Cardiovascular Revascularization Medicine xxx (2018) xxx–xxx

Contents lists available at ScienceDirect

Cardiovascular Revascularization Medicine

Revascularization strategies in cardiogenic shock complicating acute myocardial infarction: A systematic review and meta-analysis

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ARTICLE INFO

Article history:
Received 8 April 2018
Received in revised form 24 May 2018
Accepted 6 June 2018
Available online xxxx

Keywords:
Cardiogenic shock
Acute myocardial infarction
Culprit-only revascularization
Instant multi-vessel revascularization

ABSTRACT

Background: The optimal revascularization strategy in patients with multi-vessel disease (MVD) presenting with acute myocardial infarction (AMI) and cardiogenic shock (CS) remains unclear.
Objective: To investigate the comparative differences between culprit-only revascularization (COR) versus instant multi-vessel revascularization (IMVR) in AMI and CS.
Methods: 13 studies were selected using MEDLINE, EMBASE and the CENTRAL (Inception - 31 November2017). Outcomes were assessed at short-term (in-hospital or ≤30 days duration) and long-term duration (≥6 months). Estimates were reported as random effects relative risk (RR) with 95% confidence interval (CI).
Results: In analysis of 7311 patients, COR significantly reduced the relative risk of short-term all-cause mortality (RR: 0.87; 95% CI, 0.77–0.97; p = 0.01, $I^2 = 50\%$) and renal failure (RR: 0.75; 95% CI, 0.61–0.94; p = 0.01, $I^2 = 7\%$) compared with IMVR. There were no significant differences between both the strategies in terms of reinfarction (RR: 1.25; 95% CI, 0.59–2.63; p = 0.56, $I^2 = 0\%$), major bleeding (RR: 0.88; 95% CI, 0.75–1.04; p = 0.14, $I^2 = 0\%$) and stroke (RR: 0.77; 95% CI, 0.50–1.17; p = 0.22, $I^2 = 0\%$) at short term duration. Similarly, no significant differences were observed between both groups regarding all-cause mortality (RR; 1.01; 95% CI, 0.85–1.20; p = 0.93, $I^2 = 61\%$) and reinfarction (RR: 0.71; 95% CI, 0.34–1.47; p = 0.35, $I^2 = 26\%$) at long term duration.
Conclusion: In MVD patients presenting with AMI and CS, IMVR was comparable to COR in terms of all-cause mortality at long term follow up duration. These results are predominantly derived from observational data and more randomized controlled trials are required to validate this impression.

1. Introduction

Urgent percutaneous coronary intervention (PCI) is the mainstay of the management in patients with acute myocardial infarction (AMI) complicating cardiogenic shock (CS) [1]. There has been an ongoing effort to determine whether patients with multi-vessel disease (MVD) presenting with AMI should receive revascularization of culprit artery only (COR) or complete revascularization of non-culprit arteries. The PRAMI (Randomized trial of preventive angioplasty in myocardial infarction) [2], DANAMI-3 PRIMULTI (Complete revascularization versus treatment of the culprit lesion only in patients with ST- segment elevation myocardial infarction and multi-vessel disease) [3], and CvLPRIT (Randomized trial of complete versus lesion-only revascularization in patients undergoing primary percutaneous coronary intervention for STEMI and multi-vessel disease) [4] trials have endorsed revascularization of non-infarct related arteries in stable AMI patients. This was further supported by meta-analyses demonstrating reduced major adverse cardiovascular events with instant or staged complete revascularization [5–7]. Subsequently, 2015 American College of Cardiology/ American Heart Association guidelines suggest primary PCI of non-culprit lesions for hemodynamically stable subjects with STEMI and MVD either during the index procedure or as staged procedure (Class II b) [8]. However, the American guidelines are not clear whether this approach can be extended to hemodynamically unstable patients [9]. Conversely, the European Society of Cardiology (ESC) 2017 guidelines takes a more vivid stance and state that non-infarct related artery revascularization should be considered during index procedure in patients with STEMI and CS (Class IIa C) [10].

Contrary to the ESC guidelines, the recent CULPRIT-SHOCK trial (Prospective Randomized Multicenter Study Comparing Immediate

Abbreviations: AMI, acute myocardial infarction; CI, confidence interval; COR, culprit-only revascularization; CS, cardiogenic shock; CV, cardiovascular; ESC, European Society of Cardiology; HTN, hypertension; IMVR, instant multi-vessel revascularization; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; MVD, multi-vessel disease; OS, observational study; PCI, percutaneous coronary intervention; RCA, right coronary artery; RCT, randomized controlled trial; RD, risk difference; RR, relative risk; STEMI, ST-elevation myocardial infarction.

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https://doi.org/10.1016/j.carrev.2018.06.004
1553-8389/

Multivessel Revascularization by PCI Versus Culprit Lesion PCI With Staged Non-culprit Lesion Revascularization in Patients With Acute Myocardial Infarction Complicated by Cardiogenic Shock) have demonstrated contrasting results with reduced short-term mortality with COR compared to instant multi-vessel revascularization (IMVR) in AMI with CS [11]. Two former meta-analyses on this issue also provided contradictory results regarding optimal revascularization strategy in this subset of patients [12, 13]. Consequently, we performed a meta-analysis on all the studies comparing COR versus IMVR in MVD patients presenting with AMI and CS to address this controversy.

2. Methods

The meta-analysis is conducted and reported according to the Cochrane collaboration guidelines [14] and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) report [15].

2.1. Search strategy

Search was conducted by two authors (HR and SUK) using MEDLINE (PubMed), EMBASE and the CENTRAL from inception of data bases to 31st November 2017. We used following words and MeSH terms in combination: “percutaneous coronary intervention”, “revascularization”, “cardiogenic shock”, “shock”, “acute myocardial infarction”, “ST-elevation myocardial infarction”, “STEMI”, “NSTEMI”, “culprit-only”, “non-infarct”, “multi-vessel”, “complete revascularization” and “multi-vessel disease”. Restrictions were applied to “Humans” only, however there were restrictions on article types, text availability or publication dates. The search strategy is reported in Supplementary material. Electronic data base search was supplemented with review of bibliographies of the relevant articles. All citations were downloaded into EndNote X7 (Thompson ISI ResearchSoft, Philadelphia, Pennsylvania, USA). Duplicates were removed manually and by EndNote X7.

2.2. Selection criteria

Studies were included if (1) participants had MVD and presented with AMI and CS, (2) compared COR with or without staged PCI with IMVR (3) reported at least all-cause mortality. No restriction was applied regarding language, co-morbidities and follow-up duration.

2.3. Data extraction and quality assessment

Studies were assessed at title and abstract level followed by full text screening by two authors (SUK and ANL) independently based on a priori inclusion criteria. Any disagreements were resolved by third party review (HR). Data was extracted using four different data collection forms incorporating baselines characteristics of participants (sample size, demographics, co-morbidities), study characteristics (study design, exclusion and follow-up duration), procedural characteristics (vascular access, type of stents, contrast dose and medical therapy) and outcomes (events, sample size, event rate and crude point estimates). Although, definition of CS was variable in the studies but systolic blood pressure (SBP) <90 mm Hg and end organ hypo-perfusion in setting of AMI was common in all the studies, which constituted the definition of CS in this review. Quality assessment of RCT was done on the Cochrane bias risk assessment (supplementary (S) Table S6), while observational studies were assessed on New Castle-Ottawa Scale (NOS) (Table S7). The score ≥ 6 out of 8 on NOS was merit good quality for the study. PRISMA chart check list is provided in Table S8.

2.4. Outcome measures

The outcomes were measured at short-term duration (in-hospital or ≤30-days of revascularization) or long-term duration (≥6 months after index procedure). The primary focus was on short-term mortality. Secondary endpoints assessed at short-term duration were reinfarction, stroke, renal failure and major bleeding. The long-term outcomes were all-cause mortality, cardiovascular (CV) mortality, reinfarction and repeat revascularization. Renal failure was defined as elevation of creatinine by two times or >2 mg/dL or new requirement of renal-replacement therapy. Rests of the outcomes were defined as reported in the included trials.

2.5. Statistical analysis

Meta-analysis was conducted according to DerSimonian and Laird random effects model. We used random effects model to account for any between study variance [16]. The principal summary measure was risk ratio (RR) with 95% confidence interval (CI), supplemented by risk difference (RD). Since both the RR and RD represent same data, we used RR estimates for forest plots in this review. However, RD estimates are reported in Table S4. A p value of 0.05 was set as significant. Heterogeneity was assessed using Q statistics with I^2 with values >50% consistent with a high degree of heterogeneity [17]. A sensitivity analysis exclusively for STEMI patients was done to compare effect of both interventions on primary outcome.

Moment of methods Meta regression analysis was conducted to assess the effect of various study characteristics in the COR group on the short-term all-cause mortality. Publication bias was assessed using Egger's regression test. Comprehensive Meta-analysis software version 3.0 (Biostat, Englewood, NJ) was used for conducting all analyses.

3. Results

Initial database search recovered 21,235 articles, 17,201 were duplicates, and 3731 records were removed at title and abstract level. Additional 290 studies were removed if desired outcomes were not reported or if studies were systematic reviews and meta-analyses. Ultimately 13 studies (one RCT and 12 observational studies) were selected [11, 18–30] (Fig. 1). Six studies exclusively recruited STEMI patients [20, 22–25, 28, 29] and one study enrolled patients with cardiac arrest [26]. Only two studies [11, 19] provided percentages of patients undergoing staged PCI with rest of studies either excluded staged PCI or did not report it. In total of 7311 participants, 76.9% (5623 patients) underwent COR and 23.1% (1688 patients) had IMVR. The mean (SD) age of the participants was 67.3 ± 2.3 years, 68.5% were males and 91.0% had STEMI. Three studies [11, 26, 27] used ≥70% stenosis cutoff for the MVD and the rest applied ≥50% stenosis cutoff. The culprit lesion in the COR group was right coronary artery (RCA, 45.2%), left anterior descending artery (LAD, 37.9%) and left circumflex artery (LCX, 14.2%). Use of intra-aortic balloon pump (IABP) was slightly more frequent in patients undergoing IMVR as mentioned in Table S3. The mean follow-up duration was ~9 months. The baseline features of the participants are illustrated in Table 1. The study characteristics and procedural characteristics are provided in the supplementary material Table S1–S3.

3.1. Outcomes assessed at short-term duration

a) **All-cause mortality**: In patients with MVD who presented with AMI and CS, COR significantly reduced the RR of short term all-cause mortality compared with IMVR (31% vs 40%; RR: 0.87; 95% CI, 0.77–0.97; $p = 0.01$, $I^2 = 50\%$, Fig. 2). In sensitivity analysis of six studies with 100% STEMI patients, COR was consistently superior to IMVR in terms of reducing short-term mortality (27% vs 34%; RR: 0.81; 95% CI, 0.69–0.96; $p = 0.01$, $I^2 = 34\%$, Fig. S1).
b) **Secondary outcomes** (Fig. 3): COR reduced the relative risk of renal failure compared with IMVR (7% vs 11%; RR: 0.75; 95% CI, 0.61–0.94; $p = 0.01$, $I^2 = 7\%$). There were no significant differences in risk of reinfarction (2% vs 1%; RR: 1.25; 95% CI, 0.59–2.63; $p = 0.56$, $I^2 = 0\%$), stroke (2% vs 2%; RR: 0.77; 95% CI, 0.50–1.17; $p = 0.22$, $I^2 =$

Please cite this article as: Rahman H, et al, Revascularization strategies in cardiogenic shock complicating acute myocardial infarction: A systematic review and meta-analysis, Cardiovascular Revascularization Medicine (2018), https://doi.org/10.1016/j.carrev.2018.06.004