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Impact of intraprocedural thrombotic events on short- and long-term outcomes following percutaneous coronary intervention. Evidence from a meta-analysis

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ABSTRACT

Background: Data regarding the effects of intraprocedural thrombotic events (IPTE) are scarce. Hence we aim to perform a meta-analysis to examine the outcomes of IPTE compared to non-IPTE during PCI.
Methods: We performed a literature search of all published full-length articles of studies that reported data on patients with IPTE compared with non-IPTE during PCI. We calculated odd ratios via random effects model.
Results: A total of 26,697 patients, of which 1572 patients had IPTE, were included in this analysis. In-hospital, IPTE was associated with higher mortality (odds ratio (OR) 5.36, 95% confidence interval (CI) [2.31, 12.41]; $p < 0.0001$), myocardial infarction (MI) and major bleeding compared to non-IPTE. At 30 days, IPTE was also associated with higher mortality (OR 4.57, 95% CI [2.43, 8.60]; $p < 0.0001$), MI, repeat revascularization, stent thrombosis and major bleeding compared to non-IPTE group. IPTE was also associated with higher long-term mortality (OR 2.19, 95% CI [1.35, 3.53]; $p = 0.001$). Among IPTE patients, intraprocedural stent thrombosis was associated with greater odds of MI compared to both no reflow and distal embolization events.
Conclusion: IPTE during PCI is associated with more adverse ischemic events, including mortality, during the index hospitalization, at 30 days and long-term.

1. Introduction

Intra-procedural thrombotic events (IPTE) represent an important group of percutaneous coronary intervention (PCI) related complications, and include slow flow, no reflow, distal embolization, abrupt vessel closure, loss of a coronary artery side branch, new or worsening thrombus formation and intraprocedural stent thrombosis. Prior studies demonstrated that patients with non-ST-elevation acute coronary syndrome (NSTEACS) or ST-segment elevation myocardial infarction (STEMI) are at a greater risk for intra-procedural thrombotic complications, these are associated with higher rates of major adverse cardiovascular events and increased mortality [1–6]. Few studies examined these different intraprocedural complications, mostly in a small sample size of patients. It is thought that they carry worse prognosis. No reflow refers to the inability to reperfuse myocardial tissue after opening the blocked epicardial coronary artery and it is thought to be associated with large myocardial necrosis. Distal embolization refers to the visualization of embolized atherothrombotic material distal to the culprit lesion as a filling defect. While development of new thrombus in or near a newly deployed stent is identified as intraprocedural stent thrombosis (IPST). These angiographic complications of PCI are a product of microvascular dysfunction, myocardial edema, reperfusion injury and embolization of atherosclerotic and thrombotic material. We aim to perform the first meta-analysis to examine clinical outcomes in patients with IPTE compared to those without IPTE during PCI, including primary PCI for STEMI, urgent PCI for NSTEACS as well as elective PCI. We further aim to explore whether any particular IPTE may be associated with more adverse events.

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2. Methods

2.1. Data sources and search strategy

We searched the online databases including PubMed, Cochrane CENTRAL, EMBASE, Web of Science and CINAHL databases through December 2014 for all English language published articles, which compared patients with IPTE with non-IPTE during PCI. Our inclusion criteria were: 1) studies published in English language, 2) full length articles, 3) studies comparing IPTE patients versus those without IPTE during PCI, 4) IPTE included no reflow or slow flow, distal embolization, abrupt vessel closure, intraprocedural stent thrombosis (IPST) and new or worsened thrombus formation, and 5) reporting any of the following outcomes of interest; mortality during in-hospital, 30-day and long-term follow-up, myocardial infarction (MI), repeat revascularization, stent thrombosis and major bleeding. The following keywords were used in our search: "percutaneous coronary intervention", "no-reflow", "intraprocedural thrombotic events", "slow flow", "abrupt vessel closure", "intraprocedural stent thrombosis", "STEMI", "NSTEACS", and "distal embolization". In addition, we manually searched clinical trial databases, review articles, reference lists of all retrieved reports for potential relevant studies not found in our initial electronic database search. Two reviewers identified the studies of interest and discrepancies were resolved with other authors by consensus.

2.2. Study selection, endpoints and definitions

We used the published strengthening Meta-analysis of Observational Studies in Epidemiology (MOOSE) checklist to perform this analysis [7]. Objective assessment of the trials were done using the method specified in the Cochrane Handbook of Systematic Reviews and New Castle–Ottowa scale for case control and cohort studies [8,9]. We analyzed in-hospital, 30-day and long-term (more than 6 months) adverse events comparing IPTE versus non-IPTE during PCI. Our primary analysis compares IPTE versus non-IPTE in PCI and reports the following outcomes: mortality, MI, repeat revascularization, stent thrombosis and major bleeding. Definition of major bleeding used in each trial is detailed in supplementary table 1. We then performed a subgroup analysis of mortality in STEMI only patients comparing those who develop IPTE with non-IPTE. We also report MI events according to type of IPTE; No reflow, distal embolization (DE) and intraprocedural stent thrombosis (IPST) compared to non IPTE. Secondary analysis reports outcomes according to longest follow-up available.

2.3. Statistical analysis

Outcomes were reported as odds ratios and their respective 95% confidence intervals (CI) for each study and for the meta-analysis of all studies comparing patients who develop IPTE with non-IPTE during PCI. We assessed for heterogeneity using the Cochran Q test and the Higgins I^2 test. A Cochran's Q $p < 0.10$ and $I^2 > 50\%$ were considered significant to demonstrate heterogeneity in this analysis. Random effects model described by Der-Simonian and Laird was used for the main analysis. p-Value for interaction was calculated among subgroups and considered significant if 0.10 or less. Statistical analysis was performed with Review Manager (RevMan; Cochrane Collaboration, version 5.4) [10]. All p-values were 2-tailed with statistical significance level at 0.05, and CI was calculated to 95%.

3. Results

Our initial search identified 1257 articles. After the initial screening process, we reviewed the abstracts and the articles to identify 13 studies that met our search inclusion criteria. Two of those studies were excluded as duplicate data and overlap of the results were present [11,12] (Fig. 1). Our final analysis included 11 studies meeting search criteria comparing patients with IPTE versus non-IPTE during PCI and reporting clinical outcomes of interest [1–5,13–18]. Table 1 summarizes the

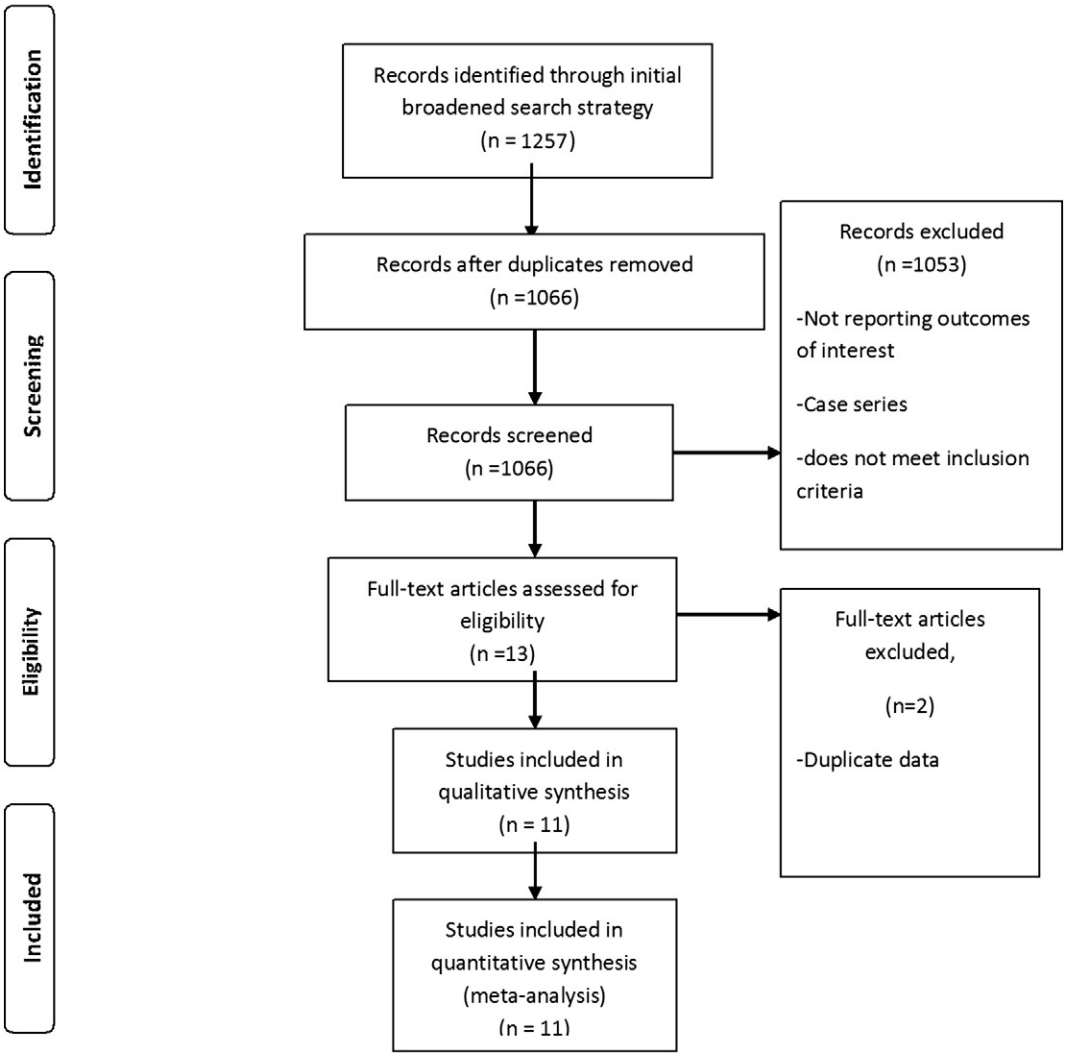

Fig. 1. Search strategy and study selection per PRISMA flow diagram.