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Comparison of drug-eluting balloon versus drug-eluting stent in patients with in-stent restenosis: Insight from randomized controlled trials

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ABSTRACT

Backgrounds: In-stent restenosis (ISR) remains an important issue even in the current drug-eluting stent (DES) era. We performed a meta-analysis to assess the clinical efficacy and safety of drug-eluting balloon (DEB) as compared with DES for the treatment of ISR.
Methods: The published literature was scanned by formal searches of electronic databases from January 2005 to February 2014. All randomized controlled trials were eligible for inclusion if they compared DEB with DES in patients with ISR.
Results: Prespecified criteria were met by 4 trials involving 803 patients. There was no significant difference in the primary endpoint (12-month major adverse cardiac events) between the 2 groups (risk ratio [RR] 1.04, P = 0.80). The incidence of death (RR 0.81, P = 0.62), myocardial infarction (RR 0.66, P = 0.29), and target lesion revascularization (RR 1.35, P = 0.12) in the DEB group was also similar to those in the DES group.
Conclusions: This meta-analysis showed that DEB was associated with comparable clinical outcomes to DES for the treatment of ISR. DEB might be the preferred interventional strategy for patients with ISR by obviating the need of additional stent layer.

1. Introduction

In-stent restenosis (ISR) remains an important issue even in the current drug-eluting stent (DES) era [1]. As compared with conventional therapeutic strategies, DES had been demonstrated to result in superior angiographic and clinical outcomes in patients suffered from ISR [2–5]. However, repeat metal scaffold implantation may further reduce the flexibility of the coronary artery and limit the repeatability of the interventional procedure. In recent years, drug-eluting balloon (DEB) has emerged as an alternative option for the treatment of ISR. Although the superiority of the DEB over the conventional balloon angioplasty (BA) in treatment of ISR had been widely demonstrated [6–9], the relative safety and efficacy of DEB versus DES remain undetermined. Recently, the results of several randomized controlled trials (RCTs) comparing DEB versus DES for ISR lesions have been reported [10–13]. However, the primary endpoints were angiographic parameters in all of these studies, and none had enough statistical power regarding the clinical outcomes [10–13]. Meta-analysis of randomized trials has the potential to increase the power and improve the precision of treatment effects and safety [14]. Therefore, we performed a meta-analysis based on all currently available RCTs to assess the clinical efficacy and safety of the DEB angioplasty as compared with the DES implantation for the treatment of ISR.

2. Methods

2.1. Study selection criteria and data extraction

We included published RCTs that compared the DEB angioplasty with the DES implantation in patients with ISR. There were no language restrictions. The published literature was scanned by a comprehensive search of electronic databases (MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials) to identify relevant articles from January 2005 to February 2014. Search terms included percutaneous coronary intervention, drug-eluting balloon, drug-coated balloon, paclitaxel-eluting balloon, paclitaxel-coated balloon, stent, and restenosis. All review articles, editorials, and Internet-based sources of information on trials of interest were also reviewed. Data abstraction was independently performed by two investigators. In addition to pertinent data on the outcomes of interest, we gathered information on study characteristics, patient characteristics, and treatment information. Disagreements were resolved by consensus. Data were managed according to the intention-to-treat principle. A flow diagram depicting the overall search strategy is demonstrated in Fig. 1.

2.2. Study endpoints

Primary endpoint in the present study was a composite of major adverse cardiac events (MACEs) at 1 year follow-up. The secondary endpoints included all-cause mortality, myocardial infarction (MI), target lesion revascularization (TLR), recurrent binary

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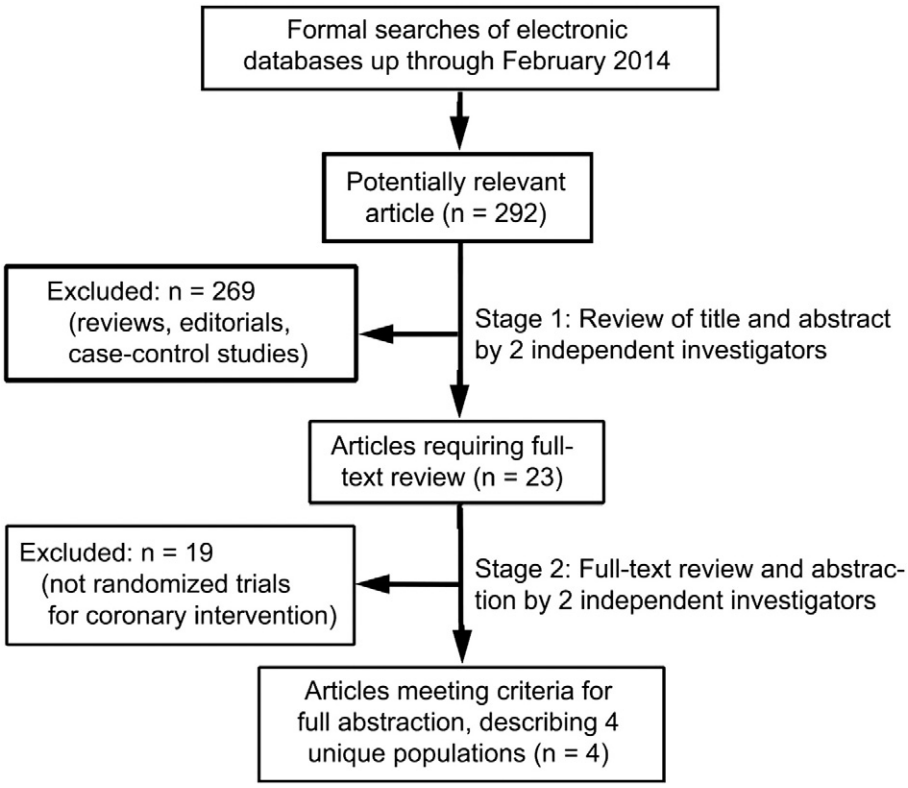

Fig. 1. Flow diagram depicting the selection of studies included in the meta-analysis.

Table 1
The event definitions used in individual trials.

Authors	Trial, published date	MI	TLR	MACE
Unverdorben et al. [10]	–, 2009	Two of the following 5 criteria were present: chest pain lasting longer than 30 min; substantial changes on ECG that were typical of acute MI; a substantial increase in the level of CK or CK-MB (at least 3 times the ULN); new, clinically significant Q waves; and chest pain leading to angiography up to 6 h after the onset of the pain, with angiographic evidence of a totally occluded vessel	Percutaneous reintervention or coronary-artery bypass grafting involving the target lesion	TLR, MI, ST, or all-cause death
Alfonso et al. [11]	RIBS V, 2013	Two of the following: prolonged (>30 min) chest pain; rise in CK levels > twice the local ULN (with abnormal MB fraction); and development of persisting ischemic ECG changes	Repeat revascularization by percutaneous coronary intervention or surgery of the target lesion	Death, MI, or TLR
Byrne et al. [12]	ISAR-DESIRE 3, 2009	Either an increase in CK-MB (or CK) ≥3 ULN and at least 50% over the most recent pre-PCI levels, or the development of new ECG changes consistent with MI and CK-MB (CK) elevation higher than the ULN at two measurements for patients undergoing DES implantation in setting of stable angina pectoris or non-ST-segment elevation acute coronary syndrome and falling or normal CK-MB (CK) levels	Any revascularisation procedure involving the target lesion because of luminal renarrowing with symptoms or objective signs of ischemia at 1 year of follow-up	Death, MI, or TLR
Xu et al. [13]	PEPCAD China ISR, 2014	Non-Q-wave MI was defined as a CK-MB or troponin-T/troponin-I increase to >3 times ULN combined with clinical signs of MI, in the absence of pathological Q waves and not related to an interventional procedure. Q-wave MI was defined as development of new pathological Q waves in 2 or more contiguous leads together with clinical signs of MI	Any repeat percutaneous coronary intervention or aortocoronary bypass surgery because of restenosis ≥ 50% associated with symptoms or objective signs of ischemia	Death, MI, or all-cause revascularization

MI = myocardial infarction; TLR = target lesion revascularization; MACE = major adverse cardiac event; ST = stent thrombosis; ULN = upper limit of normal; CK = creatine kinase; MB = myocardial band isoform; ECG = electrocardiogram.