Impact of Incomplete Percutaneous Revascularization in Patients With Multivessel Coronary Artery Disease: A Systematic Review and Meta-Analysis

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Background—Up to half of patients undergoing percutaneous coronary intervention have multivessel coronary artery disease (MVD) with conflicting data regarding optimal revascularization strategy in such patients. This paper assesses the evidence for complete revascularization (CR) versus incomplete revascularization in patients undergoing percutaneous coronary intervention, and its prognostic impact using meta-analysis.

Methods and Results—A search of PubMed, EMBASE, MEDLINE, Current Contents Connect, Google Scholar, Cochrane library, Science Direct, and Web of Science was conducted to identify the association of CR in patients with multivessel coronary artery disease undergoing percutaneous coronary intervention with major adverse cardiac events and mortality. Random-effects meta-analysis was used to estimate the odds of adverse outcomes. Meta-regression analysis was conducted to assess the relationship with continuous variables and outcomes. Thirty-eight publications that included 156,240 patients were identified. Odds of death (OR 0.69, 95% CI 0.61-0.78), repeat revascularization (OR 0.60, 95% CI 0.45-0.80), myocardial infarction (OR 0.64, 95% CI 0.50-0.81), and major adverse cardiac events (OR 0.63, 95% CI 0.50-0.79) were significantly lower in the patients who underwent CR. These outcomes were unchanged on subgroup analysis regardless of the definition of CR. Similar findings were recorded when CR was studied in the chronic total occlusion (CTO) subgroup (OR 0.65, 95% CI 0.53-0.80). A meta-regression analysis revealed a negative relationship between the OR for mortality and the percentage of CR.

Conclusion—CR is associated with reduced risk of mortality and major adverse cardiac events, irrespective of whether an anatomical or a score-based definition of incomplete revascularization is used, and this magnitude of risk relates to degree of CR. These results have important implications for the interventional management of patients with multivessel coronary artery disease.

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Key Words: complete revascularization • incomplete revascularization • major adverse cardiovascular events • mortality • percutaneous coronary intervention

Percutaneous coronary intervention (PCI) is the most common form of coronary revascularization in patients with stable coronary artery disease and acute coronary syndromes (ACS).1 Multivessel coronary artery disease is common and affects more than half of patients who have an ACS.2,3 In these patients there is a lack of evidence on whether revascularization that is restricted to the culprit artery is sufficient or whether multivessel PCI would lead to an improved prognosis. Angiographically incomplete revascularization (IR) has been considered to be a poor prognostic feature in multiple...
observational studies and post hoc analyses of randomized controlled trials. The only prospective randomized controlled trial (RCT) outside the context of ST-elevation myocardial infarction (STEMI) comparing the safety, efficacy, and costs of complete versus “culprit” vessel revascularization in multivessel coronary artery disease treated with PCI showed no difference in major adverse cardiovascular event (MACE) rates between the 2 strategies, with a lower cost associated with the culprit-only strategy in the shorter term, although costs equalized in the longer term.9

Recent data from randomized trials including the PRAMI,10 CvLPRIT,11 and DANAMI-3-PRIMULTI trials,12 which recruited patients presenting with STEMI undergoing primary PCI, have shown that multivessel “complete” revascularization is associated with better outcomes than culprit-only revascularization. However, despite these data, important uncertainties still exist about the optimal strategy for such patients. Furthermore, in patients with stable coronary artery disease, international PCI guidelines do not provide guidance about the performance of complete revascularization (CR) versus IR, although functional assessment of lesions using noninvasive tests or fractional flow reserve (FFR) is recommended to avoid unnecessary treatment of nonsignificant stenosis because this is associated with adverse outcomes.

In a previous meta-analysis by Garcia et al16 including ~90 000 individuals with multivessel disease, incomplete revascularization in 25 938 CABG patients (29% from 16 studies) and 63 945 PCI patients (71% from 24 publications) was associated with increased risk of mortality, myocardial infarction, and repeat revascularization irrespective of the revascularization strategy employed. Since then many studies have been published including large registry data, post hoc analyses of randomized trials, and observational studies to assess effectiveness of complete coronary revascularization.

Our objectives were to assess and update the current evidence for complete revascularization and its prognostic impact in PCI by performing a meta-analysis of 38 studies including over 150 000 patients (excluding the STEMI and surgical revascularization cohorts).

Methods

Eligibility Criteria

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines were followed. Studies were selected of patients who underwent PCI, reporting mortality or cardiovascular events among patients with and without complete revascularization with no restriction based on study design or the indication for PCI. Publications that did not report either mortality or MACE were excluded.

Search Strategy

A search was done of PubMed, EMBASE, MEDLINE, Current Contents Connect, Google Scholar, Cochrane library, Science Direct, and Web of Science to October 2016. We used the following search terms: “Complete revascularization” OR “Incomplete revascularization” AND “Percutaneous coronary intervention” OR “PCI.” These keywords were searched as text words as well as exploded medical subject headings when feasible. The search strategy example for MEDLINE is as follows: 1 Complete revascularization.mp. (913), 2 Incomplete revascularization.mp. (358), 3 1 or 2 (1125), 4 exp *Percutaneous Coronary Intervention/ (31 192), 5 3 and 4 (292). We excluded the STEMI and surgical revascularization cohorts. The definitions of “complete revascularization” are given in Table 1. Studies in all languages were included. The bibliographies of the included studies and relevant review articles were checked for additional relevant articles.

Study Selection and Data Extraction

Two reviewers (V.N. and M.M.) independently checked all titles and abstracts for studies potentially meeting the inclusion criteria. The full reports of these studies were retrieved, and data were independently extracted on study design, participant characteristics, complete revascularization definition, outcome events, and follow-up.

Quality Assessment

The Newcastle-Ottawa Scale (NOS) was used as an assessment tool for selection, comparability, and outcome assessment. Study quality was rated on a scale from 1 (very
Data Analysis

The program Comprehensive Meta-analysis (version 2.0) was used to conduct DerSimonian and Laird random-effects meta-analysis.29 Risk ratio (RR) and 95% confidence intervals (CI) were calculated. Adjusted or propensity-matched risk estimates were used when available. Meta-regression analysis was conducted to assess the relationship with continuous variables and outcomes. The Cochrane Q-statistic ($I^2$) was used to assess the consistency among studies, with $I^2<$25% considered low, $I^2=$25-50% moderate, and $I^2>75%$ high heterogeneity.30

Results

Study Population

A total of 425 publications were screened; then, 38 relevant studies* including 156 240 patients met our selection criteria (Figure 1). We excluded previous meta-analysis16,54-66 and trials comparing target lesion revascularization versus upfront revascularization STEMI.10-12,67-70 The studies included were mostly observational and included large registries,13,17,50,53 or post hoc analyses of randomized trials such as the SYNTAX trial,6 FAME trial,18 ARTS trial,31 ARTS-II Study,44 MASS II trial,36 BARI trial,33 CABRI trial,34 and the ACUITY trial.8 Only 1 randomized single-center trial9 has been published so far that compares the outcomes of complete and incomplete percutaneous revascularization.

The publication dates ranged from 1988 to 2016, and the follow-up period for patients ranged between 1 and 11 years. The numbers of patients in each study were variable and ranged between 192 and 23 342 individuals. Most of these participants were male, and the percentage of females ranged from 7% to 37%; the mean age reported in the studies varied from 52 to 68 years. The percentage of ACS ranged from 0% to 100%.

Most of the studies used an anatomic definition for complete revascularization. Only 1 study used a functional definition (coronary lesions with fractional flow reserve $<0.75$ to 0.80 received a stent),43 and 7 others utilized a score-based assessment (SYNTAX score; a residual score of 0 is considered to be complete revascularization).5,6,17,19,21-23 The percentage of complete revascularization ranged from 17% to 70% with a mean of 42.7%. The study characteristics have been tabulated in Table 2. The results of the studies that evaluated incomplete revascularization and adverse outcomes are shown in Table 3.

Outcomes: Overall and Subgroup Analysis Based on CR Definition and Chronic Total Occlusion Revascularization

There was a significantly lower risk of death with complete revascularization (Figure 2, OR 0.69, 95% CI 0.61-0.78) among 36 studies† that reported this outcome. This lower risk of mortality was maintained after performing subgroup analysis based on the anatomic definition of complete revascularization‡ (OR 0.69, 95% CI 0.61-0.79), although this did not reach statistical significance for score-based definitions§ (OR 0.73, 95% CI 0.50-1.07). Similar findings were recorded in the complete chronic total occlusion (CTO)-revascularization cohort (5 studies,** (OR 0.65, 95% CI 0.53-0.80) and in the non-CTO cohort (OR 0.71, 95% CI 0.61-0.82).§

The outcome of repeat revascularization was reported in 17 studies,† and there was statistically significantly lower rate in complete revascularization populations (Figure 3, OR 0.60, 95% CI 0.45-0.80). After subgroup analysis with respect to definition of complete revascularization, this benefit was maintained in studies that used anatomic§ (OR 0.58, 95% CI 0.41-0.82) and score-based definitions§ (OR 0.64, 95% CI 0.54-0.76).

Myocardial infarction was reported in 17 studies,‡‡ and a statistically significantly lower rate was observed (Figure 4, OR 0.63, 95% CI 0.50-0.79). This finding was maintained with respect to anatomic‡‡ (OR 0.60, 95% CI 0.45-0.81) and score-based definitions‡‡ (OR 0.64, 95% CI 0.51-0.79) of complete revascularization.

MACE was reported in 14 studies,‡‡‡ and a significantly lower rate was observed (Figure 5, OR 0.66, 95% CI 0.51-0.85). This finding was maintained with respect to anatomic‡‡ (OR 0.64, 95% CI 0.46-0.89) and score-based definitions‡‡ (OR 0.68, 95% CI 0.50-0.93) of complete revascularization.

Stent thrombosis was reported in only 3 studies,** and there was no impact of complete revascularization in its incidence (Figure 6, OR 0.81, 95% CI 0.49-1.33).

In a subgroup analysis of 2 studies§§ that reported on outcomes in patients who exclusively had acute coronary syndromes (ACS), no significant benefit was observed.

References

1References 4-9, 13, 17, 18, 20-24, 31-53, 71.
2References 4, 7, 9, 13, 17, 20-24, 31-37, 40-43, 45, 47-50, 52, 53.
3References 5-9, 13, 17, 18, 20-24, 31-37, 39-47, 49, 53.
4References 6, 8, 9, 13, 17-20, 31, 33, 37, 41, 49, 53, 71.
5References 9, 13, 17, 20, 31, 33, 37, 41, 49, 53, 71.
6References 6, 8, 9, 13, 17-20, 31, 33, 37, 41, 49, 53, 71.
7References 9, 13, 17, 20, 31, 33, 37, 41, 49, 53, 71.
8References 6-9, 13, 17-20, 35, 39, 47, 53, 56.

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OR 0.71, 95% CI 0.44-1.11) in mortality or MACE (OR 0.79, 95% CI 0.54-1.17).

Regression Analysis Based on Proportion of CR
A regression analysis was conducted, and a negative relationship was observed between the mortality and the percentage of CR. From the regression model, there was very strong evidence that the OR of mortality was inversely related to CR with a \( P < 0.001 \) (df=34). Log OR of mortality decreased by 1.25 (95% CI –1.64 to –0.88) for every 1% increase in CR. There was no relationship between the odds ratio of mortality and year of publication.

Heterogeneity and Publication Bias
There was significant heterogeneity noted among the different studies that could be explained by diverse population groups.

The degree of heterogeneity reduced to a minimal amount once subgroup analysis was performed based on a score-based definition of complete revascularization, suggesting similar study designs and population cohorts. The results have been summarized in Table 4. There was no publication bias identified using the Egger regression model.

Discussion
In our meta-analysis of 38 studies including over 156 240 patients undergoing PCI, we observed that fewer than half of all patients with multivessel coronary artery disease have CR. We observed that CR is associated with a lower rate of mortality, myocardial infarction, and MACE, irrespective of whether an anatomical or a score-based definition of IR was used, and that the magnitude of risk relates to degree of CR on meta-regression. Our analysis builds on the work done by Garcia et al\textsuperscript{16} by placing a focus on PCI and including new studies.

Figure 1. Flow diagram of included studies. STEMI indicates ST-elevation myocardial infarction.
| Name                        | Country          | Year | Study Type                  | CR Definition                                                                 | IR Definition                                                                 | Number of Patients | ACS% | Follow Up Years | CR Prevalence | % Female | Mean Age, y | NOS |
|-----------------------------|------------------|------|-----------------------------|------------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------|------|----------------|---------------|----------|-------------|-----|
| Appleby et al32             | Canada           | 2010 | Observational study         | Anatomic                                                                     | Greater than 70% stenosis in epicardial vessel, assessed angiographically at the end of the procedure | 12 662             | 53   | 3.7            | 35            | 28       | 63          | 7   |
| Bourassa et al33            | USA and Canada   | 1999 | Post hoc analysis of the BARI trial | Anatomic: Angiographically significant lesions were defined as ≥50% stenosis in a vessel 1.5 mm as measured by electronic calipers | NA                                                                             | 896                | 63   | 5              | 64            | 23       | 62          | 6   |
| Breeman et al34             | Netherlands      | 2001 | Post hoc analysis of the CABRI trial | Anatomic: If all lesions were successfully dilated—ie, if there were no remaining lesions with diameter stenosis <50% and incomplete otherwise | NA                                                                             | 267                | 25   | 1              | 38            | 19       | 61          | 6   |
| Capodanno et al21           | Italy            | 2013 | Observational study         | Score-based: The baseline SYNTAX score and residual SYNTAX score were derived from the summation of the individual scorings for each lesion (defined as ≥50% stenosis in vessel ≥1.5 mm) on angiograms | Residual SYNTAX score >1                                                      | 400                | 62   | 2              | 48.75         | 23       | 67          | 6   |
| Chung et al35               | Korea            | 2012 | Observational study         | Anatomic: Absence of diameter stenosis ≥50% in major epicardial coronary arteries or their side branches with a diameter ≥2.5 mm after successful PCI during index admission irrespective of the function or viability of relevant myocardium | NA                                                                             | 845                | 28   | 3.9            | 66.3          | 36.8     | 64          | 6   |
| D’Oliveira Vieira et al36   | Brazil           | 2012 | Post hoc analysis of the MASS II trial | Anatomic                                                                     | NA                                                                             | 192                | 0    | 10             | 36            | 33       | 59          | 8   |
| Deligonul et al37           | USA              | 1988 | Observational study         | Anatomic: Successful dilation of all major coronary or branch vessels and absence of residual stenosis ≥50% in a major coronary vessel | NA                                                                             | 397                | 49   | 2              | 59            | 24       | NA          | 6   |

Continued
| Name           | Country    | Year | Study Type                      | CR Definition                                                                                           | IR Definition                                                                                     | Number of Patients | ACS% | Follow Up Years | CR Prevalence | % Female | Mean Age, y | NOS |
|----------------|------------|------|---------------------------------|----------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------|--------------------|------|----------------|---------------|----------|-------------|-----|
| Gao et al⁷     | China      | 2013 | Observational study             | Anatomic: Angiographic CR, which entailed successful angioplasty of all diseased lesions in the major epicardial coronary vessels and their first-degree side branches (diameter ≥ 2.5 mm) | Patients not meeting the definition of CR were defined as having IR divided into 4 subgroups: (1) 1 IR vessel with no total occlusion; (2) 1 IR vessel with total occlusion; (3) ≥2 IR vessels with no total occlusion; and (4) 2 IR vessels with total occlusion | 7065               | 61.2 | 1.3            | 16.8          | 20.94    | 58          | 7   |
| Généreux et al⁶| Multicenter| 2015 | Post hoc analysis of the SYNTAX trial | Score-based: The baseline SYNTAX score and residual SYNTAX score were derived from the summation of the individual scorings for each lesion (defined as ≥50% stenosis in vessel ≥1.5 mm) on angiograms | The SYNTAX Revascularization Index was calculated with the following formula: (Δ SS / baseline SYNTAX score × 100). Classified into SRI = 100%, SRI 50% to <100%, and SRI <50% | 903                | 28.5 | 5              | 43.5          | 23.7     | 65          | 8   |
| Hambraeus et al¹³ | Sweden    | 2016 | Observational study             | Anatomic                                                                                                  | Defined as any nontreated significant (at least 60%) stenosis in a coronary artery supplying >10% of the myocardium | 23 342             | 80   | 1              | 35            | 27.2     | 68.1        | 7   |
| Hannan et al⁴  | USA        | 2006 | Observational study             | Anatomic: Defined as attempting all lesions with ≥50% stenosis in major epicardial coronary vessels (proximal, mid, and distal right coronary artery, left anterior descending, and left circumflex) either during the index hospitalization or any time within 30 days after discharge from the index hospitalization but before suffering a new myocardial infarction | Patients not meeting the definition of CR were defined to have IR                                      | 21 945             | NA   | 3              | 31            | 31       | NA          | 6   |

Continued
| Name             | Country | Year | Study Type         | CR Definition                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | IR Definition                                                                                                                                                                                                 | Number of Patients | ACS% | Follow Up Years | CR Prevalence | % Female | Mean Age, y | NOS |
|------------------|---------|------|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------|------|-----------------|---------------|----------|-------------|-----|
| Hannan et al38    | USA     | 2009 | Observational study| Anatomic: Defined as successfully attempting all diseased (≥70% stenosis) lesions in major epicardial coronary vessels (proximal, mid, and distal segments; major left anterior descending diagonals; and circumflex marginal branches) with PCI either during the index hospitalization or at any time within 30 days after discharge from the index hospitalization for PCI but before suffering a new MI. Success was defined as a reduction in stenosis of at least 20% and a residual stenosis of less than 50% | Patients not meeting the definition of CR were defined to have IR                                                                                   | 11 294           | 37   | 1.5             | 31            | 33       | NA          | 6   |
| Ijsselmuiden et al9 | Netherlands | 2004 | RCT                | Anatomic: Randomly assigned to undergo PCI of either the coronary artery thought to be responsible for ischemia (culprit vessel) or of all ≥50% stenosis (CR)                                                                                                                                                                                                                                                                                                      |                                                                                                                                                                                                                 | 219              | 37   | 5               | 50            | 26       | 62          | 9   |
| Kobayashi et al18 | Multicenter | 2016 | Post hoc analysis of FAME trial | Score-based: The baseline SYNTAX score and residual SYNTAX score were derived from the summation of the individual scorings for each lesion (defined as ≥50% stenosis in vessel ≥1.5 mm) on angiograms                                                                                                                                                                                                                                                                                                | Residual SYNTAX score of 0, >0 to 4, >4 to 8, and >8, and with SYNTAX revascularization index of 100%, 50% to <100%, and 0% to <50% | 427              | 31.9 | 2               | 14.5          | 25.5     | 64.7        | 8   |
| Kim et al39       | Korea   | 2011 | Observational study | Anatomic: Angiographic CR-1, according to the SYNTAX classification, was defined as angioplasty or grafting in all diseased coronary segments (≥1.5 mm), consisting of the right coronary artery (segments 1, 2, and 3) and its main branches, including the posterior descending artery (segment 4 or 15) and the posterolateral branch (segment 16); the left anterior descending artery (segments 5, 6, 7, and 8) and its major diagonal branches (segment 9 or 10); and the left circumflex artery (segments 11 and 13) and its major obtuse marginal branches (segment 12 or 14). Angiographic CR-2 was defined as revascularization in all diseased segments ≥2.5 mm in diameter | Patients not meeting these criteria were considered IR patients                                                                                           | 1400             | 42   | 5               | 41            | 29       | 61          | 6   |

Continued
| Name          | Country   | Year | Study Type           | CR Definition                                                                 | IR Definition                                                                 | Number of Patients | ACS% | Follow Up Years | CR Prevalence | % Female | Mean Age, y | NOS |
|--------------|-----------|------|----------------------|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------|-------------------|------|-----------------|--------------|----------|-------------|-----|
| Kip et al 40 | USA       | 1999 | Post hoc analysis of the BARI trial | Anatomic: Angiographically significant lesions were defined as >50% stenoses in a vessel >1.5 mm, as measured by electronic calipers. A reduction in stenosis of ≥20% with residual stenosis of <50% and TIMI grade 3 flow defined successful lesion dilation | | 2047 | NA | 5 | 59 | NA | 61 | 6 |
| Kloeter et al 41 | Switzerland | 2001 | Observational study | Anatomic: No remaining main coronary artery stenosis of >50% | | 250 | NA | 2.5 | 60 | 18 | 59 | 6 |
| Malkin et al 22 | United Kingdom | 2013 | Observational study | Score-based: SYNTAX score and residual SYNTAX score were derived from the summation of the individual scorings for each lesion (defined as ≥50% stenosis in vessel ≥1.5 mm) on angiograms | Residual SYNTAX score of >0 | 353 | 53 | 3.4 | 48.7 | NA | 68 | 7 |
| Malkin et al 23 | United Kingdom | 2013 | Observational study | Score-based: SYNTAX score and residual SYNTAX score were derived from the summation of the individual scorings for each lesion (defined as ≥50% stenosis in vessel ≥1.5 mm) on angiograms | Residual SYNTAX score of >0 | 240 | 38 | 2.6 | 41 | 26 | 66.9 | 7 |
| Mariani et al 71 | Italy | 2001 | Observational study | Anatomic: Defined as successful management of all significant stenoses in major epicardial vessels, whereas IR was defined as the residual presence of >50% stenosis in a major segment after the procedure | | 208 | 100 | 1 | 24 | 17 | 63 | 6 |
| Nikolsky et al 42 | Israel | 2004 | Observational study | Anatomic | | NA | 658 | 22 | 3 | 27 | 27 | 61 | 6 |
| Norwa-Otto et al 43 | Poland | 2010 | Observational study | Functional: CR was defined as successful PCI of all coronary artery lesions with significant narrowing not fulfilling the above criteria | Functionally driven IR was defined as dilation of all segments with >70% stenosis, with the exception of arteries supplying an area of previous transmural MI or a small amount of myocardium | 908 | 33 | 11 | 31 | 18 | 52 | 6 |

Continued
| Name                | Country    | Year | Study Type            | CR Definition                                                                 | IR Definition                                                                 | Number of Patients | ACS% | Follow Up Years | CR Prevalence | % Female | Mean Age, y | NOS |
|---------------------|------------|------|-----------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------|------|----------------|---------------|----------|-------------|-----|
| Park et al<sup>17</sup> | Korea      | 2014 | Observational study   | Score-based; The baseline SYNTAX score and residual SYNTAX score were derived from the summation of the individual scorings for each lesion (defined as ≥50% stenosis in vessel ≥1.5 mm) on angiograms | Residual SYNTAX score of 0, >0 to <7, and >7                                  | 5088               | 64.5 | 1              | 42.7          | 32       | 62          | 7   |
| Rosner et al<sup>8</sup> | USA        | 2012 | Post-hoc analysis of ACUITY trial | Anatomic                                                                      | Was variably defined as any lesion with a final DS ranging from ≥30% to ≥70% (in 10% increments) with a reference vessel diameter (RVD) ≥2.0 mm by QCA was left untreated after PCI in any epicardial coronary artery | 2954               | 100  | 1              | 63            | 31       | 60          | 8   |
| Sarno et al<sup>44</sup> | The Netherlands | 2010 | Post-hoc analysis of the ARTS-II Study | Anatomic; Patients were considered to have CR if all lesions with >50% diameter stenosis had been successfully treated | Those patients in whom attempt was made to treat 1 significant lesion or whose treatment resulted in a final diameter stenosis >50% were considered to have IR | 567                | 45   | 5              | 61.2          | 23       | 62.5        | 6   |
| Sohn et al<sup>20</sup> | Korea      | 2014 | Observational study   | Anatomic; CR was defined as the absence of ≥70% diameter stenosis in major epicardial coronary arteries or their branches with a diameter ≥2.0 mm after successful PCI |                                                                            | 263                | 29   | 3.3            | 57            | 25.8     | 67          | 6   |
| Song et al<sup>45</sup> | Korea      | 2012 | Observational study   | Anatomic; CR strategy was defined as attempting all lesions with >50% stenosis in major epicardial coronary vessels and their major branches during the index hospitalization |                                                                            | 873                | 48   | 1.5            | 48.9          | 30       | 64          | 6   |
| Srinivas et al<sup>46</sup> | USA        | 2007 | Observational study   | Anatomic; CR required that at least 1 lesion had to be treated in each of the major territories with diameter stenosis >50% |                                                                            | 1406               | 36.5 | 1              | 22            | 33       | 62          | 6   |
| Name                  | Country     | Year | Study Type          | CR Definition                                                                 | IR Definition                                                                 | Number of Patients | ACS% | Follow Up Years | CR Prevalence | % Female | Mean Age, y | NOS |
|-----------------------|-------------|------|---------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------|--------------------|------|----------------|---------------|----------|-------------|-----|
| Tamburino et al47     | Italy       | 2008 | Observational study | Anatomic: Revascularization was defined as complete, when all lesions with >50% diameter stenosis located in segment of at least 2.25 mm diameter, by quantitative coronary analysis, were successfully treated either during the index hospitalization or staged electively within 3 months after the initial procedure |                                                                              | 508                | 50   | 3              | 42            | 21       | 62          | 7   |
| Valenti et al48       | Italy       | 2008 | Observational study | Anatomic: CR was defined as a restoration of TIMI grade 3 flow with residual stenosis <30% on visual assessment in the 3 coronary arteries and their major branches (branch diameter ≥2 mm) |                                                                              | 486                | 37.5 | 2              | 62            | 17       | 68          | 6   |
| Van den Brand et al31 | Multicenter | 2002 | Post-hoc analysis of the ARTS Trial | Anatomic: if all lesions of ≥50% diameter stenosis had been successfully treated | If no attempt was made to treat 1 or more significant lesions, or if treatment resulted in a final diameter stenosis ≥50%, these patients were considered to be incompletely revascularized | 576                | 38   | 1              | 70            | 21       | 61.5        | 8   |
| Wu et al5             | USA         | 2011 | Observational study | Anatomic: Revascularization was defined as reduction of stenosis to <50% in all diseased (≥70% stenosis) lesions in major epicardial coronary vessels (left anterior descending artery and major diagonals; left circumflex artery and large marginal branches; and right coronary artery and right posterior descending artery) in the index hospitalization or within 30 days after discharge from the index hospitalization before having a new MI. However, if the patient had an MI before the CR was completed, this was not regarded as CR because of the occurrence of an adverse event before CR was attained | When a CR was not achieved during a stenting procedure, it was defined as a procedure with IR. | 13 016              | NA   | 8              | 30            | 31       | NA          | 6   |
| Name          | Country | Year | Study Type       | CR Definition                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | IR Definition                                                                                                                                                                                                                                                                                                                                                                           | Number of Patients | ACS% | Follow Up Years | CR Prevalence | % Female | Mean Age, y | NOS |
|---------------|---------|------|------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------|------|-----------------|---------------|----------|-------------|-----|
| Wu et al24    | USA     | 2013 | Observational study | Anatomic: CR was defined when the postprocedural stenosis in each of the lesions was reduced to <50% in the index hospitalization or within 30 days in staged PCI procedures following discharge from the index hospitalization before the occurrence of a new MI. When CR was not achieved after the stenting procedure in the index admission or within 30 days of discharge, the revascularization was defined as IR. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 21,767            | NA   | 5               | 31.4          | 33.5     | NA          | 7   |
| Yang et al49  | China   | 2010 | Observational study | Anatomic: Clinical lesions were defined as >50% stenosis of a main coronary artery or >70% stenosis of its primary branches. The definition of CR was the treatment of all lesions in the main coronary artery and primary branches. Incomplete coronary revascularization (ICR) was defined as treatment of main culprit lesions but not other clinical lesions. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 324               | 92   | 1.5             | 22            | 22       | 61          | 6   |
| George et al50| UK      | 2014 | Observational study | Successful PCI to the target CTO and postprocedural obstruction of <50% in all major epicardial coronary arteries. Successful PCI to the target CTO but with residual obstruction of >50% in ≥1 other vessels. |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | 13,443            | NA   | 2.65            | NA            | 21       | 63.5        | 6   |
| Hannan et al51| USA     | 2016 | Observational study | Defined as a residual stenosis of <50% for all lesions with preprocedural stenoses of at least 70%. The reference category for the variable was successful CTO PCI and CR of all other lesions with preprocedural stenosis of at least 70%. Also, if a CTO or non-CTO PCI was successful in a staged admission, that patient was regarded as having undergone a successful PCI. | NA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 4,030             | NA   | 1.8             | 61            | 22.4     | 63.2        | 6   |
| Danzi et al52 | Italy   | 2013 | Observational study | Defined as a TIMI flow grade 3 with residual stenosis of <30% on visual assessment in the 3 coronary arteries and their major branches (branch diameter of ≥2 mm). | NA                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | 120               | 33.3 | 2               | 63.3          | 7.5      | 68          | 6   |
| Chang et al53 | South Korea | 2016 | Prospective cohort study | Absence of diameter stenosis ≥50% in major epicardial coronary arteries or their side branches with a diameter ≥2.5 mm after successful stent implantation during index hospitalization irrespective of the function or viability of relevant myocardium. | Not meeting the CR criteria                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | 3,901             | 54.1 | 4.9             | 50            | 30       | 63          | 8   |

ACS indicates acute coronary syndrome; CR, complete revascularization; CTO, chronic total occlusion; IR, incomplete revascularization; NOS, Newcastle-Ottawa Scale; PCI, percutaneous coronary intervention; SRI, SYNTAX revascularisation index; SYNTAX, Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery; TIMI, thrombolysis in myocardial infarction.
### Table 3. Results of Studies That Evaluated Incomplete Revascularization and Adverse Outcomes

| Study | Results |
|-------|---------|
| Appleby et al<sup>32</sup> | Better survival with CR (87±1% vs 78±1%, \(P<0.001\)). Residual disease significant independent predictor of the need for repeat procedures |
| Bourassa et al<sup>33</sup> | CR (n 579) (%) IR (n 317) (%) \(P\)Value  
Death 87.5 84.0 0.13  
MI 83.8 84.1 0.91  
Repeat revascularization 46.3 42.8 0.48  
Angina 79.8 75.6 0.22 |
| Breeman et al<sup>34</sup> | At 1 month  
PTCA Remaining lesions 0 1 2 ≥3  
Death (%) 2.1 0.7 0.8 2.5  
MI (%) 4.9 2.8 3.3 5.0  
(Repeat revascularization) CABG (%) 2.8 1.4 7.4 20.2  
(Repeat revascularization) PTCA (%) 4.2 3.5 5.7 5.9  
At 1 year  
PTCA Remaining lesions 0 1 2 ≥3  
Death (%) 5.4 2.0 3.3 5.0  
MI (%) 5.4 3.4 4.9 6.7  
(Repeat revascularization) CABG (%) 7.4 9.5 18.0 37.0  
(Repeat revascularization) PTCA (%) 25.0 22.5 23.8 19.3 |
| Capodanno et al<sup>21</sup> | Cardiac mortality at 2 years: 3.3%, 4.5%, and 19.8% in the CR |
| Chung et al<sup>35</sup> | Propensity score-matched (n = 550)  
Adjusted HR [95% CI]  
Death 0.66 [0.34-1.28]  
Death and MI 0.51 [0.28-0.95]  
Death, MI, and repeat revascularization 0.84 [0.60-1.19]  
Cardiac death 0.50 [0.18-1.40]  
Cardiac death and MI 0.39 [0.16-0.96]  
Any adverse cardiac events 0.93 [0.64-1.35] |
| D’Oliveira Vieira et al<sup>26</sup> | A statistically significant difference was observed for the PCI group (CR, 6 individuals died, IR 20 individuals died) |
| Deligonul et al<sup>37</sup> | Outcomes Events/CR Total Events/IR Total  
Repeat revascularization CABG/PTCA 24/118, 73/255  
MI 3/118, 9/255  
Death 6/118, 14/255 |
| Gao et al<sup>7</sup> | At 36 months, cardiac death was significantly greater in the IR cohort (2.55% vs 1.13%, log-rank test: \(P=0.016\)), but there was no difference in the 3-year rates of MI, TVR, and MACE between the 2 cohorts. Angiographic IR had a greater risk of cardiac death (adjusted hazard ratio [HR] 2.56, 95% confidence interval [CI] 1.03-6.41) |
| Généréux et al<sup>6</sup> | At 60 months, rates of MACE were linked with IR |
| Hambraeus et al<sup>13</sup> | Unadjusted HR (IR compared with CR): repeat revascularization 2.05 (95% CI 1.80-2.32; \(P=0.0001\)); combined endpoint of death/MI, HR was 1.92 (95% CI 1.77-2.09; \(P=0.0001\)) for IR compared with CR |
| Hannan et al<sup>4</sup> | Adjusted HR for IR patients compared to CR patients for death was 1.15 (95% CI 1.01-1.30). Repeat revascularization: 10.09% for CR patients and 11.46% for IR patients (\(P=0.16\)) |
| Hannan et al<sup>38</sup> | (IR vs CR) 18-month mortality (adjusted HR 1.23, 95% CI 1.04-1.45) and 18-month MI/mortality (adjusted HR 1.27, 95% CI 1.09-1.47). The adjusted survival rates for CR and IR were 94.9% and 93.8% (\(P=0.01\)), and the freedom-from-MI rates were 93.3% and 91.7% (\(P=0.002\)) |
| Ijsselmuiden et al<sup>9</sup> | (IR vs CR) MACE rates at 1 month (14.4% vs 9.3%), 1 year (32.4% vs 26.9%), and 46.4±1.2 years (40.4% vs 34.6%) were similar in both cohorts |
| Kobayashi et al<sup>18</sup> | Patients with MACE had comparable RSS and SRI after PCI: RSS 6.0 [IQR 3.0-10.0] vs 5.0 [IQR 2.0-9.5], \(P=0.51\); SRI 60.0% [IQR 40.9%-78.9%] vs 58.8% [IQR 26.7%-81.8%], \(P=0.24\), respectively. Kaplan-Meier analysis showed comparable 12-month rate of MACE with different RSS/SRI (log-rank \(P=0.55\) and 0.54, respectively) |
| Kim et al<sup>29</sup> | (CR vs IR) MACE HR 0.82 (95% CI 0.58-1.15), MACCE HR 0.90 (95% CI 0.75-1.09) |
| Kip et al<sup>60</sup> | Outcomes Events/CR Total Events/IR Total  
Repeat revascularization 328/59, 237/399  
Death 55/595, 47/399 |

Continued
### Table 3. Continued

| Study        | Outcomes Events/CR Total Events/IR Total | Results                                                                 |
|--------------|------------------------------------------|-------------------------------------------------------------------------|
| Kloeter et al[41] | Repeat revascularization 10/101 23/149 | Complete revascularization had considerably higher clinical restenosis (35% vs 22%, P<0.02) |
| Malkin et al[22] | Complete revascularization was significantly linked with survival (Adjusted OR 3.1, 95% CI 1.7-5.6) |
| Malkin et al[23] | Outcomes Events/CR Total Events/IR Total | Death 6/98 29/142 P<0.001 |
| Mariani et al[71] | Outcomes Events/CR Total Events/IR Total | Death 6/98 29/142 P<0.001 |
| Nikolsky et al[42] | Survival in CR was 94.5%, vs 83.0% for those with IR (P<0.001). MI-free survival was considerably greater in patients with CR than in those with IR (92.9% vs 79.9%, respectively). IR was a prognosticator of mortality (95% CI 1.54-7.69; P=0.003) |
| Norwa-Otto et al[43] | Outcomes Events/CR Total Events/IR Total | MACCE in the 87% of the CR cohort at 24 months and 75% at 60 months. Definite stent thrombosis occurred in 2.6% of the IR cohort and 3.9% of the CR cohort (P=0.45); definite or probable stent thrombosis occurred in 6.5% in the IR cohort vs 8.6% in the CR cohort (P=0.41) |
| Park et al[17] | Outcomes Events/CR Total Events/IR Total | MACCE 114/2173 29/2915 Death 28/2173 65/2915 Myocardial infarction 4/2173 19/2915 Unplanned revascularization 86/2173 225/2915 Definite/probable stent thrombosis 11/2173 21/2915 |
| Rosner et al[8] | (IR vs CR) Unadjusted HR (95% CI) for IR vs CR: death 1.43 (0.90-2.27); repeat revascularization 1.58 (1.28-1.96); MI 1.50 (1.18-1.89); MACE 1.47 (1.24 -1.74) |
| Sarno et al[44] | MACCEs in the 87% of the CR cohort at 24 months and 75% at 60 months. Definite stent thrombosis occurred in 2.6% of the IR cohort and 3.9% of the CR cohort (P=0.45); definite or probable stent thrombosis occurred in 6.5% in the IR cohort vs 8.6% in the CR cohort (P=0.41) |
| Sohn et al[20] | (CR vs IR) MACCE 34.7% vs 45.1%; adjusted hazard ratio [HR] 0.65, 95% CI 0.44-0.95, P=0.03; all-cause death adjusted HR 0.48, 95% CI 0.29-0.80, P=0.01 |
| Song et al[45] | (CR vs IR) MACE HR 0.64, 95% CI 0.46-0.88, P=0.01; revascularization HR 0.61, 95% CI 0.42-0.90, P=0.01; death HR 0.87, 95% CI 0.48-1.57, P=0.64; MI HR 0.62, 95% CI 0.23-1.67, P=0.35. The rate of periprocedural MI and stent thrombosis was comparable in the 2 cohorts (4.7% in the CR group vs 3.6% in the IR group, respectively) |
| Srinivas et al[46] | (CR vs IR) mortality HR 1.10 (95% CI 0.58-2.10) and repeat revascularization HR 0.92 (96% CI 0.66-1.29) |
| Tamburino et al[47] | (CR vs IR) primary composite endpoint HR 0.43 (0.29-0.63, P=0.0001), cardiac death HR 0.37 (0.15-0.92, P=0.03), combination of cardiac death or MI HR 0.34 (0.16-0.75, P=0.008), and repeat revascularization HR 0.45 (0.29-0.69, P=0.0003) |
| Valenti et al[48] | The survival rates were 91.6% and 87.4% in the CR and IR cohorts, respectively (P=0.025). CR was inversely proportional to mortality (HR 0.44, 95% CI 0.22-0.87, P=0.021) |
| Van den Brand et al[21] | Outcomes Events/CR Total Events/IR Total | Unplanned revascularization 34/406 61/170 Myocardial infarction 20/406 10/170 Death 7/406 6/170 |
| Wu et al[5] | Death (HR 1.12, 95% CI 1.01-1.26, P=0.04). Eight-year survival was 78.5% and 80.8% for IR and CR (P=0.04). Mortality IR vs CR (adjusted HR 1.16, 95% CI 1.06-1.26, P=0.001) |
| Wu et al[24] | Among 6511 propensity-matched individuals (IR compared to CR) (79.3% vs 81.4%, P=0.004), and death (HR 1.16, 95% CI 1.06-1.27). Five-year survival rate (IR 79.3% vs CR 81.4%, P=0.004) |
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The decision not to undertake CR by the operator may re

cluded in this analysis are derived from registry data; hence,

contribute to the associations reported. Most of the studies

registry data, is signi

ences in baseline characteristics, the possibility of unmea-

sured confounding, particularly in studies derived from

registry data, is significant. Furthermore, the increased risk

associated with IR may relate to the complexity/extensive-

ness of coronary artery disease at baseline. For example, a

post hoc analysis of the ARTS trial revealed that IR was

associated with worse outcomes only in patients in the

highest SYNTAX score tertile, whereas in the low and middle
tertiles IR was not an independent predictor of adverse
outcomes.44

Our analysis does not allow comparison of outcomes of
patients undergoing IR in different settings such as elective
versus the ACS because the majority of studies do not report
outcomes by clinical presentation. The subgroup analysis of
ACS of 2 studies8,71 did not show any difference in mortality or
MACE between the 2 cohorts. The studies were hetero-
geneous, and 1 of them71 was not large enough to detect the
difference among the cohorts. Nevertheless, it has been
demonstrated that complete revascularization in STEMI
confers survival benefit.10-12 More recently, for example, the
DANAMI-3-PRIMULTI trial reported a 44% reduction in the
primary endpoint of all-cause mortality, nonfatal myocardial
infarction, and repeat revascularization (HR 0.56, 95% CI 0.38-
0.83; P=0.004). Following these trials, multiple meta-
analyses56,63,65,74-76 have suggested a significant survival
advantage in complete revascularization in patients with
STEMI. Similarly, in the post hoc analysis of the ACUITY Trial,8
which included 2954 ACS patients, IR is associated with an
increased risk of MACE. Unstable angina accounted for
approximately one third of the patients in the SYNTAX5 and
FAME trials.18,77,78 In the post hoc analysis18 of the FAME
trial, CR was compared to IR in patients who underwent FFR-
guided PCI. There was no significant difference in survival
between stable and unstable individuals at 24 months,
indicating a consistent treatment effect with the FFR inter-
vention. Further, a post hoc analysis of the SYNTAX trial8
performed subgroup analysis based on SYNTAX Revascular-
ization Index <70% versus >70%. The OR for patients with
unstable angina was 3.25 (95% CI 3.37-11.25), clearly
indicating a survival advantage for patients with CR.

Our meta-regression analysis suggests that outcomes
relate to the degree of CR, in agreement with several previous
studies. Indeed, post hoc analysis of the SYNTAX trial
suggests higher degrees of IR, as measured by the SYNTAX
revascularization index, were associated with increased
5-year cardiac death, AMI, and major adverse cardiac or
cerebrovascular events (MACCE).6 Similarly, Park et al17
showed in the EXCELLENT registry that patient-orientated

| Study | Results |
|-------|---------|
| Yang et al49 | No differences in outcomes between the 2 cohorts at follow-up. Outcomes Events/CR Total Events/IR Total Repeat revascularization 4/99 17/255 MI 1/99 4/255 Death 3/99 7/255 |
| George et al50 | (CR vs IR) Mortality (adjusted HR 0.70, 95% CI 0.56-0.87, P=0.002) |
| Hannan et al51 | 2.5-year Mortality CR vs CR for CTO, incomplete for ≥1 other lesions adjusted HR 1.11 (0.74, 1.68). 2.5-year mortality CR vs IR for CTO adjusted HR 1.63 (1.28, 2.08), P=0.0001 |
| Danzi et al52 | Two-year cardiac death-free survival was better in the CR cohort compared to IR (96 vs 78 P=0.002) |
| Chang et al53 | IR with drug-eluting stents in multivessel disease was associated with increased MI risk (HR 1.86, 95% CI 1.08-3.19, P=0.024) and similar risk of death (HR 1.03, 95% CI 0.80-1.32; P=0.83) compared to CR |

CABG indicates coronary artery bypass grafting; CR, complete revascularization; CTO, chronic total occlusion; IR, incomplete revascularization; MACE, major adverse cardiac events; MI, myocardial infarction; PCI, percutaneous coronary intervention; PTCA, percutaneous transluminal coronary angioplasty; RSS, residual SYNTAX score; SRI, SYNTAX revascularisation index.
composite endpoint rates (POCE) increased with increasing residual syntax score tertiles. Finally, CTO revascularization has been a matter of debate in recent years.50,79-81 Contemporary evidence from a large UK registry of 13 443 individuals with CTO suggests that complete revascularization had a survival advantage over partial revascularization with a hazard ratio of 0.70 (95% CI 0.56-0.87). Our study confirms survival benefit regarding complete revascularization of CTO with an OR of 0.69 (95% CI 0.61-0.78). Similarly, a meta-analysis of 7288 patients suggested that successful CTO recanalization had a survival advantage and reduced surgical revascularization.

Figure 2. Risk of death with complete vs incomplete revascularization. The odds of death (OR:0.69, 95% CI: 0.61–0.78) was significantly lower in the patients who underwent complete revascularization. CR indicates complete revascularization; IR, incomplete revascularization.
Limitations

There are several limitations associated with our analysis. First, although we report an association between IR and adverse clinical outcomes, we cannot infer a causal relationship. We have shown an association between IR and adverse outcomes, but it cannot be assumed that treating such patients with IR with additional PCI to attain CR would improve their prognosis. Second, for anatomical based definitions of IR, there are no universally accepted definitions of lesion “significance” with studies defining significant lesions as those with diameter stenosis (DS) varying between ≥50% and ≥70% in vessels of diameter ≥1.5 mm in some studies to ≥2.5 mm in other studies. Many of the studies included in this analysis used visual assessment to define lesion severity, which is known to have greater interobserver variability and to overestimate percentage DS compared with quantitative coronary angiograph (QCA). Interestingly, a post hoc analysis of the ACUITY trial using QCA illustrated that even when DS ≥30% was used to define a significant lesion, IR was independently associated with an increased risk of MACE (HR 1.36, 95% CI 1.11-1.68), although the risk increased with increasing DS thresholds (for DS threshold of ≥70%, HR 1.59, 95% CI 1.30-1.93). Score-based definitions of IR, such as the residual SYNTAX score, overcome some of the limitations around differences in anatomical definitions of lesion significance used across studies, allowing comparisons to be made more easily. In the current analysis we report a similar prognostic impact of IR irrespective of whether this is defined by anatomical or score-based definitions.

Figure 3. Risk of repeat revascularization with complete vs incomplete revascularization. The odds of repeat revascularization (OR: 0.60, 95% CI: 0.45–0.80) was significantly lower in the patients who underwent complete revascularization. CR indicates complete revascularization; IR, incomplete revascularization.
Third, contemporary studies have shown that the functional significance of lesions on the basis of fractional flow reserve is a more important determinant of future cardiac events than anatomical/angiographic appearances. Operators may choose not to revascularize lesions due to their functional nonsignificance or location within vessels supplying infarcted and nonviable myocardium. A recent post hoc analysis of the FAME study demonstrated that IR (as defined by residual SYNTAX score and SYNTAX revascularization index) was not associated with adverse outcome in the setting of complete functional revascularization, supporting the hypothesis that functional CR is more important than anatomical CR. The remaining studies that report outcomes following IR included in this analysis (with the exception of the aforementioned study) do not differentiate between the anatomical and the functional significance of incompletely revascularized lesions. The differences in the prognostic impact of incomplete revascularization across the different studies analyzed in this meta-analysis may relate to the above limitations, mainly variability in the definition of what is considered to be a significant coronary lesion, the site of the lesion, whether the lesions that were not revascularized were in infarcted nonviable territories or were functionally significant, the sample size of the cohort studied, and whether this would be adequately powered to detect a statistically significant difference and the nature of the cohort studied. Finally, most of the studies included in this analysis are derived from registry data; hence, the decision not to undertake CR by the operator may reflect

**Figure 4.** Risk of myocardial infarction with complete vs incomplete revascularization. The odds of myocardial infarction (OR: 0.64, 95% CI: 0.50-0.81) was significantly lower in the patients who underwent complete revascularization. CR indicates complete revascularization; IR, incomplete revascularization.
**Figure 5.** Risk of MACE with complete vs incomplete revascularization. The odds of MACE (OR: 0.66, 95% CI: 0.51–0.85) were significantly lower in the patients who underwent complete revascularization. CR indicates complete revascularization; IR, incomplete revascularization, MACE, major adverse cardiac events.

**Figure 6.** Risk of stent thrombosis with complete vs incomplete revascularization. There was no difference in the rate of stent thrombosis among the two cohorts. CR indicates complete revascularization; IR, incomplete revascularization.
uncaptured comorbidity or general frailty of the patient and so act as a surrogate of poor health status of the patients that will contribute to the poorer outcomes reported. Although nearly all of the studies have adjusted for differences in baseline characteristics, there remains a possibility of unmeasured confounding.

In conclusion, our analysis of data derived from over 150,000 patients undergoing PCI suggests that fewer than half of all patients with multivessel coronary artery disease have CR following PCI. We observe that CR is associated with decreased incidence of mortality, myocardial infarction, and MACE, irrespective of whether an anatomical or a score-based definition of IR was used and that the magnitude of risk relates to degree of CR. The findings of our analysis have several practical implications for interventional cardiologists. Our reported associations between IR and adverse clinical outcomes suggest that in patients with MVD, consideration should be given to the degree of CR that can be achieved by PCI when discussing choice of revascularization modality within the heart team, in addition to consideration of lesion complexity, functional significance, patient characteristics, and syntax score in line with current international recommendations.\textsuperscript{86} At the very least these data speak of the need for further carefully conducted randomized trials to address this question.

### Author Contributions

Mamas conceived and planned the study. Nagaraja and Ooi performed the search, screened relevant studies, extracted data from the studies, and performed the analysis. Mamas wrote the first draft of the paper. All authors contributed to the interpretation of the findings and reporting of the work and edited the manuscript for significant intellectual content.

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### Disclosures

None.

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### Table 4. Pooled OR and 95% CI for the Studies Included in the Meta-Analysis

| Outcome          | Subgroup Analysis | OR   | 95% CI      | $i^2$  | $P$ Value |
|------------------|-------------------|------|-------------|--------|-----------|
| Death            | All               | 0.69 | 0.61 to 0.78| 77.03  | <0.001    |
|                  | Anatomic          | 0.69 | 0.61 to 0.79| 80.60  | <0.001    |
|                  | Scored based      | 0.73 | 0.50 to 1.07| 60.81  | 0.03      |
|                  | CTO               | 0.65 | 0.53 to 0.80| 68.13  | <0.001    |
|                  | Non-CTO           | 0.71 | 0.61 to 0.82| 78.6   | <0.001    |
|                  | ACS               | 0.71 | 0.44 to 1.11| 0      | 0.95      |
| Repeat revascularization | All              | 0.60 | 0.45 to 0.80| 92.87  | <0.001    |
|                  | Anatomic          | 0.58 | 0.41 to 0.82| 94.23  | <0.001    |
|                  | Scored based      | 0.64 | 0.54 to 0.76| 0      | 0.59      |
| MI               | All               | 0.63 | 0.50 to 0.79| 62.4   | <0.001    |
|                  | Anatomic          | 0.60 | 0.45 to 0.81| 65.86  | 0.07      |
|                  | Scored based      | 0.64 | 0.51 to 0.79| 0.00   | 0.72      |
| MACE             | All               | 0.66 | 0.51 to 0.85| 93.29  | <0.001    |
|                  | Anatomic          | 0.64 | 0.46 to 0.89| 94.5   | <0.001    |
|                  | Scored based      | 0.68 | 0.50 to 0.93| 70.87  | 0.02      |
|                  | ACS               | 0.79 | 0.54 to 1.17| 81.86  | 0.02      |
| Stent thrombosis | All               | 0.81 | 0.49 to 1.33| 49.2   | 0.14      |

ACS indicates acute coronary syndrome; CI, confidence interval; CTO, chronic total occlusion; $i^2$, Cochrane Q-statistic; MACE, major adverse cardiovascular event; MI, myocardial infarction; OR, odds ratio.
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