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Duration of dual antiplatelet therapy after various drug-eluting stent implantation

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ABSTRACT

Objective: To evaluate efficacy and safety of long duration dual anti-platelet therapy i.e., >12 months (L-DAPT) and short duration DAPT i.e., ≤12 months (S-DAPT) after various drug-eluting stent (DES) implantation.
Methods: We searched Medline, Embase, and Cochrane Central Register of Controlled Trials (CENTRAL) to identify randomized controlled trials (RCTs) assessing the effect of L-DAPT versus S-DAPT after sirolimus-eluting (Cypher®); paclitaxel-eluting stents (Taxus®); zotarolimus-eluting (Endeavor®) and everolimus-eluting stents (Xience V®) implantation. Odds ratio (OR) and 95% confidence intervals (CI) were calculated using random-effects models. Subgroup analyses were performed comparing two second generation DES and for RCTs comparing S-DAPT and L-DAPT.
Results: We included six RCTs that randomized 19,012 patients to S-DAPT versus L-DAPT (4638 in first generation DES; 14,374 in second generation DES; 8099 EES; 4876 in ZES). Compared with L-DAPT, S-DAPT was associated with a higher rate of myocardial infarction (MI) and stent thrombosis (ST) after first [2.65 (1.88, 3.73) and 3.85 (2.14–6.93) respectively] and a higher rate of MI after second generation DES [1.33 (1.06, 1.67)]. There were no significant differences in the rates of all cause mortality, cardiovascular (CV) mortality and stroke with L-DAPT and S-DAPT after implantation of first [0.97 (0.52, 1.81); 1.19 (0.52–2.70); and 1.12 (0.36–3.52) respectively] and second generation DES [0.93 (0.69, 1.25); 0.93 (0.63, 1.36); and 0.58 (0.19, 1.75), respectively]. On further analysis of type of second generation DES, S-DAPT continues to show a higher rate of MI and ST after EES implantation [1.54 (1.11, 2.13) and 2.68 (1.20–5.94) respectively]; however there was no significant difference in the rate of MI and ST with S-DAPT and L-DAPT after ZES implantation [1.07 (0.44, 2.61) and 1.11(0.39, 3.13), respectively].
Conclusion: 1) Compared with L-DAPT, S-DAPT was associated with a higher rate of MI without any significant difference in the rate of all cause mortality, CV mortality and stroke after first and second generation DES.
2) Rate of ST was also higher with S-DAPT compared to L-DAPT after first generation DES implantation; however, it was not significantly different after second generation DES. 3) On further subgroup analysis of second-generation stent there was no significant difference in the rate of all cause mortality, CV mortality, MI, ST and stroke with S-DAPT and L-DAPT after ZES implantation. S-DAPT may be optimal for newer generation stents particularly ZES.

1. Introduction

Dual antiplatelet therapy (DAPT) using a combination of aspirin and a P2Y12 inhibitor is used for the prevention of ischemic complications after drug-eluting stent (DES) implantation. It is estimated that more than 10 million DESs have been implanted globally; however, the optimal duration of DAPT after DES implantation still remains unclear [1]. The American Heart Association/American College of Cardiology (AHA/ACC) recommends 12 months or longer duration of DAPT, if there is a low bleeding risk [2]. On the other hand, the guidelines of

Abbreviations: CV, Cardiovascular; CI, confidence interval; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; EES, everolimus-eluting stents; L-DAPT, long duration dual antiplatelet therapy; MI, myocardial infarction; OR, odds ratio; PES, paclitaxel-eluting stent; RCT, randomized controlled trial; S-DAPT, short duration dual antiplatelet therapy; SES, sirolimus-eluting stent; ST, stent thrombosis; ZES, zotarolimus-eluting stents.

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the European Society of Cardiology (ESC) support DAPT for a *maximum of 12 months* after acute coronary syndrome (ACS), and for *6 months* after DES for non-acute coronary syndrome indications [3].

AHA/ACC recommendations on DAPT duration were primarily on the basis of observational and pathological studies involving mainly first generation DES [2]. Second generation of DES utilizes thinner stent struts, has improved polymer biocompatibility and lower drug concentration and is shown to have superior endothelialization in animal models and human autopsy studies [4,5]. Thus, short duration DAPT (S-DAPT) might be sufficient for patients with second generation DES. In this study we performed a meta-analysis of randomized control trials (RCTs) to compare the efficacy and safety of S-DAPT (i.e., ≤12 months) and long duration DAPT (L-DAPT;i.e., >12 months) in patients with first and second generations of DES. In a subgroup analysis we further compare efficacy and safety of S-DAPT and L-DAPT after most commonly used second generation DES: zotarolimus-eluting (ZES;Endeavor®) and everolimus-eluting stents (EES;Xience V®).

2. Methods

2.1. Study design

We followed the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) statement for reporting systematic reviews and meta-analyses of RCTs for the protocol of our meta-analysis [6].

2.2. Data sources and search strategy

We systematically searched PubMed, CINAHL, Cochran CENTRAL, Embase, Scopus and Web of Science databases for randomized clinical trials comparing different durations of DAPT after DES implantation. Pertinent trials were also searched in clinicaltrials.gov and in the proceedings of major international cardiology meetings (ACC, AHA, ESC, The Society for Cardiac Angiography and Interventions). DAPT was defined as aspirin plus a P2Y12 receptor inhibitor, after coronary DES implantation. S-DAPT and L-DAPT were defined as duration of DAPT after DES implantation </=12 months and >12 months respectively. All relevant combinations of following keywords "aspirin", "P2Y12 receptor inhibitor ", "clopidogrel", "Plavix", "prasugrel", "Effient", "ticagrelor", "Brilinta", "thienopyridine", "dual antiplatelet therapy", "DAPT", "drug eluting stents", "DES", "first generation DES", sirolimus-eluting stent, SES, paclitaxel eluting stent, PES, second generation DES, zotarolimus eluting stent, ZES, everolimus eluting stent, "EES", "death", "mortality", "survival", "cardiac mortality", "stent thrombosis", "Thrombolysis In Myocardial Infarction (TIMI) bleeding", stroke, myocardial infarction, "randomized controlled trial", "random", "random allocation", "double-blind", and "single-blind" were included for database search. We manually searched references of identified studies. The search period took place from 1 January 2002 to 30 June 2015. No language restrictions were applied. Studies, which did not report the numbers of events with each specific DES type, were excluded from the analysis. first generation DES included sirolimus-eluting stent

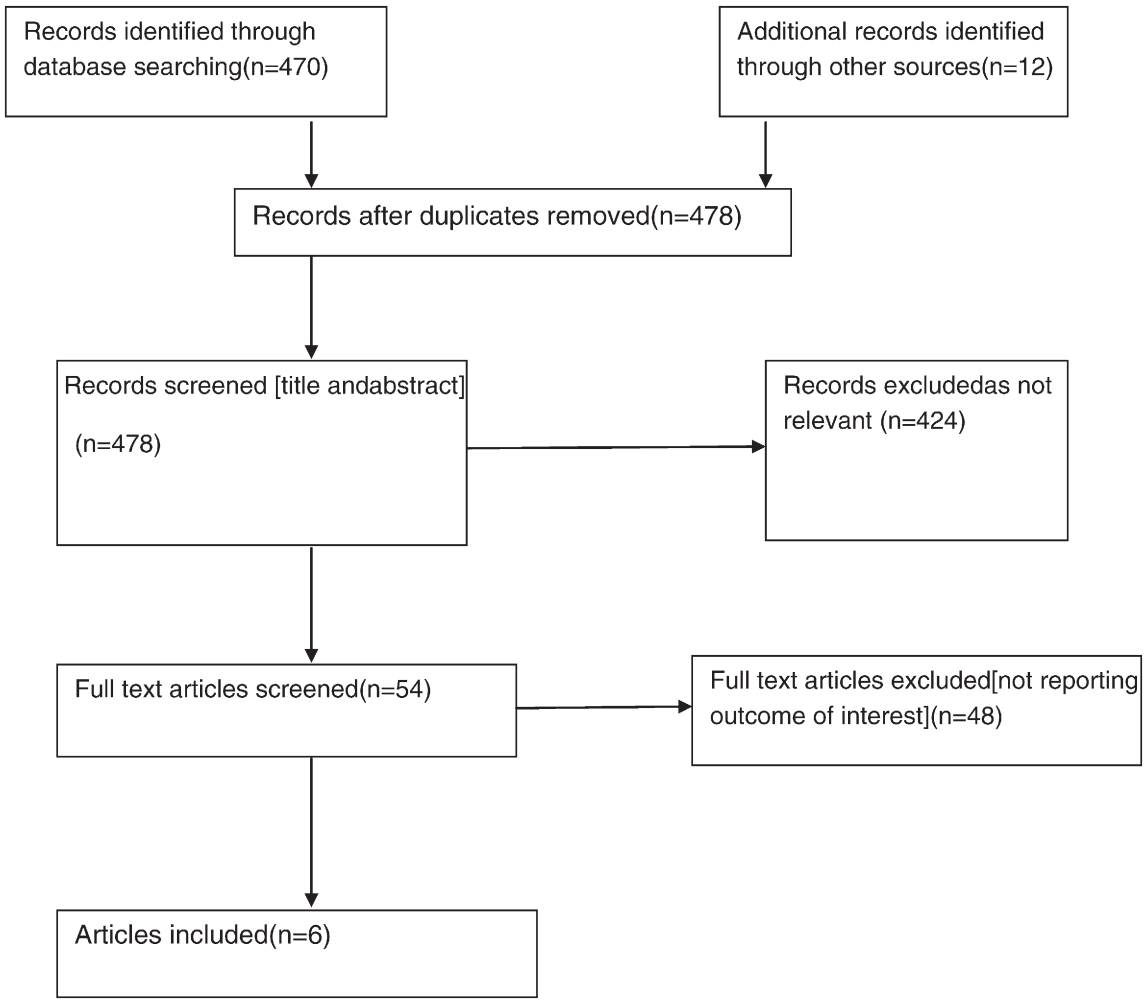

Fig. 1. The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow chart for the trial selection process.