International Journal of Cardiology 218 (2016) 126–135

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Comparison of drug-eluting balloon versus drug-eluting stent treatment of drug-eluting stent in-stent restenosis: A meta-analysis of available evidence

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ARTICLE INFO

Article history:
Received 15 April 2016
Accepted 12 May 2016
Available online 14 May 2016

Keywords:
Coronary artery disease
In-stent restenosis
Drug-eluting balloon
Drug-eluting stent

ABSTRACT

Background: In-stent restenosis (ISR) remains an important concern despite the recent advances in the drug-eluting stent (DES) technology. The introduction of drug-eluting balloons (DEB) offers a good solution to such problem.
Objectives: We performed a meta-analysis to assess the clinical efficiency and safety of DEB compared with DES in patients with DES-ISR.
Methods: A systematic search was conducted and all randomized and observational studies which compared DEB with DES in patients with DES-ISR were included. The primary outcome measure—major adverse cardiovascular events (MACE)—as well as individual events as target lesion revascularization (TLR), stent thrombosis (ST), myocardial infarction (MI), cardiac death (CD) and all-cause mortality, were analyzed.
Results: Three randomized and 4 observational studies were included with a total of 2052 patients. MACE (relative risk [RR] = 1.00, 95% confidence interval (CI) 0.68 to 1.46, P = 0.99), TLR (RR = 1.15 [CI 0.79 to 1.68], P = 0.44), ST (RR = 0.37[0.10 to 1.34], P = 0.13), MI (RR = 0.97 [0.49 to 1.91], P = 0.93) and CD (RR = 0.73 [0.22 to 2.45], P = 0.61) were not different between patients treated with DEB and with DES. However, all-cause mortality was lower in patients treated with DEB (RR = 0.45 [0.23 to 0.87, P = 0.019) and in particular when compared to only first generation DES (RR 0.33 [0.15–0.74], P = 0.007). There was no statistical evidence for publication bias.
Conclusions: The results of this meta-analysis showed that DEB and DES have similar efficacy and safety for the treatment of DES-ISR.

1. Introduction

Percutaneous coronary intervention (PCI) is the most commonly used method for myocardial revascularization in patients with coronary artery disease (CAD) [1]. However, the rate of in-stent restenosis (ISR) remains high, particularly in patients receiving bare metal stents (BMS), with almost one third of treated patients needing intervention for ISR lesions [2]. Compared to BMS, the drug-eluting stents (DES), introduced in the last decade, improved clinical outcome by reducing the rates of ISR [2]. Despite substituting the early generation of DES by new generation, thin-strut DES, with improved safety and efficacy profile [3,4], 5–10% of patients still develop ISR [5,6], a problem that is contributed to by the disease complexity [2]. Patients with ISR have been shown to have worse clinical outcome compared to those without [2,7], and their ideal treatment remains debatable [2]. Different strategies are currently in use for the treatment of ISR including conventional balloon PCI, which has recently been compared with the newly introduced drug-eluting balloon (DEB) with respect to clinical outcome [8–11]. However, the available limited evidence on the safety of the latter restricts the relevant guidelines [12,13] from suggesting DEB as the best treatment method for ISR-DES. In addition, patients presenting with DES-ISR are particularly challenging and there is still limited information on the best therapeutic strategy in this setting.

Therefore, we conducted this systematic review and meta-analysis of randomized and observational studies, to assess the clinical efficiency and safety of the two strategies: DEB compared with DES, in treating patients with DES-ISR. This is the first meta-analysis that included only DES-ISR and the outcomes of its treatment by DEB vs. DES.

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http://dx.doi.org/10.1016/j.ijcard.2016.05.040
0167-5273/

Table 1
Studies' characteristics and definition of the outcomes. AMI — acute myocardial infarction, CK — creatine kinase, SHF — systolic heart failure, NYHA — New York Heart Association, ESRD — end stage renal disease, CAG - coronary angiography.

Study (trial) year	DEB no	DES no	Inclusion criteria	Exclusion criteria	DEB type	DES type	Repeat revascularization indication	MI definition	MACE definition	TLR definition	CAG F/U	Clinical F/U
Almalla 2014	46	40	Presentation with angina pectoris, and/or positive stress test, and angiographically proven significant ISR (>50%)	AMI	SeQuence Please	Xience V 2nd stent		Presence of new Q waves in >2 contiguous ECG leads or an elevation of CK-MB at least three times normal.	Death (all) MI or TLR.	Need for TLR was determined based on significant narrowing of the lumen within the stent or the lesion including 5-mm distal or proximal to the stent (>50% angiographic diameter stenosis) in the presence of symptoms or objective signs of ischemia.	N/A	12 mo
Kufner (ISAR DESIRE 3) 2015	137	131	Ischemic symptoms or evidence of myocardial ischemia (inducible or spontaneous) in the presence of a restenosis >50% located in a native vessel DES or proximal or distal margins.	A target lesion located in the left main stem or in a coronary bypass graft; AMI within the preceding 48 h, cardiogenic shock, severe renal insufficiency, malignancies, or other comorbid conditions with life expectancy <12 months, contraindications to antiplatelet therapy, paclitaxel, stainless steel, pregnancy	SeQuent Please	Taxus Liberté	Symptoms or documented ischemia with stenosis >50% in target lesion.	Either an increase in CK-MB (or CK) ≥3 and at least 50% over the most recent pre-PCI levels, development of new ECG changes consistent with MI and CK-MB (CK) elevation at two measurements for patients undergoing	Death (all), MI or TLR	Any revascularization procedure involving the target lesion because of luminal renarrowing with symptoms or objective signs of ischemia at 1 year of follow-up	6–8 mo	36 mo
Alfonso (RIBS IV) 2015	154	155	Angina or objective evidence of ischemia and showed DES-ISR on angiography (>50% diameter stenosis)	Small vessels (<2.0 mm in diameter), very long lesions (>30 mm in length), or total occlusions. ST, very early (<1 month) DES-ISR, AMI, severe peripheral vascular disease,	SeQuent Please	Xience Prime 2nd	Symptoms or documented ischemia with stenosis >50% in target vessel.	2 of the following: prolonged (>30 min) chest pain; rise in CK levels more than twice (with abnormal MB fraction); and development of new persisting ischemic	CD, MI, or TLR	Repeat revascularization by PCI or surgery of the target lesion	6–9 mo	12 mo

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