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Percutaneous Coronary Interventions for the Treatment of Stenoses in Small Coronary Arteries

A Network Meta-Analysis

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ABSTRACT

OBJECTIVES This study evaluated the most appropriate percutaneous coronary intervention (PCI) for the treatment of stenoses in small coronary arteries.

BACKGROUND PCI in small coronary arteries is associated with an increased risk of lesion failure and restenosis.

METHODS Randomized trials comparing different PCI strategies were identified through a broad search of published reports. Primary angiographic outcome was %DS (%DS). A pairwise meta-analysis was performed by using random effects model, followed by a network meta-analysis synthesizing direct and indirect evidence.

RESULTS Overall, 19 trials were eligible, which included 5,072 patients comprising a network without closed loops among 5 identified interventions (early generation sirolimus-eluting stents [SES], paclitaxel-eluting stents [PES], drug-coated balloons [DCB], bare-metal stents [BMS], and balloon angioplasty [BA]). No dedicated trial was identified evaluating new generation drug-eluting stents. Early generation SES yielded the best angiographic results according to %DS. For %DS, SES was ranked as the most effective treatment, followed by PES (standardized mean differences [SMD]: -0.44; 95% confidence interval [CI]: -0.92 to 0.05 vs. SES) and DCB (SMD: -0.89; 95% CI: -1.53 to -0.25 vs. SES). In terms of absolute differences, SES yielded a reduction of 18% in diameter stenosis compared to DCB. SES significantly reduced the risk of target-lesion revascularization compared to PES (odds ratio [OR]: 0.39; 95% CI: 0.16 to 0.93), DCB (OR: 0.34; 95% CI: 0.10 to 0.97), BMS (OR: 0.21; 95% CI: 0.13 to 0.36), and BA (OR: 0.16; 95% CI: 0.09 to 0.29).

CONCLUSIONS Early generation SES yielded the most favorable angiographic and clinical outcomes for the treatment of stenoses in small coronary arteries. New generation DES need to be evaluated against this standard in future randomized trials. (J Am Coll Cardiol Intv 2016;9:1324–34) © 2016 by the American College of Cardiology Foundation.

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Small-vessel coronary artery disease (CAD) is common among patients undergoing percutaneous coronary intervention (PCI) and has been documented in 30% to 40% of cases (1,2). Myocardial revascularization of small vessels remains challenging owing to an increased rate of technical failure in the domain of coronary artery bypass grafting (3) and an increased risk of restenosis resulting in repeat intervention in the field of PCI (4). Although drug-eluting stents (DES) and, more recently, drug-coated balloons (DCB) have shown promising results, the optimal treatment strategy of patients undergoing PCI for small coronary arteries remains poorly defined. Current evidence derived from randomized trials is limited to relatively few and small-scale studies, and evidence from head-to-head comparisons of the available interventions is lacking. Therefore, we performed a network meta-analysis of all randomized trials to comprehensively evaluate available interventions for the treatment of small-vessel disease, to obtain more precise results, to estimate the relative effectiveness between pairs of interventions that have never been compared head-to-head, and to provide a hierarchy of treatments according to the outcomes of interest.

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METHODS

SEARCH STRATEGY. Randomized trials comparing any PCI strategy for the treatment of coronary stenoses located exclusively in vessels of small diameter were identified through a broad systematic search of PubMed, EMBASE, and Cochrane Library Central Register of Controlled Trials (CENTRAL). Clinical trial registries (ClinicalTrials.gov and Current Controlled Trials [controlled-trials.com] registries) also were scrutinized. A search algorithm that included a combination of relevant text terms and key words was used for each database (Online Appendix). We did not consider reports of trials that had been presented only at conferences when the full manuscript was not available at the time of our search (last search, August 2015). Finally, we scrutinized the reference lists of retrieved publications for other eligible studies and any relevant meta-analyses in the field. Two investigators (G.C.M.S., F.P.) scrutinized all entries for eligibility in titles and abstracts.

ELIGIBLE TRIALS AND INTERVENTIONS CONSIDERED FOR THIS REVIEW. We included randomized trials that investigated any type of PCI technique under different clinical settings for the treatment of stenoses in small coronaries. Trials with 2 or more arms of interventions were eligible. No language, year of publication, or sample size restrictions were applied. We excluded studies that allowed a mixture of interventions of interest in 1 study arm (i.e., balloon angioplasty followed by stenting based on operator discretion) and studies that were not completed at the time of our search.

We considered trials that compared 2 or more of the following PCI techniques for the treatment of coronary stenoses in small vessels: balloon angioplasty (BA), bare-metal stent (BMS), DCB, or DES with different antiproliferative drugs. For the primary and any additional analyses, we considered DES separately according to the type of antiproliferative agent. We also included in our analysis cases of PCI strategies other than those that were pre-specified that were identified through our search and were deemed eligible. We were interested mainly in PCI that used DES or DCB, because DES is considered the preferred strategy for the treatment of native coronary stenosis, and DCB has emerged as an alternative treatment for lesions in small coronary vessels and in-stent restenosis (5).

DATA COLLECTION AND OUTCOMES. Citations were independently screened and subjected to full-text review by 2 investigators (G.C.M.S., F.P.) using the predetermined selection criteria. Disagreements were resolved by consensus with a third investigator (S.W.). We extracted data that included clinical design characteristics, selection criteria, relevant population demographics and lesion characteristics, quantitative angiographic measurements, length of clinical and angiographic follow-up, and clinical outcomes of interest. We extracted outcomes of interest at the longest available follow-up time according to the intention-to-treat principle.

Because most of the clinical trials applied primary angiographic endpoints for the assessment of the efficacy of different PCI strategies, %DS (%DS) was chosen as the primary endpoint in the present study to provide sufficient precision and to arrive at a conclusive answer. It is known that PCI techniques for the treatment of small-vessel CAD have limited effect on measurable clinical outcomes and that most trials have been underpowered to detect any differences for such outcomes. Therefore, %DS is an appropriate endpoint, sensitive enough for the evaluation of angiographic effectiveness compared to binary restenosis, which is included as a secondary endpoint in our analysis. We extracted any given summary metric (mean ± SD) or median (interquartile

ABBREVIATIONS AND ACRONYMS

%DS = percent diameter stenosis
BA = balloon angioplasty
BMS = bare-metal stent(s)
CAD = coronary artery disease
DCB = drug-coated balloon(s)
DES = drug-eluting stent(s)
PCI = percutaneous coronary interventions
PES = paclitaxel-eluting stent(s)
SES = sirolimus-eluting stent(s)
TLR = target-lesion revascularization