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Original article

Short- versus standard-term dual antiplatelet therapy after percutaneous coronary intervention with drug-eluting stent implantation: A meta-analysis

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ABSTRACT

Background: Twelve months of dual antiplatelet therapy (DAPT) is recommended after percutaneous coronary intervention (PCI) with drug-eluting stent (DES) implantation. However, certain clinical scenarios may require premature discontinuation of therapy (e.g. urgent surgical procedure, major bleeding). The objective of this systematic review and meta-analysis was to investigate clinically relevant outcomes associated with a shorter duration of DAPT after PCI with DES implantation.
Methods: A systematic search of Medline and Embase (inception to December 2015) was conducted. Included were randomized controlled trials that compared 6 months (or less) of DAPT (defined as acetylsalicylic acid 75–200 mg daily and a P2Y12 inhibitor) to the standard of 12 months. Outcomes of interest included death (all-cause and cardiac), myocardial infarction (MI), definite/probable stent thrombosis, and bleeding (major and overall). An odds ratio (OR) and 95% confidence interval (CI) were calculated for each outcome using a random effects model.
Results: Six trials (five open-label, one double-blind) were included ($N = 13{,}900$). Four studies investigated 6 months of DAPT, and two studies investigated 3 months. Median follow-up was 12 months. There was no statistically significantly difference between groups regarding all-cause death (OR 0.88, 95% CI 0.64–1.20), cardiac death (OR 1.00, 95% CI 0.64–1.55), MI (OR 1.16, 95% CI 0.87–1.56), and stent thrombosis (OR 1.22, 95% CI 0.70–2.15). Both major and any bleeding were significantly decreased with shorter-term DAPT (OR 0.58, 95% CI 0.34–0.98, and OR 0.62, 95% CI 0.47–0.81, respectively).
Conclusions: Shorter duration (3–6 months) of DAPT, as compared to 12 months, was not associated with a higher risk of death, MI, or stent thrombosis, but a lower rate of major and overall bleeding.

Introduction

Percutaneous coronary intervention (PCI) is a common form of coronary revascularization for obstructive coronary artery disease (CAD). Current practice involves the implantation of a drug-eluting stent (DES), which has been demonstrated to have a lower rate of mortality, myocardial infarction (MI), definite stent thrombosis, and target-vessel revascularization compared to bare metal stents (BMS) [1,2]. However, DES possesses a higher risk of late stent thrombosis and thus requires a longer duration of dual antiplatelet therapy (DAPT) with acetylsalicylic acid (ASA) and a P2Y12 inhibitor. Until recently, the current standard of practice for patients that receive PCI with DES implantation was 12 months of DAPT [3–7]. However, certain clinical scenarios may require premature discontinuation of therapy, such as urgent surgical procedures or episodes of major bleeding. Initial registry data suggested that 3–6 months of DAPT in patients who received a DES [49–73% presented with an acute coronary syndrome (ACS)] was

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associated with a low rate of cardiovascular (CV) events that was similar to a longer duration of DAPT [8,9].

In recent years, several randomized controlled trials have been published investigating 3–6 months of DAPT, compared to 12 months, in patients who underwent PCI with DES implantation. In response, the American College of Cardiology/American Heart Association (ACC/AHA) published updated guidelines for the duration of DAPT in patients with CAD [10]. The authors continue to recommend 12 months of DAPT as the standard of practice to prevent late stent thrombosis and ischemic CV events in patients who present with an ACS and undergo PCI (regardless of stent type); however, in selected patients who develop a high risk of bleeding or experience significant overt bleeding, it may be reasonable to discontinue DAPT after 6 months. For patients with stable ischemic heart disease who undergo PCI with DES implantation, the updated guidelines recommend that patients receive 6 months of DAPT, and that a longer duration may be reasonable in selected patients who did not experience overt bleeding after 6 months, and are not at high risk of bleeding.

The new ACC/AHA recommendations represent a shift in practice; however, the studies on which these guidelines were based have been criticized for being underpowered to detect differences in clinically meaningful outcomes such as CV events, stent thrombosis, and major bleeding. Thus, the objective of this systematic review and meta-analysis was to investigate clinically relevant efficacy and safety outcomes associated with a shorter duration DAPT (6 months or less), compared to 12 months, in patients post-PCI with DES implantation.

Methods

This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [11]. A systematic search of Medline, Medline In-Progress & Other Non-Indexed Citations, and Embase from inception to December 2015 was conducted utilizing the search terms: *dual antiplatelet therapy*, *drug-eluting stent*, and *duration*. The search was limited to human participants ≥18 years of age. Included were randomized controlled trials that compared 6 months or less to 12 months of DAPT in patients who underwent PCI with DES implantation for any indication. DAPT was defined as ASA 75–200 mg daily and a P2Y12 inhibitor (clopidogrel 75 mg daily, prasugrel 60 mg daily, or ticagrelor 90 mg twice daily). Outcomes of interest included death from any cause, cardiac death, myocardial infarction (MI), definite or probable stent thrombosis, major bleeding, and any bleeding. Major bleeding was defined based on the definition used in the clinical trials. An odds ratio (OR) and 95% confidence interval (CI) were calculated for each outcome using a Mantel-Haenszel random effects model (Review Manager, version 5.3, Cochrane Collaboration, Copenhagen, Denmark). Methodological quality of the studies was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach [12]. Statistical heterogeneity was assessed using the I^2 statistic, and a value of >50% was deemed to be significantly heterogeneous. A p-value of <0.05 was considered to be statistically significant. Publication bias was assessed using a funnel plot for the outcome of MI.

Results

The search strategy identified 65 studies. A PRISMA study flow diagram is included in Fig. 1. Twenty-eight duplicate and/or post hoc analysis articles were removed. The remaining 37 citations were screened for relevance based on title and/or abstract by one author (ARB). Eight articles were identified as potentially eligible and reviewed in full by both authors. Of those, two studies were excluded due to a duration of DAPT of >12 months in the comparator group. Thus, six studies were selected for inclusion in the quantitative analysis [13–18]. One study investigated 6 versus 24 months of DAPT, but reported outcomes at 12 months; therefore, it was included [18]. A summary of the trials is included in Table 1. Five studies utilized an open-label design, and one study was double-blinded. The total population was 13,900 patients. Approximately half of the patients underwent elective PCI for stable angina or silent ischemia. Four studies investigated 6 months of DAPT, and two studies investigated 3 months.

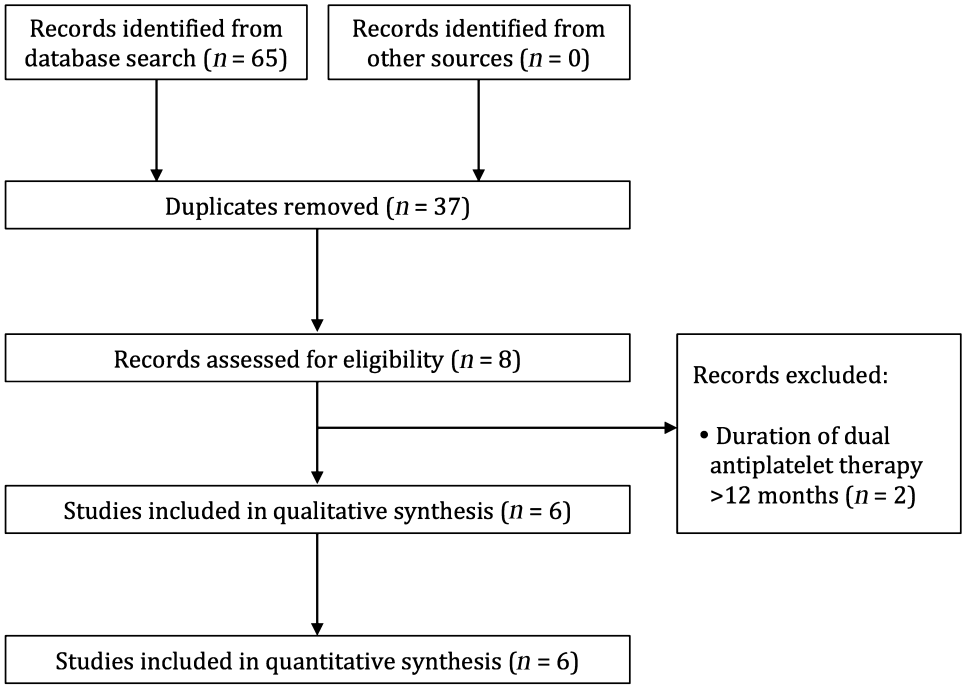

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) study flow diagram.

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