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Original article

Clinical outcome of treatment with or without a final kissing balloon technique for bifurcation in-stent restenosis lesions☆

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ABSTRACT

Background: The treatment strategy for in-stent restenosis (ISR) with bifurcation lesions has not been well explored. We examined the clinical outcomes between final kissing balloon technique (FKBT) after stent implantation and single-stent implantation without FKBT for bifurcation ISR lesions.
Methods: We identified 115 consecutive ISR with bifurcation lesions among 108 patients who underwent drug-eluting stent implantation. The patients were divided into the FKBT group (34 patients, 35 lesions) and the non-FKBT group (74 patients, 80 lesions).
Results: Thrombolysis in myocardial infarction flow grade of side branch was significantly greater in the patients with FKBT than those without FKBT after coronary intervention (2.80 ± 0.46 vs. 2.65 ± 0.68, $p = 0.04$), but this difference was attenuated and was no longer statistically significant at the time of follow-up (2.80 ± 0.48 vs. 2.80 ± 0.60, $p = 0.97$). During a mean follow-up of 47.8 ± 23.6 months, there were no significant differences in the incidence of major adverse cardiac events (MACE). In multivariate analysis, estimated glomerular filtration rate (hazard ratio: 0.96, 95% confidence interval: 0.92–0.99, $p = 0.02$) was an independent predictor of MACE. Contrast volume (170.71 ± 47.17 ml vs. 136.46 ± 55.56 ml, $p = 0.002$) and radiation dose (1.44 ± 1.65 Gy vs. 0.96 ± 0.46 Gy, $p = 0.02$) were significantly higher in the FKBT group than in the non-FKBT group.
Conclusions: Single-stent implantation without FKBT may be a sufficient treatment strategy for bifurcation ISR lesions.

Introduction

Although drug-eluting stents (DESs) have been widely used for coronary artery disease and have reduced the incidence of in-stent restenosis (ISR) and target lesion revascularization (TLR) compared with bare-metal stents (BMSs) [1–3], TLR after DES implantation is sometimes needed in the patients at high risk, such as those with complex lesions [1,4,5]. The current rates of restenosis after coronary stenting with BMS or first- or second-generation DES remain higher than 20% [6]. Thus, the management of the patients with ISR is challenging, and the optimal therapeutic strategy remains unclear [7]. Further, approximately 15% to 20% of percutaneous coronary interventions (PCIs) are performed to treat coronary bifurcation lesions [8,9], a complex subset of coronary lesions or jailed side-branch stenosis [10]. The management of these lesions represents a challenge associated with a lower rate of procedural success and a higher rate of restenosis when compared with procedures done for non-bifurcation lesions [11–13].

Given the above, coronary bifurcation ISR lesions are specially challenging to treat. Revascularization using a drug-coated balloon (DCB) has recently been used as a treatment strategy for bifurcation ISR lesions and may be a potential alternative in order to avoid metal layers. However, a recent clinical trial reported that the DCB did not show a significant benefit in terms of treatment for coronary bifurcation ISR when compared with the second-generation DES [14]. Thus, the optimal treatment strategy for such lesions remains debatable [14,15].

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The objective of the present study was to evaluate the clinical outcomes of final kissing balloon technique (FKBT) after DES implantation versus single-stent implantation without FKBT for coronary bifurcation ISR lesions.

Methods

Patient population

Between January 2006 and April 2014, we identified 115 consecutive ISR with bifurcation lesions among 108 patients who underwent DES implantation at Omori Medical Center, Toho University Faculty of Medicine (Tokyo, Japan). All patients were treated by DES implantation for ISR with bifurcation lesions for recurrent symptoms or the presence of ischemia. Bifurcation was defined as lesions with at least one clinically important side branch, a reference vessel diameter (RVD) with ≥2.0 mm by visual estimate, or requiring guide-wire insertion for the purpose of protection or treatment. Restenosis was defined as >50% diameter stenosis by quantitative coronary angiography (QCA) within the stent segment, including the 5-mm margins proximal and distal to the stent edge. The patients were divided into the following: (1) the FKBT group (34 patients, 35 lesions), which was defined as FKBT after main vessel stent implantation or a two-stent strategy for bifurcation ISR lesions; and (2) the non-FKBT group (74 patients, 80 lesions), which was defined as main vessel single-stent implantation without FKBT. This protocol was approved by the ethics committee of our hospital.

PCI strategy and antiplatelet therapy

Invasive coronary angiography was performed in accordance with the American College of Cardiology/American Heart Association Guidelines for Coronary Angiography [16]. All patients received 100 mg of aspirin and 75 mg of clopidogrel or 200 mg of ticlopidine before PCI. In the catheterization laboratory, intravenous unfractionated heparin (100 U/kg) was administered for anticoagulation during the procedure; it was given as a loading dose followed by additional boluses to maintain the activated clotting time between 250 and 300 s. During the period from January 2006 to February 2010, first-generation DESs, including a sirolimus-eluting stent (SES) (CYPHER; Cordis/Johnson & Johnson, Warren, NJ, USA) and a paclitaxel-eluting stent (PES) (TAXUS; Boston Scientific, Natick, MA, USA), were implanted. Implantation using second-generation DESs, including a zotarolimus-eluting stent (E-ZES) (Endeavor; Medtronic, Santa Rosa, CA, USA), an everolimus-eluting stent (EES) (XIENCE PRIME, XIENCE V, and XIENCE Xpedition; Abbott Vascular, Santa Clara, CA, USA or PROMUS, and PROMUS Element; Boston Scientific), a biolimus-eluting stent (BES) (NOBORI; Terumo, Tokyo, Japan), and a zotarolimus-eluting stent (R-ZES) (Resolute Integrity; Medtronic), was performed during the period from March 2010 to April 2014. The choices of DESs, the treatment strategy, and decision to perform FKBT were made by the operators. Complexity of PCI, including contrast volume, fluoroscopy time, or radiation dose measured by cumulative air kerma, was recorded. After PCI, all patients received aspirin 100 mg daily indefinitely and received clopidogrel 75 mg daily or ticlopidine 200 mg daily for at least 12 months.

Angiographic analysis

The patterns of restenosis were categorized into four groups according to the classifications previously described by Mehran et al. [17]. All bifurcation lesions were classified according to the Medina classification [18], and Medina classification type (1.1.1), (1.0.1), and (0.1.1) were defined as true bifurcation lesions. The widest bifurcation angle between the main vessel and side branch was measured at the angiographic projection. The blood flow of side branch was assessed pre-procedure, post-procedure, and at follow-up and was classified according to the Thrombolysis In Myocardial Infarction (TIMI) flow-grade system [19]. Coronary angiograms were analyzed using the CCIP310 system (Gadelius Medical Co., Tokyo, Japan). Diastolic frames were taken at the angle that showed the least shrinkage of the lesions; the same angle was used before and after treatment for recording the image. RVD, minimal lumen diameter (MLD), and percentage of diameter stenosis (%DS) of the main vessel were measured at baseline, post-procedure, and at follow-up, and those of side branch were also measured at baseline and post-procedure. For the main vessel, RVD was the average of the proximal and distal reference lumen diameters. For the side branch, RVD was defined as the distal reference lumen diameters. In-stent late loss was defined as post-procedure MLD minus MLD at follow-up. Post-procedure %DS of less than 30% in the main vessel was considered to be an angiographic success. Angiographic restenosis was defined as %DS >50 by QCA within the target lesion including the 5-mm margins proximal and distal to the stent edge at follow-up.

Study definitions and follow-up

Clinical follow-up was performed by office visit or telephone contact at 12 months after the procedure. Angiographic follow-up was performed at 12 months post-procedure. We analyzed TIMI flow grade of the side branch, angiographic restenosis, target lesion revascularization (TLR), target vessel revascularization (TVR), myocardial infarction (MI), cardiac death, major adverse cardiac events (MACE), including cardiac death, non-fatal MI, or TVR, and stent thrombosis. Further, the improvement rate of side branch TIMI flow grade, defined as any TIMI flow grade increase on follow-up coronary angiograms, was also assessed. TLR was defined as any repeat percutaneous intervention or surgical bypass for stenosis >50% within the stent or within the 5-mm proximal or distal to the stent edge. TVR was defined as revascularization of the target vessel. MI was defined as >2 times the upper limit of normal of creatine kinase-MB fraction and new ST-segment elevations or new Q-waves on the electrocardiogram. Stent thrombosis was defined according to the Academic Research Consortium classification [20].

Statistical analysis

Statistical analysis was performed using statistical software (SPSS version 20 IBM, Chicago, IL, USA). Continuous variables were compared between the FKBT and non-FKBT groups using paired Student's *t*-tests and are presented as means ± SD. Categorical variables are summarized as counts and percentages, and comparisons between the two groups were done using the χ^2-test or Fisher's exact test as appropriate. Cumulative MACE-free survival during the chronic phase was determined using the Kaplan–Meier method, and survival curves were compared by the log-rank test. An independent predictor of MACE was analyzed using multivariate Cox proportional hazard model after adjusting for variables in which *p*-values were <0.20 in univariate analysis. A *p*-value of <0.05 was considered to represent statistical significance.

Results

In the DES implantation for bifurcation ISR lesions, FKBT was performed in 34 patients (31.5%), and single-stent implantation without FKBT was performed in 74 patients (68.5%). The patient baseline clinical characteristics are shown in Table 1. There were

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