were counted as a repeat revascularization procedure. Therefore, repeat coronary revascularization may simply represent part of an initial procedural strategy rather than inadequate response to medical therapy or restenosis. Finally, the role of contemporary medical therapy in patients with residual CAD, although not the focus of our study, should not be underestimated (34). Optimization and standardization of medical therapies based on residual CAD burden has the potential to improve clinical outcomes.

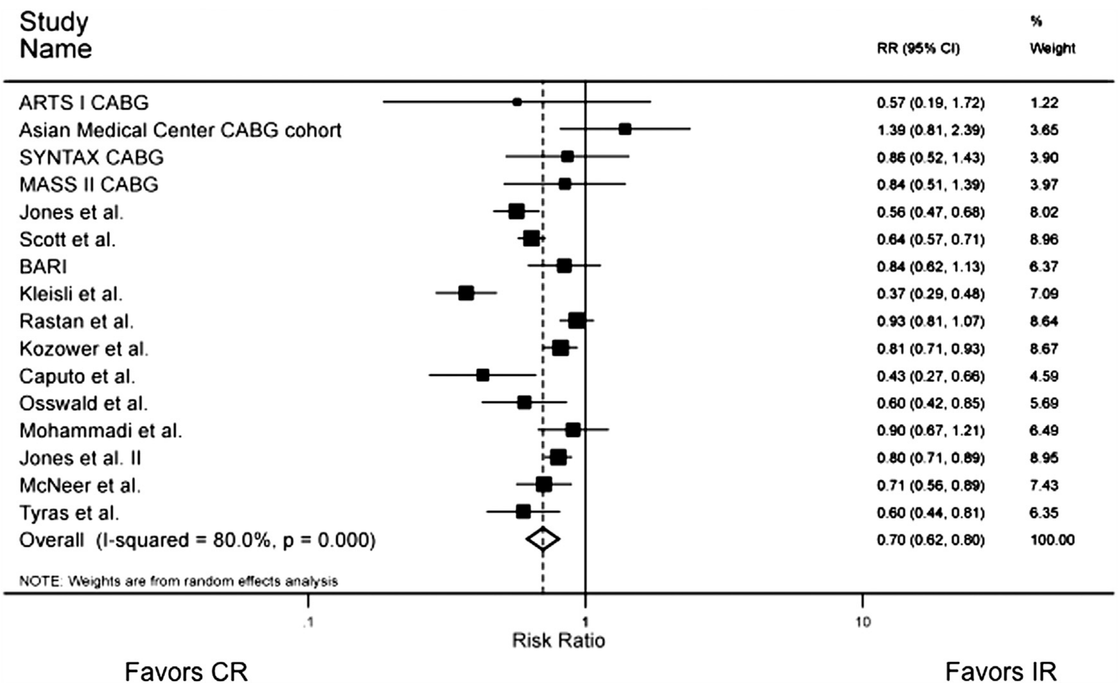


**Figure 3** **Pooled Analysis in CABG Studies**

Pooled analysis with RR and 95% CI for the occurrence of total mortality in CABG studies. **Boxes** are the relative risk estimates from each study; the **horizontal bars** are 95% CI. The size of the **box** is proportional to the weight of the study in the pooled analysis. MASS = Second Medicine, Angioplasty, or Surgery Study; other abbreviations as in Figures 1 and 2.

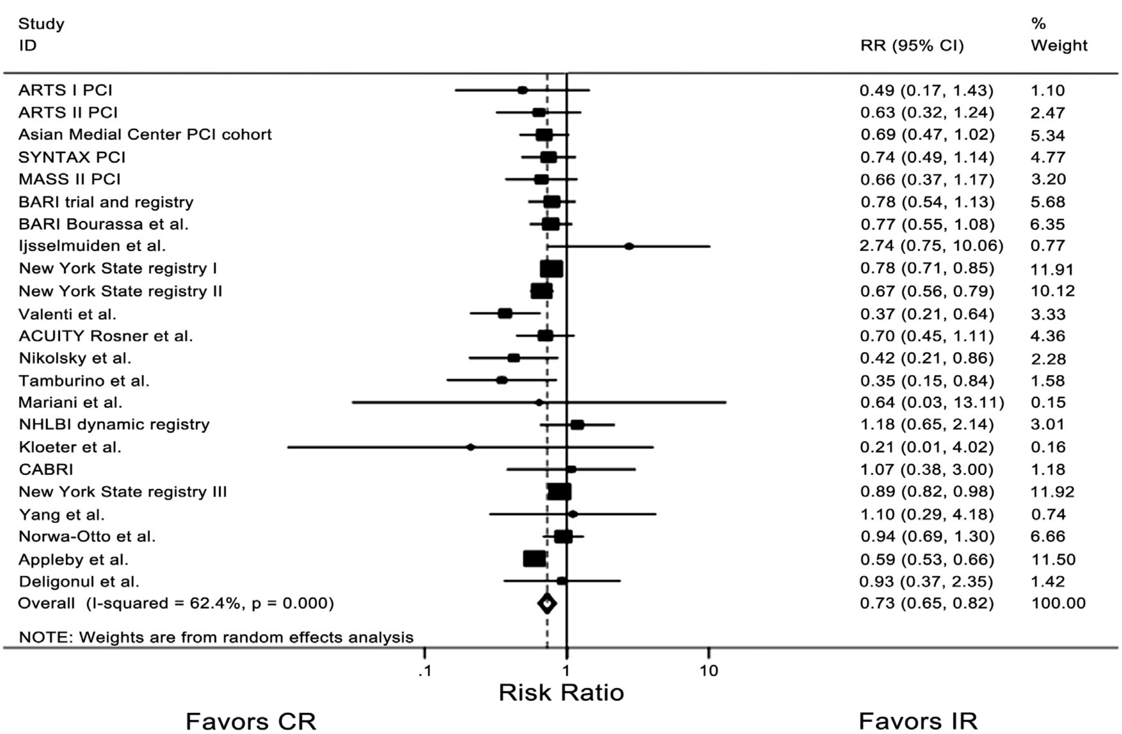


**Figure 4** **Pooled Analysis in PCI Studies**

Pooled analysis with RR and 95% CI for the occurrence of total mortality in PCI studies. **Boxes** are the relative risk estimates from each study; the **horizontal bars** are 95% CI. The size of the **box** is proportional to the weight of the study in the pooled analysis. Abbreviations as in Figures 1 and 2.

## Conclusions

In this first systematic review and meta-analysis of CR versus IR in patients with multivessel CAD undergoing revascularization with CABG or PCI, CR was associated with lower morbidity and mortality. Hence, the likelihood of achieving CR with either revascularization modality should inform the decision to proceed with CABG or PCI.

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**Reprint requests and correspondence:** Dr. Santiago Garcia, Department of Cardiology, University of Minnesota and Minneapolis VA Medical Center, One Veterans Drive (111-C), Minneapolis, Minnesota 55417. E-mail: garci205@umn.edu.

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**Key Words:** complete revascularization ■ coronary artery bypass surgery ■ coronary artery disease ■ meta-analysis ■ percutaneous coronary intervention.

## APPENDIX

**For the list of studies included in the meta-analysis, as well as supplemental references, definitions, tables, and figures, please see the online version of this paper.**

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