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Research Letter

Three Time Loser or Third Time's the Charm? PCI of Recurrent Restenosis After Overlapped Drug-Eluting Stents

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Although drug-eluting stents (DES) have significantly reduced restenosis after percutaneous coronary intervention (PCI), repeat target vessel revascularization (TVR) after treatment with new-generation DES is approximately 10% at 2 years.[1] For patients who develop in-stent restenosis (ISR) after an initial DES procedure, current American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography & Interventions revascularization guidelines give a class I recommendation for use of a second DES during repeat PCI.[2] When an overlapped second DES is used to treat ISR, 10% to 20% of patients will subsequently develop recurrent restenosis, requiring a third TVR procedure.[3,4] The outcome of performing further PCI after recurrent restenosis of DES is unclear because there is a paucity of studies on this patient cohort.[4–6] The goal of this study was to evaluate longer-term outcomes of patients treated with repeated PCI for recurrent ISR after 2 DES procedures.

This was a retrospective institutional review board–approved study of 44 consecutive patients who underwent a third PCI for recurrent ISR after 2 DES procedures on the same lesion. The primary outcome was freedom from a major adverse cardiac event (MACE) defined as death, myocardial infarction (MI), stroke, or TVR. The mean follow-up was 49 ± 13 months. Event-free survival was determined by Kaplan-Meier analysis. A binary logistic regression analysis was performed to assess potential predictors of TVR at 3 years.

The study population consisted of 29 men and 15 women, aged 66 ± 13 years. Diabetes was common (22/44, 50%), and 16 (36%) patients presented with chronic kidney disease. A history of tobacco use was also common, with 5 (11%) current and 27 (61%) former smokers. Most patients had underwent coronary artery bypass graft surgery (27, 61%) and had a history of MI (28, 64%). Clinical presentations of recurrent ISR prompting the third PCI were MI in 6 (13%), unstable angina in 22 (50%), stable angina in 14 (32%), and silent ischemia in 2 (5%). Interval between the last PCI and presentation was 30 ± 34 months. Target vessel was the left anterior descending artery in 11 (25%), left circumflex artery in 10 (23%), right coronary artery in 11 (25%), saphenous vein grafts in 11 (25%), and radial artery graft in 1 (2%). Mehran ISR classes included 22 (50%) focal, 12 (27%) diffuse, 4 (9%) proliferative, and 6 (14%) total occlusion.

A third PCI was initially successful in all 44 patients. Treatment of recurrent ISR entailed additional DES in 31 (70%), bare metal stents in 3 (7%), atherectomy without stent placement in 4 (9%), and balloon angioplasty alone in 6 (14%). There were no major periprocedural complications. MACE-free survival and TVR-free survival are shown in Figure 1. TVR-free survival was 67.4% at 1 year, 34.8% at 3 years, and 27.8% at 5 years. MACE-free survival was 60.5% at 1 year, 23.1% at 3 years, and 19.2% at 5 years. Thus, within 3 years, more than 3 out of 4 patients experienced a MACE. A logistic regression analysis revealed no significant association of any clinical characteristic (such as age, sex, and diabetes) or use of additional DES with TVR at 3 years.

Our findings are consistent with those in the study by Theodoropoulos et al[5] who described "resistant" DES restenosis as recurrence of ISR after previous successful treatment of ISR. As in this study, there was a high prevalence of diabetes (62%). At 2 years, the rates of target lesion failure and MACE were 51% and 59%, respectively. The initial episode of DES restenosis was treated by a second DES in only 53%, with 21% involving new-generation DES; by contrast, all patients in this study presented with 2 overlapped DES layers, with new-generation DES in 55%.

A limitation of this study is its size. However, the relatively small number of patients reflects that recurrent ISR after multilayered DES is an infrequent event. Based on the available data, it can be estimated that approximately 1% to 2% of patients undergoing PCI will develop resistant ISR.[3–5] Although uncommon, our findings highlight the difficult challenge presented by recurrent DES restenosis when it occurs.

Keywords: drug-eluting stents; percutaneous coronary intervention; restenosis.

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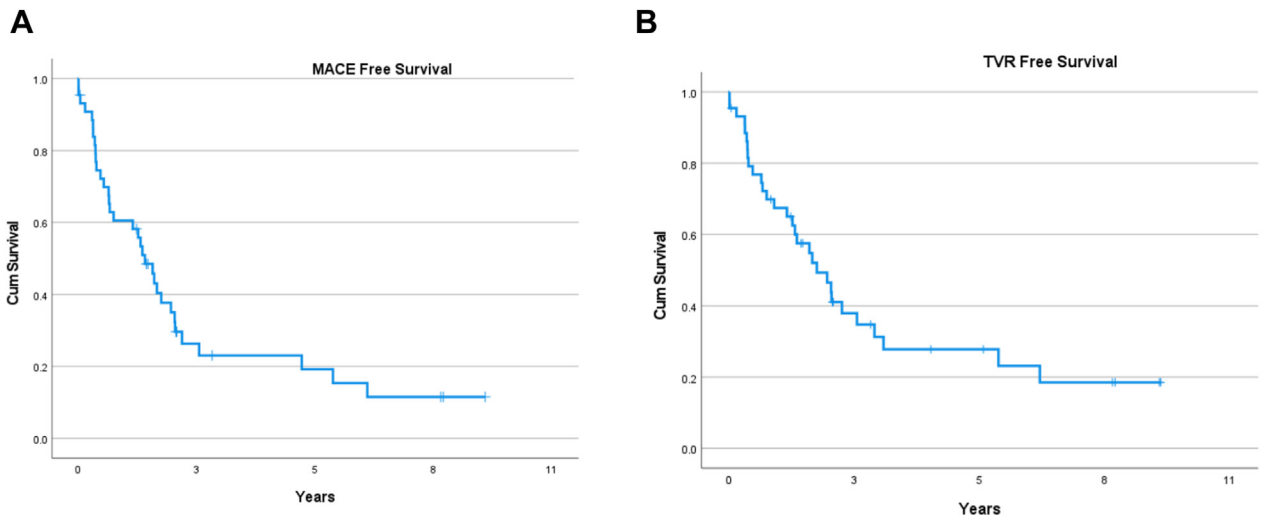

Figure 1.
Long-term outcomes after a third PCI for recurrent restenosis of 2 overlapped layers of drug-eluting stents. (**A**) MACE-free survival. (**B**) TVR-free survival. Within 3 years, more than 3 out of 4 patients experienced TVR or other MACE. MACE, major adverse cardiac event; PCI, percutaneous coronary intervention; TVR, target vessel revascularization.

Another limitation is the lack of information on intravascular imaging. Owing to the retrospective design, there was no uniform protocol for intravascular imaging because it was performed at the operator's discretion.

In conclusion, patients undergoing a third PCI to treat recurrent restenosis after 2 layers of overlapped DES exhibit a poor prognosis. Most of the patients will experience a subsequent TVR or other MACE in <3 years. Further studies are needed to assess the role of alternative therapies, such as intravascular brachytherapy or drug-eluting balloons, in the management of this perplexing problem.

Declaration of competing interest

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Ethics statement and patient consent

This retrospective study was approved by the Institutional Review Board of Thomas Jefferson University.

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