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Intracoronary Brachytherapy for Recurrent Drug-Eluting Stent Failure

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ABSTRACT

OBJECTIVES The study sought to report safety and long-term clinical efficacy of intravascular brachytherapy (VBT) for recurrent drug-eluting stent in-stent restenosis (DES-ISR).

BACKGROUND Recurrent DES-ISR remains a therapeutic challenge, and VBT has been used selectively in recurrent DES failure.

METHODS Patients undergoing VBT for recurrent DES-ISR were enrolled from a percutaneous coronary intervention registry. Clinical, procedural, VBT, and outcome data were collected for DES-ISR treated with radiation. Follow-up was obtained by phone call and clinic visits.

RESULTS A total of 186 patients (283 lesions) were included. Mean age was 65 ± 11 years, and 115 (61.8%) were men. Mean time to failure from last failed DES implantation was 450.65 ± 50 days. Majority (95%) had >2 episodes of target lesion revascularization (TLR). Commonest presentation of DES-ISR was unstable angina (68, 30%). All lesions were treated with balloon angioplasty followed by VBT using Beta-Cath system (Best Vascular Inc., Springfield, Virginia) with a dose of 23 to 25 Gy at 2 mm from source center. Radiation was delivered to site of ISR, without procedural adverse events, in 99% cases. Incidence of TLR was 3.3% at 6 months, 12.1% at 1 year, 19.1% at 2 years, and 20.7% at 3 years. No subacute thrombosis event was noted. One patient had late thrombosis during a 3-year follow-up.

CONCLUSIONS VBT for recurrent DES-ISR is safe, with low recurrence rates at 12 months post-procedure, and can be safely used as an effective short-term strategy. Overtime, there is a gradual attrition in patency requiring repeat intervention. (J Am Coll Cardiol Intv 2016;9:1259–65) © 2016 by the American College of Cardiology Foundation.

Coronary stents are a mainstay of therapy in percutaneous coronary intervention (PCI). Stents act as scaffolds and eliminate elastic recoil and late vessel contraction. However, stents are associated with a proliferative response with neointimal hyperplasia of smooth muscle cells that results in renarrowing of the stent lumen, a phenomenon described as in-stent restenosis (ISR) (1–3). Drug-eluting stents (DES) have reduced rate of ISR compared with bare-metal stents (BMS) (3). However, even with newer generations of DES, the hazard of DES-ISR remains 4% to 8% in first year and, thereafter, up to 2% per year (3).

Causes of DES-ISR are multifactorial and are related to stent, procedure, or patient characteristics. Mechanical and biological factors lead to neointima formation, resulting in narrowing of stent lumen. Patient-specific factors include, but are not limited to, resistance to the drug and the inflammatory reaction to the polymer. Recurrent episodes of DES-ISR are more common in patients with diabetes, chronic kidney disease, and in long, calcified and complex lesions, such as bifurcation lesions and vein grafts and chronic total occlusions (2–6).

Due to its recurrent and recalcitrant nature, DES-ISR remains a challenge (1). Conventional modalities for recurrent DES-ISR, including plain old balloon angioplasty (POBA); cutting balloons; atherectomy devices, such as excimer laser; and repeat DES. Even newer modalities such as drug-coated balloons result

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ABBREVIATIONS AND ACRONYMS

BMS = bare-metal stent(s)

DES = drug-eluting stent(s)

ISR = in-stent restenosis

MACE = major adverse cardiovascular event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

POBA = plain old balloon angioplasty

TLR = target lesion revascularization

TVR = target vascular revascularization

VBT = vascular brachytherapy

in failure rates of up to 20% within the first year of treatment (2–4,6–11). Thus, the optimal management strategy for DES-ISR remains undefined.

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Intracoronary vascular brachytherapy (VBT) inhibits cell proliferation via cell cycle inhibition. VBT was approved for clinical use in the United States for the treatment of BMS-ISR over a decade ago but falls short to treatment with DES and drug-coated balloons. However, over past years, the main indication for VBT has been recurrent DES-ISR (10,11,12,13). Logistical issues have limited use of VBT to only a few centers in the United States. Due to this, data on efficacy and safety of VBT for recurrent DES-ISR is sparse (12,13).

This study aimed to report the clinical experience of treatment of recurrent DES-ISR with VBT and to follow the outcomes up to 3 years.

METHODS

STUDY POPULATION. The study cohort was selected from an ongoing clinical PCI registry at our institution between 2004 and 2012. Patients with recurrent failure of DES were referred to our center from a wide referral base. Consecutive patients with angina and angiographic evidence of DES-ISR undergoing VBT were included. Patients presenting acutely with ST-segment elevation myocardial infarction (MI), cardiogenic shock, or angiographic evidence of stent thrombosis were excluded. Patients with <3 years of follow-up were also excluded for this analysis. All patients provided written consent for PCI and VBT procedure. This study was conducted under local Institutional Review Board approval.

BASELINE DEMOGRAPHIC, CLINICAL, AND PROCEDURAL DATA. Baseline data were collected from prospective VBT registry records, including medical history, medications, and details of previous PCI, including type and size of DES used.

All PCI procedures were performed using standard technique via femoral approach. Patients were treated with aspirin 325 mg prior to PCI and loaded with thienopyridine. During PCI, patients received anticoagulation with either bivalirudin (intravenous bolus of 0.75 mg/kg, followed by infusion at 1.75 mg/kg/h) or unfractionated heparin (intravenous bolus of 70 to 100 U/kg and additional heparin as needed) to achieve an activated clotting time of 250 to 300 seconds. Intravenous platelet glycoprotein IIB/IIIA inhibitors were used when deemed appropriate by the operator. Adjunctive mechanical devices, such as atherectomy, cutting balloons, and intravascular imaging with intravascular ultrasound, were used in selected cases. All patients received dual antiplatelet therapy for a minimum of 12 months post-procedure.

DETAILS OF VASCULAR BRACHYTHERAPY. Radiation system used in this study was the Beta-Cath system of Novoste (Best Vascular Inc., Springfield, Virginia). A 40- and 60-mm train of strontium-90/yttrium-β source was used for delivering VBT to target sites of DES-ISR. The catheter system consisted of 3 components: 1) delivery catheter; 2) transfer device; and 3) radiation source. The triple lumen rapid exchange catheter is closed end, coronary catheter used for delivering the train of radiation source, a lumen for fluid delivery and a lumen for guidewire. Prescription dose ranged from 23 to 25 Gy at 2 mm from center of the source based on vessel diameter. For large vein grafts, a dose of 25 Gy at 2 mm was applied (13). VBT was performed following conventional PCI with either POBA or cutting balloons. A BMS or DES was rarely used in combination with VBT. Coverage length of radiation therapy consisted of the treated segment with ~5 mm of segments both proximally and distally to sufficiently cover from the healthy proximal to healthy distal segments both side of the ISR lesion.

CLINICAL ENDPOINTS AND DEFINITIONS. The primary endpoint of the study was clinically driven target lesion revascularization (TLR) at 30 days and 1, 2, and 3 years of follow-up. TLR was defined as percutaneous revascularization for a stenosis within a stent or in the 5-mm segments proximal or distal to the stent. Target vessel revascularization (TVR) was defined as either percutaneous or surgical revascularization of the stented epicardial vessel. Procedural angiographic success was defined as a residual stenosis <30% with Thrombolysis In Myocardial Infarction (TIMI) flow grade 3. MI was defined per Universal definition (14). Acute coronary syndrome was defined as either MI or unstable angina arising from a de novo culprit lesion. Acute coronary syndrome presentations in the absence of biomarker elevations were defined as unstable angina. A major adverse cardiac event (MACE) was defined as composite of death, MI, and TLR. Time to failure was defined as time from DES implantation to subsequent failure treated with VBT. ISR was defined as >50% luminal stenosis within the stent or 5 mm proximal or distal to stent. Focal ISR was defined as a restenotic lesion length <10 mm, intermediate ISR as restenotic