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# Multi-vessel versus culprit-vessel and staged percutaneous coronary intervention in STEMI patients with multivessel disease: a meta-analysis of randomized controlled trials $^{\stackrel{\sim}{\sim}, \stackrel{\sim}{\sim}, \stackrel{\star}{\sim}}$



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#### ABSTRACT

Introduction: Percutaneous coronary intervention (PCI) is preferred in patients with acute ST-elevation myocardial infarction (STEMI). In patients with acute STEMI with multivessel disease (MVD), the guidelines recommend culprit vessel PCI (CV-PCI) in the absence of hemodynamic instability. We performed a meta-analysis of all randomized controlled trials (RCTs) comparing multi-vessel PCI (MV-PCI) with CV-PCI or staged PCI (S-PCI) in patients with acute STEMI and MVD.

*Methods*: PubMed, EMBASE and CENTRAL were searched for publications since inception to December 2013. Random effects model was used to compute summary effects.

Results: Four RCTs (840 patients) were identified. MV-PCI compared to CV-PCI significantly reduced the risks of major adverse cardiac events (MACE)—a composite of MI, revascularization and all-cause mortality (RR: 0.46, 95% CI: 0.35–0.60, P < 0.00001) by reducing the risks of MI (0.35, 0.17–0.71, P = 0.004) and revascularization (0.35, 0.24–0.52, P < 0.00001). The risk of all-cause mortality was not different (0.69, 0.39–1.21, P = 0.19). S-PCI and MV-PCI had similar risks of MACE (0.96, 0.59–1.57, P = 0.87), MI (0.60, 0.20–1.78, P = 0.36), revascularization (0.86, 0.47–1.54, P = 0.60) and all-cause mortality (1.50, 0.44–5.07, P = 0.57).

Conclusions: MV-PCI compared to CV-PCI resulted in lower risks of MACE driven by lower MI and revascularization in patients with STEMI and multi-vessel disease.

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#### 1. Introduction

Coronary angioplasty, hereafter called percutaneous coronary intervention (PCI), is the preferred treatment in patients with acute ST-elevation MI (STEMI) [1–3]. In patients with STEMI, 40–50% have been reported to have multi-vessel disease (MVD), the stenosis of >50% in more than one coronary artery [4,5]. The patients with MVD have worse outcomes of death, future MI and revascularization in comparison to patients with single vessel disease [4,6,7]. The current guidelines recommend PCI of culprit vessel (CV-PCI) in patients who present with

Abbreviations: CABG, Coronary artery bypass grafting; CI, Confidence interval; CV-PCI, Culprit vessel percutaneous coronary intervention; IRA, Infarct related artery; MI, Myocardial infarction; MVD, Multi-vessel disease; MV-PCI, Multi-vessel percutaneous coronary intervention; RCT, Randomized controlled trial; S-PCI, Staged percutaneous coronary intervention; STEMI, ST-elevation myocardial infarction.

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STEMI without hemodynamic instability and do not recommend PCI of non-infarct related artery (IRA) [1]. A previous meta-analysis with both observational studies and randomized controlled trials showed worse mortality outcomes with multi-vessel PCI (MV-PCI) in comparison to CV-PCI and staged PCI (S-PCI) and supported the current guidelines [8]. The Preventive Angioplasty in Acute Myocardial Infarction (PRAMI) trial showed that MV-PCI was superior to CV-PCI by significantly reducing adverse cardiovascular events [9]. Similarly, the Complete versus Lesion-only Primary PCI Trial (CvLPRIT) showed significantly lower rates of major adverse cardiac events (MACE) with complete versus culprit vessel revascularization [10]. To define the best revascularization strategy from published studies, we performed a meta-analysis of all randomized controlled trials (RCTs) that compared the effects of MV-PVI with CV-PCI or S-PCI in patients with STEMI and MVD.

#### 2. Methods

#### 2.1. Search criteria and study selection

This meta-analysis was designed in accordance with PRISMA statement [11]. Two authors (K.D. & J.R.) independently searched PubMed,

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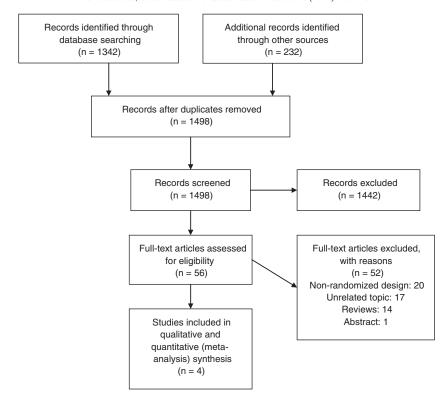


Fig. 1. Flow diagram of study selection.

EMBASE and Cochrane Central Register of Controlled Trials for Englishlanguage publications since inception in December 2013 with pre-specified terms "multi-vessel PCI", "staged PCI", "culprit vessel PCI", "STEMI", "multivessel disease" and "randomized trials". The ClinicalTrials.gov was searched for past or ongoing trials of interest. A hand search was performed for all relevant references. Algorithm of study selection is shown (Fig. 1).

All randomized controlled trials comparing MV-PCI with either S-PCI or CV-PCI in adult patients (>18 years) with STEMI and multivessel disease without hemodynamic instability were included. The studies were excluded from the analysis if they were abstracts, non-randomized or non-human studies.

#### 2.2. Data extraction

Data were independently extracted by two persons (K.D. & J.R.) from the selected RCTs using standardized data-extraction table in Microsoft Excel 2010. A consensus was reached in case of disagreement. We obtained data on study and patient characteristics, type of intervention, duration of follow-ups and outcomes.

#### 2.3. Definitions and outcomes

MV-PCI is defined as revascularization of one or more non-infarct arteries during the index PCI. CV-PCI is defined as the PCI of infarct-related artery only with no planned intervention of non-infarct vessels. S-PCI is defined as the planned PCI of non-infarct vessel (s) at a future date after index PCI.

Primary outcome was major adverse cardiovascular events (MACE), a composite of myocardial infarction, revascularization and all-cause mortality. The secondary outcomes were individual components of MACE.

#### 2.4. Statistical analysis

For binary outcomes, the crude events from each study were used to compute risk ratio (RR) with 95% confidence interval (CI). Categorical variables were expressed as mean ( $\pm$  standard deviation). We used funnel plot to visually examine publication bias which was further evaluated with Egger's regression intercept and Begg and Mazumdar rank correlation. The quality of studies was evaluated with Jadad scale based on randomization, blinding and attrition of participants [12]. DerSimonian-Laird random-effects model was used for meta-analysis of effect size. Study heterogeneity was evaluated with Cochran's Q and I2 index, and P < 0.1 or I2 > 60% was considered significant heterogeneity. If significant heterogeneity was detected, sensitivity analyses were performed to explore heterogeneity. The P-values are two-tailed and a P-value of < 0.05 was considered statistically significant. Statistical analyses were performed with comprehensive meta-analysis (CMA 2.2, Biostat, Englewood, NJ, USA) and review manager (RevMan 5.2, Cochrane Collaboration, Nordic Cochrane Center, Copenhagen, Denmark).

#### 3. Results

#### 3.1. Description of included studies

After removal of duplicates, 1498 total citations were retrieved for review, of which 56 full text articles were screened for eligibility. Of 56 publications, we included 4 RCTs [9,13–15] with a total of 840 patients with STEMI and MVD in meta-analysis. The individual study characteristics are presented in Table 1. Two studies compared MV-PCI with CV-PCI [9,15], while one study compared MV-PCI with S-PCI [14] and one study compared MV-PCI with both CV-PCI and S-PCI [13]. The duration of follow up was between 6 months and 5 years.

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