**Name of journal: *World Journal of Meta-Analysis***

**Manuscript NO: 35639**

**Manuscript type: Meta-Analysis**

**Complete revascularization reduces adverse outcomes in patients with multivessel coronary artery disease**

Auchoybur ML *et al.* Complete *vs* incomplete myocardial revascularization

**Merveesh L Auchoybur, Xin Chen**

**Merveesh L Auchoybur, Xin Chen,** Department of Cardiovascular Surgery, Nanjing First Hospital Affiliated to Nanjing Medical University, Nanjing Cardiovascular Disease Research Institute, Nanjing 210006, Jiangsu Province, China

**ORCID number:** Merveesh L Auchoybur ([0000-0002-6274-2187](http://orcid.org/0000-0002-6274-2187)); Xin Chen ([0000-0002-7786-1701](http://orcid.org/0000-0002-7786-1701)).

**Author contributions:** Auchoybur ML acquisition and interpretation of data, study design, drafting the article, final approval; Chen X conception and design of study, critical revision, final approval.

**Conflict-of-interest statement:** The authors declare that there is no conflict of interest regarding the publication of this paper.

**Data sharing statement:** No additional data is available.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Unsolicited manuscript

**Correspondence to:** **Xin Chen, MD, PhD, Professor, Director,** Department of Cardiovascular Surgery, Nanjing First Hospital Affiliated to Nanjing Medical University, Nanjing Cardiovascular Disease Research Institute, 68, Change Road, Nanjing 210006, Jiangsu Province, China. stevecx@njmu.edu.cn

**Telephone:** +86-25-52271363

**Received:** July 30, 2017

**Peer-review started:** August 4, 2017

**First decision:** September 7, 2017

**Revised:** September 21, 2017

**Accepted:**

**Article in press:**

**Published online:**

**Abstract**

***AIM***

To investigate the influence of complete and incomplete revascularization (ICR) in patients with multivessel coronary artery disease undergoing coronary artery bypass or percutaneous coronary intervention.

***METHODS***

We searched PubMed using the keywords “complete revascularization”, “incomplete revascularization”, “coronary artery bypass”, and “percutaneous coronary intervention”. We selected randomized controlled studies (RCT) and observational studies only for review. The main outcomes of interest were mortality, myocardial infarction (MI) and repeat revascularization. We identified further studies by hand searching relevant publications and included those that met with the inclusion criteria in our final analysis and performed a systematic review.

***RESULTS***

Ten studies were identified, including 13327 patients of whom, 8053 received complete revascularization and 5274 received ICR. Relative to ICR, CR was associated with lower ­­­mortality (RR: 0.755, 95%CI: 0.66 to 0.864, *P* = 0.765, *I*2 = 0.0%), lower rates of MI (RR: 0.759, 95%CI: 0.615 to 0.937, *P* = 0.091, *I*2 = 45.1%), lower rates of MACCE (RR: 0.731, 95%CI: 0.668 to 0.8, *P* = 0.453, *I*2 = 0.0%) and reduced rates of repeat coronary revascularization (RR: 0.691, 95%CI: 0.541 to 0.883, *P* = 0.0, *I*2 = 88.3%).

***CONCLUSION***

CR is associated with lower rates of adverse outcomes. CR can be used as a standard in the choice of any particular revascularization strategy.

**Key words:** Complete revascularization; Incomplete revascularization; Coronary artery bypass grafting; Percutaneous coronary intervention

**© The Author(s) 2017.** Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Completeness of revascularization has been documented to have lesser adverse post-operative/post-procedural outcomes as compared to incomplete revascularization (ICR). We conduct a systematic review with meta-analysis to analyze the outcomes in patients undergoing CR *vs* ICR, using any or both techniques. Ten studies were identified, including 13327 patients of whom, 8053 received CR and 5274 received ICR. CR is associated with lower rates of mortality, MI, repeat coronary revascularization procedures, and MACCE. Sub-group analysis also showed reduced rates of adverse events. CR can be used as an aim for any myocardial revascularization procedure.

Auchoybur ML, Chen X. Complete revascularization reduces adverse outcomes in patients with multivessel coronary artery disease. *World J Meta-Anal* 2017; In press

**INTRODUCTION**

Complete revascularization arose from early studies on coronary artery bypass grafting (CABG) surgery whereby some studies demonstrated that patients who were completely revascularized enjoyed a mortality benefit over those who were incompletely revascularized[1-3]. Data from the coronary artery surgery study (CASS) registry show that patients with multi-vessel coronary artery disease (CAD) and severe angina that received three or more grafts had better survival relative to patients who received one or two grafts[4]. Although CR is often easier to achieve with CABG than with percutaneous coronary intervention (PCI), with recent developments in percutaneous transluminal coronary angioplasty procedures, such as the new era of drug eluting stents (DES), the previous barriers of PCI in the treatment of multi-vessel disease are no longer insurmountable, and favorable outcomes have been recorded across multiple centers using this revascularization approach[5].

Different established standards are used to determine the degree of completeness of revascularization. Conventionally, perfusion districts are divided into three areas according to the supply of the coronary artery branches namely the left anterior descending (LAD), the left circumflex (LCX) and the right coronary artery (RCA). The most commonly used definition across studies is the (1) anatomical definition, and was used in 90% of the studies included in our meta-analysis. According to this definition, CR has been achieved if all diseased arterial segments with a vessel size (greater/equal to 1.5 mm for a graft and 2.0-2.25 mm for a stent) with at least one significant stenosis greater than or equal to 50% receive a graft or a stent. A second definition of CR is (2) numerical whereby the number of distal anastomoses is greater or equal to the number of diseased coronary segments/systems and was used in 10% of the studies included in our meta-analysis. Other definitions include the (3) functional definition whereby all ischemic myocardial territories are grafted (or stented); areas of old infarction with no viable myocardium are not required to be perfused, the (4) score-based definition whereby the stenosis in different vessels is scored and different weights are given to different vessels according to number of myocardial segments supplied (A residual score of 0 is usually considered equivalent to CR) and the (5) physiology-based definition whereby all coronary lesions with fractional flow reserve of less than equal to 0.75-0.80 receive a graft or stent.

Due to procedural difficulties associated with each technique (CABG and PCI), complete revascularization is not always achieved. Previous studies have tried to assess the outcomes following incomplete revascularization (ICR). However, since there is no specific definition for ICR, which is essentially defined as “failure to achieve complete revascularization”, it lacks objectivity as it relies on post-procedural classification of CR by the treating surgeon/physician. The SYNTAX trial, which used a more accurate method to determine the completeness of revascularization (patients were categorized as incompletely revascularized when the number of diseased segments that were treated did not match the heart team decision), and the BARI trial reported no increase in adverse outcomes in incompletely revascularized patients.

There is discrepancy between the results of different studies concerning the superiority of CR over ICR. In our meta-analysis, we aim to determine whether CR, is associated with improved post-procedural outcomes. In a subgroup analysis, we also investigate the mid/long -term outcomes of CR, along with outcomes in a > 60 years old patient population.

**MATERIALS AND METHODS**

We identified four types of studies on the PubMed database: Randomized controlled trials, observational studies, controlled clinical trials and clinical trials. The study was conducted in March 2016, using the keywords “coronary artery bypass”, “percutaneous coronary intervention”, “complete revascularization”, “incomplete revascularization”. The total number of records identified was fifty-four. We limited our search to the specific above-mentioned study types. Six of these studies met with our inclusion criteria. Through Hand-search (a methodological approach previously validated), we searched through journals related to our subject-matter and identified relevant studies and also searched the latter’s references. An additional four manuscripts were selected using the above-mentioned method[6]. A total of ten studies were included in our final analysis.

***Data sources and study search strategy***

We included two types of studies in our meta-analysis, namely randomized controlled trials and observational studies in which: (1) patients with multi-vessel CAD were enrolled for either CABG or PCI; (2) the outcomes of interest between CR and ICR were compared using any of the definitions of CR (see introduction for definitions of CR used); and (3) the outcomes included the primary outcome of interest and/or the secondary outcomes. We excluded studies in which: (1) multiple grafts were used for treatment of multi-vessel CAD without any reference to CR and/or ICR; (2) PCI was used for the treatment in the setting of ST-elevation acute myocardial infarction (MI); (3) outcomes of interest were not reported unless there was reference to CR and ICR; (4) the patients included were undergoing repeat CABG surgery; and (5) the sample size was small (< 100 patients).

***Study selection***

Our initial search using the keywords: Complete revascularization, ICR, coronary artery bypass, PCI yielded fifty-four citations on PubMed. Using the filter for article types, we selected clinical trials, controlled clinical trials, observational studies and randomized controlled trials only. Of the fifty-four citations, nine citations remained, and the abstracts from these nine citations were reviewed. Of these, one abstract was excluded due to absence of comparison between complete and ICR. The remaining eight full text manuscripts were reviewed for eligibility. Of these eight manuscripts, six met with our inclusion criteria. We hand-searched references cited in relevant publications and an additional four manuscripts that fit our inclusion criteria were included. A total of ten studies were selected and included in this meta-analysis (Figure 1).

***Data extraction***

The data was extracted by Merveesh L Auchoybur using standardized extraction forms. Extracted information included study design, method of revascularization and definition of CR used by each study, follow-up time, patient characteristics pre-operatively, and outcomes relevant to this meta-analysis. The subjects were divided into two groups, namely the complete revascularization group for those subjects who received complete revascularization and the ICR group for those subjects who were not completely revascularized. In studies where complete revascularization through CABG and PCI were reported separately, the sum total of completely revascularized patients was used for the complete revascularization group and the remaining patients were added to the ICR group.

***Outcomes***

The primary outcome used in this systematic study was all-cause mortality. Secondary outcomes were MI and repeat revascularization. Major adverse cardiovascular and cerebral events were also analyzed where present.

***Methodological quality***

In this meta-analysis, both *χ*2 based Q-statistic test and *I*2 test were considered to assess the heterogeneity across studies, and *P-*value less than or equal to 0.05 was considered significant. *I*2 is a description of the variation present across studies that is due to heterogeneity instead of chance (*I*2 value less than 50% indicates no or little heterogeneity)[7]. Weighted relative risk (RR) and its 95% confidence interval were calculated to evaluate the effect size. A fixed effect model using Mantel-Haenszel method were used to combine values from studies when heterogeneity was absent, otherwise, a random-effects model using the DerSimonian and Laird method was used[8]. Egger’s test and inverted funnel plots were utilized to provide a diagnosis of publication bias[9]. Automatic “zero cell” correction was used for studies with no events for a particular outcome. All analyses were performed using Stata version 11.1 software (Stata, College Station, TX, United States). All statistical evaluations were made assuming a two-sided test with a significance level of 0.05, unless stated otherwise.

**RESULTS**

***Study and patient characteristics***

The list of the ten studies that met with our inclusion criteria are listed in Table 1. Of the studies included, four were RCTs and six were non-RCTs. All the RCTs reported both CABG and PCI as revascularization strategies. Of the six non-RCTs included, three reported PCI, two reported both CABG and PCI simultaneously, and one reported CABG only. Of the studies comprising our analysis, nine use an anatomical definition of CR and one uses a numerical definition of CR. The current analysis includes 13327 patients of whom, 8053 (60.4%) received complete revascularization (CR) and 5274 (39.6%) received ICR. The mean age of the patients undergoing CR was 63.6 years, 20.5% had diabetes mellitus, 39.8% had suffered from previous MI, 43.5% had hypertension (Table 2). The mean age of the patients undergoing ICR was 65.1 years, 22.4% had diabetes mellitus, 46.1% had previously suffered from MI, and 52.6% had hypertension (Table 3). The mean follow-up time of the patients was 4.9 years.

***Mortality***

Of the ten studies included, eight reported mortality and were used for this analysis. CR is associated with reduced overall mortality relative to ICR (RR: 0.755, 95%CI: 0.66 to 0.864, *P* = 0.765, *I*2 = 0.0%) (Figure 2). In a subgroup analysis: mid-term follow-up of < 5 years shows that CR has lower mortality (RR: 0.710, 95%CI: 0.595 to 0.847, *P* = 0.701, *I*2 = 0.0%). Long-term follow-up of > 5 years is associated with reduced mortality (RR: 0.824, 95%CI: 0.669 to 1.016, *P* = 0.660, *I*2 = 0.0%). In the age group of > 60 years, CR is associated with reduced mortality (RR: 0.742, 95%CI: 0.641 to 0.859, *P* = 0.706, *I*2 = 0.0%) (Figure 3).

***MI***

Of the ten studies, seven reported MI and were used for this analysis. CR is associated with reduced rates of post-operative MI as compared to ICR (RR: 0.759, 95%CI: 0.615 to 0.937, *P* = 0.091, *I*2 = 45.1%) (Figure 4). In a subgroup analysis: mid-term follow-up of < 5 years group, occurrence of MI is less with CR as compared to ICR (RR: 0.608, 95%CI: 0.484 to 0.763, *P* = 0.388, *I*2 = 0.0%). Long-term follow-up of > 5 years shows that CR is associated with reduced rates of MI (RR: 0.894, 95%CI: 0.731 to 1.095, *P* = 0.419, *I*2 = 0.0%). In the age group of > 60 years, CR is associated with reduced MI (RR: 0.758, 95%CI: 0.589 to 0.974, *P* = 0.053, *I*2 = 54.1%).

***Repeat coronary revascularization***

Of the ten studies, six reported repeat revascularization and were consequently used in this analysis. CR is associated with reduced rates of revascularization (PCI and/or CABG) relative to ICR (RR: 0.691, 95%CI: 0.541 to 0.883, *P* = 0.0, *I*2 = 88.3%). In a subgroup analysis: mid-term follow-up of < 5 years shows that CR is associated with less repeat revascularizations (RR: 0.827, 95%CI: 0.651 to 1.052, *P* = 0.323, *I*2 = 11.6%). Long-term follow up of > 5 years shows that CR is associated with less repeat revascularizations (RR: 0.827, 95%CI: 0.651 to 1.052, *P* = 0.009, *I*2 = 78.9%). In the age group > 60 years, CR is associated with reduced rates of repeat revascularization (RR: 0.646, 95%CI: 0.484 to 0.863, *P* = 0.0, *I*2 = 89.2%).

***MACCE***

Of the ten studies, five reported MACCE and were used in this analysis. CR is associated with reduced MACCE relative to ICR (RR: 0.731, 95%CI: 0.668 to 0.8, *P* = 0.453, *I*2 = 0.0%). In a subgroup analysis of MACCE: Mid-term follow-up of < 5 years shows that CR is associated with lower MACCE rates as compared to ICR (RR: 0.717, 95%CI: 0649 to 0.792, *P* = 0.427, *I*2 = 0.0%). Long-term follow-up of > 5 years shows that CR is associated with reduced rates of MACCE (RR: 0.799, CI: 0.644 to 0.990, *P* = 0.427, *I*2 = 0.0%). In the age group of > 60 years, CR is associated with less MACCE (RR: 0.731, 95%CI: 0.668 to 0.8, *P* = 0.453; *I*2 = 0.0%).

**DISCUSSION**

The results of our study comparing the outcomes of CR *vs* ICR show that CR is associated with a 25% reduction in overall mortality, 24% reduction in MI, 27% reduction in MACCE, and 31% reduction in repeat revascularization procedures. Our findings are quite similar to the paper published by Santiago *et al*[5] where they reported a 30% reduction in long term mortality, a 22% reduction in MI, and a 26% reduction in repeat coronary revascularization procedures. Moreover, the results of our subgroup analysis show that independent of the modality of revascularization, CR is associated with better mid-term (< 5 years), long-term (> 5 years) outcomes and is also associated with lesser adverse outcomes in the > 60 years old patient population.

Conventionally, there are two distinct approaches to coronary artery revascularization, one of them being CABG and the other being PCI. Both of these revascularization strategies have their set of advantages and disadvantages. The advantages of PCI include use of local anesthesia, minimal post-procedural morbidity, and shorter hospital stay. New advancement in the form of DES has also allowed effective treatment of long diffuse stenosed segments. Despite these numerous advantages, PCI remains restricted with respect to its inability to overcome chronic total occlusions, whereby success rates vary and symptomatic failures eventually require CABG. CABG surgery, on the other hand, despite having the ability to overcome chronic occlusions, and necessitating fewer repeat revascularization procedures, is nevertheless associated with substantial postoperative morbidity, longer periods of hospitalization, and a slower return to normal activities. Multiple diseased vessel segments are challenging, requiring multiple grafts and longer operative times which translate into longer periods of CPB, and are associated with higher morbidity[10]. Among the main adverse outcomes, PCI is associated with higher rates of MI and repeat revascularization while CABG is associated with higher morbidity and risk of stroke[11]. Many variables have to be considered when selecting a patient for any procedure, which might be a cause for dissimilarities between the outcomes from different studies. Although SYNTAX reported a higher incidence of MACCE at 5 years, data concerning the incidence of death, MI and stroke at 5 years was inconsistent between these studies, even in the diabetic subgroup. In SYNTAX there was no significant difference reported at 5 years in any of the individual outcomes of death, MI, or stroke between PCI and CABG in either the diabetic or non-diabetic subgroups[12]. On the other hand, in the FREEDOM trial PCI was associated with higher incidence of death and MI with a lower incidence of stroke when compared to CABG[10]. Past studies have compared post-procedural outcomes of these two revascularization approaches[13-15]. The primary focus of our study is the clinical outcome(s) of complete revascularization as compared to ICR, achieved by any particular method of revascularization, or both methods simultaneously (hybrid procedures), rather than a comparison of CABG *vs* PCI.

***Benefits of CR***

The association between CR and lower risk for subsequent cardiovascular events has been documented in some studies in which the benefits of complete revascularization are reduction and often elimination of myocardial ischemia (which has been linked to worse prognosis especially when large), improvement in left ventricular function with preserved ejection fraction in heart failure patients, reduction of arrythmias, improved exercise capacity, and better tolerance to future acute myocardial ischemic events[12,16]. More importantly, the mortality benefit of CR is independent of revascularization modality and definition of CR used[17]. In a study by An Den Brand *et al*[14], the authors reported that the frequency with which CR was achieved was greater in CABG treated patients (84.1%) as compared to stented patients, despite the potential for equivalent revascularization. Although no difference in mortality or the combined endpoint of death/stroke/MI were seen, overall MACCE rates were significantly higher in the incompletely revascularized stented group, driven by an increased need for CABG within the first year of follow up.

Over the past decades, CABG has evolved to better peri-operative management, more frequent use of arterial grafting and off pump surgery, and development of minimally invasive direct coronary artery bypass grafting (MIDCAB) and robot-assisted totally endoscopic coronary artery bypass (TECAB) grafting as genuine options. PCIs, especially percutaneous transluminal coronary angioplasty (PTCA), initially developed as a strategy in the treatment of single-vessel disease. Currently, particularly with the advent of DES and new devices to treat chronic total occlusions, it is considered an alternative to CABG in the treatment of multiple vessel disease in certain cases[18,19]. These improvements in technique have increased the feasibility and practicability of complete revascularization. Although CABG and PCI have their own sets of inclusion and exclusion criteria, overlapping in selection criteria exist, where the decision to proceed with a particular technique is generally made by a heart team, consisting of both cardiac surgeons and cardiologists among others. All other factors excluded, we propose that CR/IR should influence a decision to proceed with any specific surgical approach of coronary artery revascularization.

***Mid/long-term outcomes***

The short-term, mid-term, and long-term outcomes of a strategy of revascularization are as important to the patient as it is to the doctor, and we consider it a pivotal factor in the decision making process. In our study, we sub-divided the follow-up time at the 5-year mark, and obtained the two sub-groups, namely the mid-term follow-up group (< 5 years) and long-term follow-up group (> 5 years). Statistical analysis was separately performed on each of the subgroups. CR was found to be associated with less mortality, post-op MI, reduced MACCE, and repeat revascularization procedures.

***> 60 years old***

There has been a gradual increase in the average age of patients now referred for CABG. Contemporary cohorts consist of a greater proportion of octogenarians[15,20]. The BARI trial reported no survival disadvantage associated with IR, where non-LAD territories were left ungrafted. Siamak Mohammadi *et al*[32] in their study of octogenarians undergoing CABG reported that short-term and long-term mortality were not negatively affected by a strategy of ICR during CABG. Due to the greater number of grafted vessels, CR is associated with longer procedural times. This translates into increased duration of general anesthesia, longer cardiopulmonary bypass times, which increase the incidence of negative post-procedural complication and delay discharge from the hospital. Hence, some surgeons have advocated the concept of incomplete “reasonable” revascularization[21-23]. The results of our subgroup analysis show that there is a reduction across all negative outcomes associated with CR in patients who are > 60 years old. Despite the general trend in the elderly population, we propose CR as a precautionary measure against leaving potential myocardial regions and graftable target coronary arteries un-revascularized.

***Study limitations***

There are several limitations to our meta-analysis. The results are affected by variation in study design, end-point definitions and reporting and possible publication bias. Moreover, our results and analysis are limited to the papers found on the Pubmed database and those added by hand-search.

Our study is concordant with similar studies from the past, whereby CR is associated with lower mortality, reduced post-op MI and MACCE, and lower rates of repeat procedures for revascularization. Furthermore, our study shows that CR is also associated with better mid-term and long-term outcomes, and less adverse outcomes in the > 60 years of age patient population. In our experience, CR acts as a buffer between CABG and PCI, and reduces the adverse outcomes associated with any one particular technique. With this in mind, and as dictated by the patient’s condition, the technique with which CR is most likely to be accomplished should be used, and hybrid techniques can be emphasized for complicated cases, thus maximizing the gains from both techniques while minimizing the drawbacks. Given the obvious benefits, CR should be considered as the standard to determine the strategy of revascularization in patients with multi-vessel CAD.

**ARTICLE HIGHLIGHTS**

***Research background***

Two strategies are used in the treatment of multivessel coronary artery disease (CAD), namely percutaneous coronary intervention with stenting and coronary artery bypass grafting. Previous studies have proved the importance of complete revascularization. However, the extent to which completeness of revascularization influences the outcomes is still unclear.

***Research motivation***

Nowadays with new improvements in technology and technique, the feasibility of complete revascularization is less of an issue. Hence, a thorough understanding of how complete revascularization affects post-procedural outcomes is mandatory.

***Research objectives***

To investigate the influence and outcomes of complete *vs* incomplete myocardial revascularization in patients with multivessel CAD.

***Research methods***

Database (pubmed) search coupled with hand search was performed for the identification and collection of relevant studies. Filters, inclusion and exclusion criteria were used to ensure quality and homogenecity of studies. Standard tables were used for data extraction. The data was analyzed and subjected to the appropriate tests by a statistician. A systematic review was then performed.

***Research results***

Ten studies were identified, including 13327 patients of whom, 8053 received complete revascularization and 5274 received ICR. Relative to ICR, CR was associated with lower ­­­mortality (RR: 0.755, 95%CI: 0.66 to 0.864, *P* = 0.765, *I*2 = 0.0%), lower rates of MI (RR: 0.759, 95%CI: 0.615 to 0.937, *P* = 0.091, *I*2 = 45.1%), lower rates of MACCE (RR: 0.731, 95%CI: 0.668 to 0.8, *P* = 0.453, *I*2 = 0.0%) and reduced rates of repeat coronary revascularization (RR: 0.691, CI: 0.541 to 0.883, *P* = 0.0, *I*2 = 88.3%).

***Research conclusions***

Completeness of revascularization is not mandatory for the treatment of multivessel CAD. The results of our study show that CR is associated with lower rates of adverse outcomes. We propose that the extent to which a technique can achieve complete revascularization should be a major deciding factor in the choice of any one particular technique.

***Research perspectives***

Complete revascularization is an alternative standard to decide the choice of a particular technique of revascularization. With emerging techniques of coronary revascularization, new retrospective cohort studies can be performed. Further research is needed to better understand the benefits of complete revascularization with a particular technique.

**REFERENCES**

1 **DeFrances CJ**, Lucas CA, Buie VC, Golosinskiy A. 2006 National Hospital Discharge Survey. *Natl Health Stat Report* 2008; **(5)**: 1-20 [PMID: 18841653]

2 **Yusuf S**, Zucker D, Peduzzi P, Fisher LD, Takaro T, Kennedy JW, Davis K, Killip T, Passamani E, Norris R. Effect of coronary artery bypass graft surgery on survival: overview of 10-year results from randomised trials by the Coronary Artery Bypass Graft Surgery Trialists Collaboration. *Lancet* 1994; **344**: 563-570 [PMID: 7914958 DOI: 10.1016/S0140-6736(94)91963-1]

3 **Hachamovitch R**, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. *Circulation* 2003; **107**: 2900-2907 [PMID: 12771008 DOI: 10.1161/01.CIR.0000072790.23090.41]

4 **Bell MR**, Gersh BJ, Schaff HV, Holmes DR Jr, Fisher LD, Alderman EL, Myers WO, Parsons LS, Reeder GS. Effect of completeness of revascularization on long-term outcome of patients with three-vessel disease undergoing coronary artery bypass surgery. A report from the Coronary Artery Surgery Study (CASS) Registry. *Circulation* 1992; **86**: 446-457 [PMID: 1638714 DOI: 10.1161/01.CIR.86.2.446]

5 **Garcia S**, Sandoval Y, Roukoz H, Adabag S, Canoniero M, Yannopoulos D, Brilakis ES. 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. *J Am Coll Cardiol* 2013; **62**: 1421-1431 [PMID: 23747787 DOI: 10.1016/j.jacc.2013.05.033]

6 **Adabag AS**, Ishani A, Bloomfield HE, Ngo AK, Wilt TJ. Efficacy of N-acetylcysteine in preventing renal injury after heart surgery: a systematic review of randomized trials. *Eur Heart J* 2009; **30**: 1910-1917 [PMID: 19282300 DOI: 10.1093/eurheartj/ehp053]

7 **Higgins JP**, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; **327**: 557-560 [PMID: 12958120 DOI: 10.1136/bmj.327.7414.557]

8 **DerSimonian R**, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986; **7**: 177-188 [PMID: 3802833 DOI: 10.1016/0197-2456(86)90046-2]

9 **Egger M**, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; **315**: 629-634 [PMID: 9310563 DOI: 10.1136/bmj.315.7109.629]

10 **Ong AT**, Serruys PW. Complete revascularization: coronary artery bypass graft surgery versus percutaneous coronary intervention. *Circulation* 2006; **114**: 249-255 [PMID: 16847164 DOI: 10.1161/CIRCULATIONAHA.106.614420]

11 **French JK**, Burgess S, Chew DP. Re-infarction after primary percutaneous coronary intervention. *Curr Opin Cardiol* 2015; **30**: 354-358 [PMID: 26049380 DOI: 10.1097/HCO.0000000000000193]

12 **Weintraub WS**, Grau-Sepulveda MV, Weiss JM, O'Brien SM, Peterson ED, Kolm P, Zhang Z, Klein LW, Shaw RE, McKay C, Ritzenthaler LL, Popma JJ, Messenger JC, Shahian DM, Grover FL, Mayer JE, Shewan CM, Garratt KN, Moussa ID, Dangas GD, Edwards FH. Comparative effectiveness of revascularization strategies. *N Engl J Med* 2012; **366**: 1467-1476 [PMID: 22452338 DOI: 10.1056/NEJMoa1110717]

13 **Fanari Z**, Weiss SA, Zhang W, Sonnad SS, Weintraub WS. Comparison of percutaneous coronary intervention with drug eluting stents versus coronary artery bypass grafting in patients with multivessel coronary artery disease: Meta-analysis of six randomized controlled trials. *Cardiovasc Revasc Med* 2015; **16**: 70-77 [PMID: 25662779 DOI: 10.1016/j.carrev.2015.01.002]

14 **van den Brand MJ**, Rensing BJ, Morel MA, Foley DP, de Valk V, Breeman A, Suryapranata H, Haalebos MM, Wijns W, Wellens F, Balcon R, Magee P, Ribeiro E, Buffolo E, Unger F, Serruys PW. The effect of completeness of revascularization on event-free survival at one year in the ARTS trial. *J Am Coll Cardiol* 2002; **39**: 559-564 [PMID: 11849851 DOI: 10.1016/S0735-1097(01)01785-5]

15 **Serruys PW**, Unger F, Sousa JE, Jatene A, Bonnier HJ, Schönberger JP, Buller N, Bonser R, van den Brand MJ, van Herwerden LA, Morel MA, van Hout BA; Arterial Revascularization Therapies Study Group. Comparison of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. *N Engl J Med* 2001; **344**: 1117-1124 [PMID: 11297702 DOI: 10.1056/NEJM200104123441502]

16 **Shaw LJ**, Berman DS, Maron DJ, Mancini GB, Hayes SW, Hartigan PM, Weintraub WS, O'Rourke RA, Dada M, Spertus JA, Chaitman BR, Friedman J, Slomka P, Heller GV, Germano G, Gosselin G, Berger P, Kostuk WJ, Schwartz RG, Knudtson M, Veledar E, Bates ER, McCallister B, Teo KK, Boden WE; COURAGE Investigators. Optimal medical therapy with or without percutaneous coronary intervention to reduce ischemic burden: results from the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial nuclear substudy. *Circulation* 2008; **117**: 1283-1291 [PMID: 18268144 DOI: 10.1161/CIRCULATIONAHA.107.743963]

17 **Yang ZK**, Zhang RY, Hu J, Zhang Q, Ding FH, Shen WF. Impact of successful staged revascularization of a chronic total occlusion in the non-infarct-related artery on long-term outcome in patients with acute ST-segment elevation myocardial infarction. *Int J Cardiol* 2013; **165**: 76-79 [PMID: 21872352 DOI: 10.1016/j.ijcard.2011.07.074]

18 **Kappetein AP**, Head SJ, Morice MC, Banning AP, Serruys PW, Mohr FW, Dawkins KD, Mack MJ; SYNTAX Investigators. Treatment of complex coronary artery disease in patients with diabetes: 5-year results comparing outcomes of bypass surgery and percutaneous coronary intervention in the SYNTAX trial. *Eur J Cardiothorac Surg* 2013; **43**: 1006-1013 [PMID: 23413014 DOI: 10.1093/ejcts/ezt017]

19 **Serruys PW**, Ong AT, van Herwerden LA, Sousa JE, Jatene A, Bonnier JJ, Schönberger JP, Buller N, Bonser R, Disco C, Backx B, Hugenholtz PG, Firth BG, Unger F. Five-year outcomes after coronary stenting versus bypass surgery for the treatment of multivessel disease: the final analysis of the Arterial Revascularization Therapies Study (ARTS) randomized trial. *J Am Coll Cardiol* 2005; **46**: 575-581 [PMID: 16098418 DOI: 10.1016/j.jacc.2004.12.082]

20 **Tarakji KG**, Sabik JF 3rd, Bhudia SK, Batizy LH, Blackstone EH. Temporal onset, risk factors, and outcomes associated with stroke after coronary artery bypass grafting. *JAMA* 2011; **305**: 381-390 [PMID: 21266685 DOI: 10.1001/jama.2011.37]

21 **Ferguson TB Jr**, Hammill BG, Peterson ED, DeLong ER, Grover FL; STS National Database Committee. A decade of change--risk profiles and outcomes for isolated coronary artery bypass grafting procedures, 1990-1999: a report from the STS National Database Committee and the Duke Clinical Research Institute. Society of Thoracic Surgeons. *Ann Thorac Surg* 2002; **73**: 480-489; discussion 489-490 [PMID: 11845863 DOI: 10.1016/S0003-4975(01)03339-2]

22 **Capodanno D**, Stone GW, Morice MC, Bass TA, Tamburino C. Percutaneous coronary intervention versus coronary artery bypass graft surgery in left main coronary artery disease: a meta-analysis of randomized clinical data. *J Am Coll Cardiol* 2011; **58**: 1426-1432 [PMID: 21939824 DOI: 10.1016/j.jacc.2011.07.005]

23 **Bainey KR**, Mehta SR, Lai T, Welsh RC. Complete vs culprit-only revascularization for patients with multivessel disease undergoing primary percutaneous coronary intervention for ST-segment elevation myocardial infarction: a systematic review and meta-analysis. *Am Heart J* 2014; **167**: 1-14.e2 [PMID: 24332136 DOI: 10.1016/j.ahj.2013.09.018]

24 **Bell MR**, Bailey KR, Reeder GS, Lapeyre AC 3rd, Holmes DR Jr. Percutaneous transluminal angioplasty in patients with multivessel coronary disease: how important is complete revascularization for cardiac event-free survival? *J Am Coll Cardiol* 1990; **16**: 553-562 [PMID: 2387928 DOI: 10.1016/0735-1097(90)90342-M]

25 **McLellan CS**, Ghali WA, Labinaz M, Davis RB, Galbraith PD, Southern DA, Shrive FM, Knudtson ML; Alberta Provincial Project for Outcomes Assessment in Coronary Heart Disease (APPROACH) Investigators. Association between completeness of percutaneous coronary revascularization and postprocedure outcomes. *Am Heart J* 2005; **150**: 800-806 [PMID: 16209985 DOI: 10.1016/j.ahj.2004.10.037]

26 **Sarno G**, Garg S, Onuma Y, Gutiérrez-Chico JL, van den Brand MJ, Rensing BJ, Morel MA, Serruys PW; ARTS-II Investigators. Impact of completeness of revascularization on the five-year outcome in percutaneous coronary intervention and coronary artery bypass graft patients (from the ARTS-II study). *Am J Cardiol* 2010; **106**: 1369-1375 [PMID: 21059423 DOI: 10.1016/j.amjcard.2010.06.069]

27 **Farooq V**, Serruys PW, Garcia-Garcia HM, Zhang Y, Bourantas CV, Holmes DR, Mack M, Feldman T, Morice MC, Ståhle E, James S, Colombo A, Diletti R, Papafaklis MI, de Vries T, Morel MA, van Es GA, Mohr FW, Dawkins KD, Kappetein AP, Sianos G, Boersma E. The negative impact of incomplete angiographic revascularization on clinical outcomes and its association with total occlusions: the SYNTAX (Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial. *J Am Coll Cardiol* 2013; **61**: 282-294 [PMID: 23265332 DOI: 10.1016/j.jacc.2012.10.017]

28 **Bourassa MG**, Kip KE, Jacobs AK, Jones RH, Sopko G, Rosen AD, Sharaf BL, Schwartz L, Chaitman BR, Alderman EL, Holmes DR, Roubin GS, Detre KM, Frye RL. Is a strategy of intended incomplete percutaneous transluminal coronary angioplasty revascularization acceptable in nondiabetic patients who are candidates for coronary artery bypass graft surgery? The Bypass Angioplasty Revascularization Investigation (BARI). *J Am Coll Cardiol* 1999; **33**: 1627-1636 [PMID: 10334434 DOI: 10.1016/S0735-1097(99)00077-7]

29 **Bourassa MG**, Yeh W, Holubkov R, Sopko G, Detre KM. Long-term outcome of patients with incomplete vs complete revascularization after multivessel PTCA. A report from the NHLBI PTCA Registry. *Eur Heart J* 1998; **19**: 103-111 [PMID: 9503182 DOI: 10.1053/euhj.1997.0574]

30 **Head SJ**, Mack MJ, Holmes DR Jr, Mohr FW, Morice MC, Serruys PW, Kappetein AP. Incidence, predictors and outcomes of incomplete revascularization after percutaneous coronary intervention and coronary artery bypass grafting: a subgroup analysis of 3-year SYNTAX data. *Eur J Cardiothorac Surg* 2012; **41**: 535-541 [PMID: 22219412 DOI: 10.1093/ejcts/ezr105]

31 **Schwartz L**, Bertolet M, Feit F, Fuentes F, Sako EY, Toosi MS, Davidson CJ, Ikeno F, King SB 3rd. Impact of completeness of revascularization on long-term cardiovascular outcomes in patients with type 2 diabetes mellitus: results from the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D). *Circ Cardiovasc Interv* 2012; **5**: 166-173 [PMID: 22496082 DOI: 10.1161/CIRCINTERVENTIONS.111.963512]

32 **Mohammadi S**, Kalavrouziotis D, Dagenais F, Voisine P, Charbonneau E. Completeness of revascularization and survival among octogenarians with triple-vessel disease. *Ann Thorac Surg* 2012; **93**: 1432-1437 [PMID: 22480392 DOI: 10.1016/j.athoracsur.2012.02.033]

**P-Reviewer:** Liang Y, Petrucciani N, Pani SP **S-Editor:** Ji FF **L-Editor: E-Editor:**

**Specialty type:** Medicine, research and experimental

**Country of origin:** China

**Peer-review report classification**

Grade A (Excellent): 0

Grade B (Very good): B, B

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

**Table 1 Studies included in meta-analysis**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Ref. | Type of search | Method of revascularization | Study design | Year | Definition of CR used | Follow-up (yr) |
| Bell *et al*[24] | Hand | PCI | Post hoc analysis, non-RCT | 1990 | Anatomical | 2.2 |
| Approach/catherine Mclellan *et al*[25] | Hand | PCI | Post hoc analysis, non-RCT | 2005 | Anatomical | 9 |
| ARTS II/Sarno *et al*[26] | PubMed | CABG/PCI | Post hoc analysis, non-RCT | 2010 | Anatomical | 5 |
| ARTS trial/van den Brand *et al*[14] | PubMed | CABG/PCI | Post hoc analysis, RCT | 2002 | Anatomical | 1 |
| SYNTAX trial/ Farooq *et al*[27] | PubMed | CABG/PCI | Post hoc analysis, RCT | 2013 | Anatomical | 4 |
| BARI/Bourassa *et al*[28] | PubMed | CABG/PCI | Post hoc analysis, RCT | 1999 | Anatomical | 5 |
| Bourassa *et al*[29] | Hand | PTCA | Post hoc analysis, non-RCT | 1998 | Anatomical | 9 |
| Head *et al*[30] | PubMed | CABG/PCI | Post hoc analysis, RCT | 2012 | Anatomical | 3 |
| BARI 2D/Schwartz *et al*[31] | PubMed | CABG/PCI | Post hoc analysis, non-RCT | 2012 | Numerical | 5.3 |
| Mohammadi *et al*[32] | Hand | CABG | Post hoc analysis, non-RCT | 2012 | Anatomical | 5.4 ± 3.0 |

CABG: Coronary artery bypass grafting; PCI: Percutaneous coronary intervention; CR: Complete revascularization; RCT: Randomly controlled trial.

**Table 2 Characteristics of patients undergoing complete revascularization**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Ref. | Prevalence of CR (%) | Mean age (yr) | Previous MI | No previous MI | Diabetes | No diabetes | Hypertension | No hypertension |
| Bell *et al*[24] | 41 | 60 | 122 | 234 | 46 | 319 | 148 | 217 |
| Approach/catherine Mclellan *et al*[25] | 66.9 | 62.1 | 802 | 506 | 244.6 | 1063.4 | 725.94 | 582.06 |
| ARTS II/Sarno *et al*[26] | 72.5 | 61.5 | 149 | 688 | 163 | 674 | 440 | 397 |
| ARTS trial/van den Brand *et al*[14] | 77.2 | 61 | 385 | 498 | 143.93 | 739.07 | - |  |
| SYNTAX trial/ Farooq *et al*[27] | 61.8 | 65.3 | 521 | 1088 | 429.6 | 1179.4 | 759.45 | 849.55 |
| BARI/Bourassa *et al*[28] | 65.4 | 61.3 | 612 | 584 | 204.52 | 991.48 | 578.86 | 617.14 |
| Bourassa *et al*[29] | 17.4 | 56.6 | 62 | 70 | 15.05 | 116.95 | 55.97 | 76.03 |
| Head *et al*[30] | 59.9 | 64.9 | 328 | 713 | 300 | 438 | 702 | 356 |
| BARI 2D/Schwartz *et al*[31] | 37.9 | 61.21 | - |  | - |  | - |  |
| Mohammadi *et al*[32] | 82.1 | 82.1 | 224 | 167 | 107.92 | 283.08 | 286.21 | 104.79 |

CR: Complete revascularization; MI: Myocardial infarction.

**Table 3 Characteristics of patients undergoing incomplete revascularization**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Ref. | Prevalence of CR (%) | Mean age (yr) | Previous MI | No previous MI | Diabetes | No diabetes | Hypertension | No hypertension |
| Bell *et al*[24] | 41 | 60 | 122 | 234 | 46 | 319 | 148 | 217 |
| Approach/catherine Mclellan *et al*[25] | 66.9 | 62.1 | 802 | 506 | 244.6 | 1063.4 | 725.94 | 582.06 |
| ARTS II/Sarno *et al*[26] | 72.5 | 61.5 | 149 | 688 | 163 | 674 | 440 | 397 |
| ARTS trial/van den Brand *et al*[14] | 77.2 | 61 | 385 | 498 | 143.93 | 739.07 | - |  |
| SYNTAX trial/ Farooq *et al*[27] | 61.8 | 65.3 | 521 | 1088 | 429.6 | 1179.4 | 759.45 | 849.55 |
| BARI/Bourassa *et al*[28] | 65.4 | 61.3 | 612 | 584 | 204.52 | 991.48 | 578.86 | 617.14 |
| Bourassa *et al*[29] | 17.4 | 56.6 | 62 | 70 | 15.05 | 116.95 | 55.97 | 76.03 |
| Head *et al*[30] | 59.9 | 64.9 | 328 | 713 | 300 | 438 | 702 | 356 |
| BARI 2D/Schwartz *et al*[31] | 37.9 | 61.21 | - |  | - |  | - |  |
| Mohammadi *et al*[32] | 82.1 | 82.1 | 224 | 167 | 107.92 | 283.08 | 286.21 | 104.79 |

CR: Complete revascularization; MI: Myocardial infarction.

Abstracts filtered out by selecting “clinical trials, controlled clinical trials, observational study, randomized controlled trial” in “article types” (n=45)

Manuscripts included through pubmed search (n=6)

Abstracts excluded (n=1)

Reason for exclusion: absence of CR versus ICR comparison

Full-text articles assessed for eligibility (n=8)

Potential relevant abstracts reviewed (n=9)

Records identified through pubmed search( n=54)

Full-text articles excluded(n=2)

Reason for exclusion:

Absence of CR versus ICR comparison(n=1)

Outcome of interest not reported(n=1)

Studies included in meta-analysis (n=10)

Studies identified through hand-search (n=4)

**Figure 1 Flow diagram of literature search and study selection.** ICR: Incomplete revascularization.



Risk Ratio

Favors CR Favors IR

**Figure 2 Pooled analysis with risk ratio and 95%CI for the occurrence of total mortality.** Boxes are 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. CR: Complete revascularization.



Risk Ratio

Favors CR Favors IR

**Figure 3 Pooled analysis with risk ratio and 95%CI for the occurrence of mortality in the > 60 age group.** Boxes are 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. CR: Complete revascularization.



Risk Ratio

Favors CR Favors IR

**Figure 4 Pooled analysis with risk ratio and 95%CI for occurrence of myocardial infarction.** Boxes are 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. CR: Complete revascularization.