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ORIGINAL ARTICLE

Predictors of Long-Term Outcomes After Drug-Eluting Balloon Angioplasty for Bare-Metal Stent Restenosis

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Background Clinical trials have investigated efficacy of drug-eluting balloon (DEB) angioplasty for bare-metal stent (BMS) in-stent restenosis (ISR). Few studies have investigated predictors of long-term outcomes following BMS-ISR treatment with DEB.

Methods From June 2011 to April 2015, 105 patients with 125 BMS-ISR lesions were enrolled from the Cardiovascular Atherosclerosis and Percutaneous TrAnsluminal INterventions (CAPTAIN) registry. All these lesions were treated with DEB angioplasty as final therapy. The major adverse cardiac events (MACEs) were recurrent clinically driven target lesion revascularisation (TLR), myocardial infarction, and cardiac death after DEB angioplasty.

Results After DEB angioplasty, the angiographic stenosis decreased from 84.8% ± 12.4% to 22.6% ± 10.4%. Over a mean follow-up duration of 21.7 ± 13.4 months, the rates of TLR at 1–12 months and 12–48 months were 4.8% and 4.2%, respectively. The rates of MACEs at 1–12 months and 12–48 months were 6.7% and 6.1%, respectively. Chronic haemodialysis, calcified lesion, chronic total occlusion lesion before stenting, stent with metal-to-artery ratio >16.5%, and residual stenosis >25% after DEB angioplasty were potential risk factors for MACEs in univariate analysis. After adjustment in multivariate analysis, independent predictors of long-term MACEs were identified as chronic haemodialysis, chronic total occlusion lesion before stenting, and residual stenosis >25% after DEB angioplasty.

Conclusions The long-term results of DEB angioplasty for BMS-ISR are acceptable in this real-world registry. Patient (chronic haemodialysis), lesion (chronic total occlusion) and angioplasty (residual stenosis percentage) related factors predicted long-term outcomes following BMS-ISR treatment with DEB angioplasty.

Keywords Drug-eluting balloon • Bare-metal stent • In-stent restenosis • Predictors

Introduction

Although percutaneous coronary intervention (PCI) with metallic-stent implantation is a major advancement in the management of coronary artery disease, restenosis following intervention remains a major problem in clinical practice. Approximately 20–40% of patients who have undergone PCI with bare-metal stent (BMS) implantation had in-stent restenosis (ISR) at short-term angiographic follow-up [1,2]. In-stent restenosis usually develops gradually, but it should not

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be considered a benign complication. A substantial proportion of patients with ISR can present with unstable angina or myocardial infarction (MI), leading to poorer clinical outcomes [3]. Bare-metal stent-ISR is predominantly caused by neointimal hyperplasia, with excess vascular smooth muscle cell hyperplasia and extracellular matrix deposition. Compared with plain balloon angioplasty, implantation of drug-eluting stent (DES) to treat BMS-ISR has been shown to reduce the repeat restenosis rate to 13%–20% at nine-month angiographic follow-up [2,4]. However, this stent-in-stent approach, with two or more layers of metal in coronary arteries, raised concerns about delayed arterial healing and inflammatory response, which can contribute to continuous neointimal growth, late stent thrombosis, and in-stent neoatherosclerosis, thus leading to late stent failure [5].

Drug-eluting balloon (DEB) therapy has emerged as a potentially effective treatment for ISR, and the reduction of repeat revascularisation has been demonstrated in several randomised studies, especially in patients with BMS-ISR [6–8]. Its efficacy has also been established in clinical trials [9–11]. To evaluate the long-term efficacy of DEB angioplasty for BMS-ISR across the spectrum of coronary lesions and clinical presentations in the real world, we analysed the long-term follow-up results of DEB treatment for BMS-ISR in Cardiovascular Atherosclerosis and Percutaneous TrAnsluminal INterventions (CAPTAIN) registry and identified the predictors of subsequent major adverse cardiac events (MACEs).

Materials and Methods

Patient Population

The CAPTAIN registry included consecutive patients undergoing elective or emergent PCI at a single centre whose clinical and procedural data were prospectively entered into a database [12,13]. Between June 2011 and April 2015, 105 patients with 125 BMS-ISR lesions were treated with DEB angioplasty in the CAPTAIN registry. All the patients received DEB angioplasty as first therapeutic strategy for BMS-ISR in this study. There was no patient in this cohort receiving DES or another BMS for the BMS-ISR. Patients were excluded if the target lesion was previously treated for ISR or bailout DES stenting after DEB angioplasty.

The SeQuent Please paclitaxel-coated balloon catheter (B. Braun Melsungen AG, Vascular Systems, Berlin, Germany) was used in the study. Models of BMSs used included Bx Velocity (Johnson and Johnson, Miami Lakes, FL, USA), Driver (Medtronic, Santa Rosa, CA, USA), Express (Boston Scientific, Natick, MA, USA), Integrity (Medtronic, Santa Rosa, CA, USA), Liberte (Boston Scientific, Natick, MA, USA), Multi-Link VISION (Abbott Vascular, Santa Clara, CA, USA), Omega (Boston Scientific, Natick, MA, USA), R (OrbusNeich, Hong Kong), and S7 (Medtronic, Santa Rosa, CA, USA). The metal-to-artery ratio of each stent was recorded from the manufacturer's reports. This study was conducted in accordance with the provisions of the Declaration of Helsinki and local regulations. All patients provided informed consent for the index procedure and subsequent data collection and analysis. This study was approved by the Institutional Review Board of the Chang Gung Medical Foundation.

Intervention Procedure

All the patients were pretreated with a loading dose of aspirin of 300 mg and one of two P2Y12 inhibitors, clopidogrel (300–600 mg) or ticagrelor (180 mg), before catheterisation. Heparin was administered also as an initial bolus dose, and the dose was adjusted according to the activated clotting time, with a target of 250–300 seconds. The procedures were performed according to standard techniques. In all patients, the interventional strategy and the use of adjunctive devices and pharmacotherapy were at the discretion of the operator. Predilation was performed for all ISR lesions. The length of the DEB was determined to cover both the proximal and distal stent margins. The inflation time of the DEB was more than 45 seconds. Dual antiplatelet therapy was maintained for at least one month after DEB angioplasty.

Angiographic Analysis

Coronary angiograms were obtained in multiple views after intracoronary nitrate administration. The quantitative coronary angiographic analysis was performed by two experienced interventional cardiologists and images were selected with an end-diastolic cine-frame of the most severe and non-foreshortened projection. Reference vessel diameter, minimal luminal diameter, percentage of diameter stenosis, and lesion length were measured before and after intervention. Restenosis was defined as stenosis of at least 50% of the luminal diameter.

Study Endpoints

After the index procedure, clinical follow-up was performed by telephone or clinic visit at 1, 2, 3, 6, 9, and 12 months, and every 3 months thereafter. A follow-up angiogram was obtained if patients had recurrent ischaemic symptoms and evidence of myocardial ischaemia in noninvasive stress tests. Cardiac death was defined as any death due to a cardiac cause (e.g., MI, heart failure, or fatal arrhythmia). Myocardial infarction was defined as any typical rise above the upper range limit and fall of biochemical markers of myocardial necrosis, with at least one of the following: ischaemic symptoms, development of Q waves on the ECG, and ECG changes indicative of ischaemia. Clinically driven target lesion revascularisation (TLR) was defined as any repeat PCI or bypass surgery because of recurrent ISR and clinical myocardial ischaemic symptoms or signs. We defined MACEs as composite endpoints of clinically driven TLR, myocardial infarction, and cardiac death.

Statistical Analysis

Data were prospectively collected and analysed using SPSS statistical software package (version 22.0, IBM, Armonk, New York, USA) for all statistical analyses. Continuous variables were expressed as mean ± standard deviation.

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