IMAGES IN CARDIOLOGY

Twelve-Year Outcome of Multi-Lesion PCI with Coronary Stenting: Very Late Non-Target Lesion Progression Amidst Durable Patency of Multiple Stents

Antonis S. Manolis, MD,[1] Nikolaos Patsouras, MD,[2] Christodoulos Flordellis, PhD[2]

[1]*Athens University School of Medicine, Athens,* [2]*Patras University School of Medicine, Patras, Greece*
E-mail: asm@otenet.gr

Abstract
A case of a 72-year-old gentleman with very late non-target lesion revascularization is presented illustrating late atherosclerosis progression despite long-term statin therapy, while at the same time long-lasting patency of drug-eluting stents implanted 12 years earlier is pictorially exemplified. *Rhythmos 2019;14(4):77-79*.

Key Words: coronary artery disease; coronary angiography; percutaneous coronary intervention; drug-eluting stent(s); non-target lesion revascularization; LDL-cholesterol; statin

Abbreviations: CAD = coronary artery disease; DES = drug-eluting stent; LAD = left anterior descending (coronary artery); LDL = low-density lipoprotein; QCA = quantitative coronary angiography; OCT = optical coherence tomography

A 72-year-old gentleman with a history of coronary artery disease (CAD) who had been submitted to percutaneous coronary intervention (PCI) with the implantation of 3 coronary stents in the left anterior descending (LAD) coronary artery 12 years earlier, presented with a 3-month history of crescendo angina. The patient had a history of hypercholesterolemia and a positive family history for CAD. Twelve years ago, for symptoms of angina and a positive thallium exercise test, he had a coronary angiogram, which revealed two critical lesions in the LAD (**Fig. 1**, arrows in **panels A & C**) and non-critical CAD in the right coronary artery. The LAD disease was successfully managed at that time with the implantation of 3 coronary drug-eluting stents (DES) (Endeavor® zotarolimus-eluting stent); a 3/12 mm DES was placed in the midLAD segment followed by a 2.75/14 mm DES and finally a 2.5/12 mm DES was placed at the distal segment of the LAD with excellent angiographic outcome (**Fig. 1**, **panels B & D**). He fared well over the ensuing 12 years, with normal exercise tests performed periodically, having remaining asymptomatic until 3 months prior to the current hospital admission. His medical

regimen included aspirin (100 mg qd), metoprolol (25 mg bid) and atorvastatin (20 mg qd). The LDL level had not been maintained consistently <70 mg/dl, but rather >70 and <100 for most of the time.
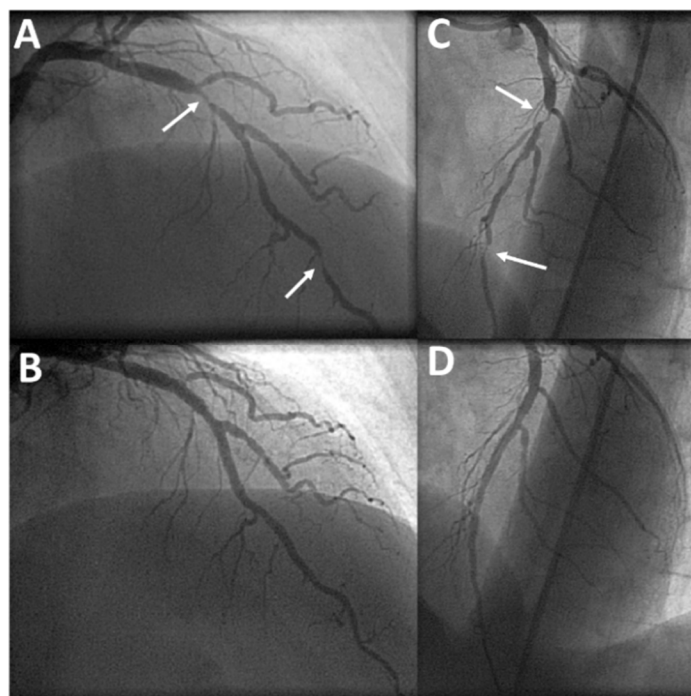

Figure 1. Right anterior oblique (RAO) views in panels A & B, left anterior oblique (LAO) views in panels C & D, all with cranial angulation

When the patient sought medical advice for his recent symptoms compatible with angina Canadian Cardiovascular Society (CCS) class II-III, a functional test with myocardial perfusion scintigraphy was promptly advised and performed. It revealed areas of ischemia with reversible perfusion defects in the anterior and septal walls of the left ventricular myocardium in the distribution areas of the LAD. The patient was subsequently scheduled to have a coronary angiogram which was performed within a week. Coronary angiography revealed a subtotal occlusion of the LAD at its proximal segment (**Fig. 2**, arrow in **panels A & C**), while all 3 stents were patent (see dotted circles with outlines of stents for respective locations in **panels B & D**). The left circumflex was free of disease and the right coronary artery had non-critical (≤50%) lesions not much different from 12 years ago, except for the origin of the posterior descending branch, which though was a very small vessel. Thus, during the same session, ad-hoc PCI of the proximal LAD lesion was performed. After pre-dilation with a 2.5/15 mm balloon, a DES was successfully implanted (everolimus-eluting stent 3.5/16 mm). After deployment of the stent and after intracoronary administration of additional nitroglycerin, a borderline

lesion between the old proximal and distal stents became apparent, which was treated with direct stenting. The final result is shown in **Fig. 3**, **panels B & D**. The procedure was completed without complications. The patient was discharged home the next day on dual-antiplatelet therapy and has fared well over the ensuing 3 months of follow-up. His hypolipidemic regimen was changed to rosuvastatin 10 mg qd plus ezetimibe 10 mg qd with the advice to maintain the LDL level <70 mg/dl.
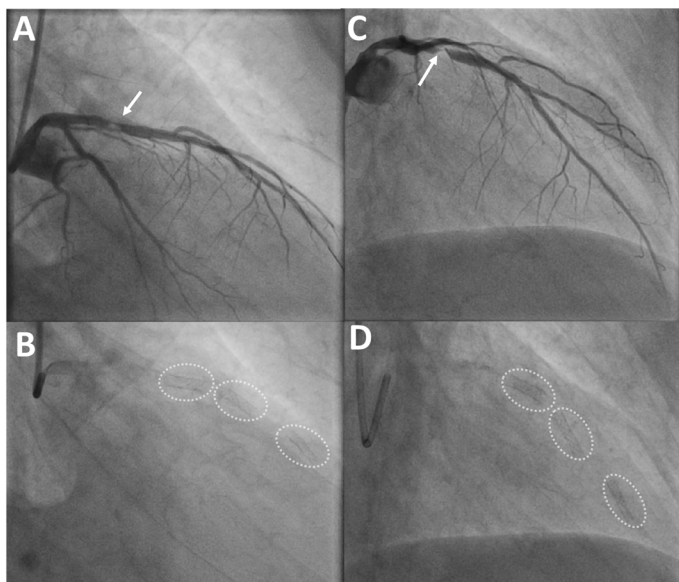
Figure 2. RAO views
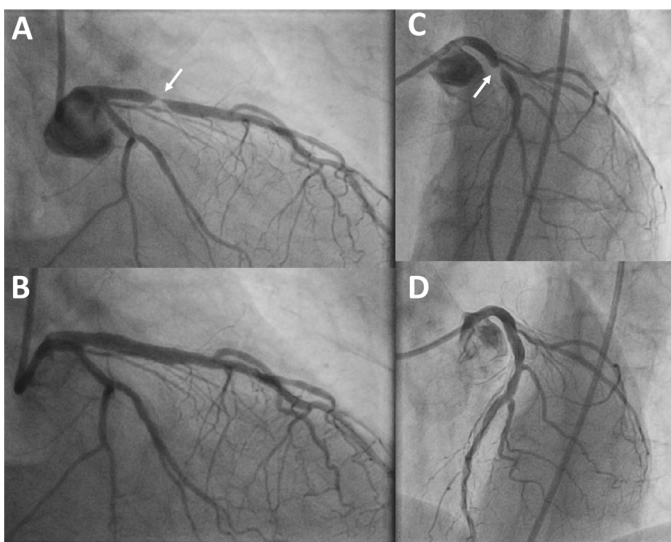
Figure 3. RAO views in panels A & B; LAO views in panels C & D with cranial angulation

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The use of drug-eluting stents (DES) has been shown to reduce intimal hyperplasia and the incidence of stent restenosis and improve prognosis after PCI. Thus, DES lead to lower rates of target lesion and target vessel revascularization. [1, 2] Despite the initial favorable outcome with the use of DES, there is a possibility for a late catch-up phenomenon, where slower intimal growth may result in a more prevalent late restenosis, which is a concern, at least with the first generation of DES.[3] The improved clinical outcome conferred by DES was confirmed in our case where 12 years later after PCI, no in-stent restenosis was detected at coronary angiography with all 3 stents found to be angiographically patent. However, non-target lesion and/or vessel status at this very late follow-up is another story. Apparently, there was native disease development and/or progression in a non-culprit atherosclerotic plaque.

Data on repeat PCI after such a long time after the index procedure are lacking, but there are some reports of new lesion PCI at shorter follow-up (5 years). According to a study evaluating the progression of new coronary lesions, among 1,214 patients, the cumulative rate of new-lesion PCI was 17.6% at 5 years.[4] Greater CAD burden (multivessel disease), low HDL, and insulin-dependent diabetes mellitus (DM) were independent predictors of progression of new culprit coronary lesions.

A study evaluated the relative clinical significance of stent-related events (in-stent restenosis or thrombosis) in target lesions compared to atherosclerotic disease progression in nontarget lesions in 2626 patients with implanted DES.[5] A total of 166 (6.3%) patients (123 men, age 65±10 years) had repeat PCI after a median period of 1 year. Angiographic evidence of target lesion in-stent restenosis or thrombosis was found in 91 patients (3.5% of the whole population), while disease progression in nontarget lesions was detected in 75 (2.8%). Interestingly, the clinical presentation at repeat PCI was different in the two groups. In the target lesion re-PCI group, 22% had stable CAD and 78% presented with ACS. In contrast, in the non-target lesion PCI group, the incidence of stable CAD was 81%, and that of ACS was 19%. Our patient, who had non-target lesion PCI, albeit many years later after the index procedure, presented with relatively stable CAD (recent onset of exertional, albeit progressive, angina).

Another study evaluated the relationship between native atherosclerosis progression of untreated coronary segments and in-stent neoatherosclerosis (NA) in 88 patients at 5 years after DES implantation with use of optical coherence tomography (OCT) for in-stent imaging and quantitative coronary angiography (QCA) for native segments.[6] In-stent NA was observed in 16% of lesions. A total of 704 non-target lesion (non-TL) segments were serially evaluated by QCA. Between baseline and 5-year follow-up, the reduction in minimal lumen diameter was significantly more pronounced in patients with NA when compared with patients without NA (P = 0.002). Similarly, non-TL revascularization was more frequent in patients with NA (78.6%) when compared with patients without NA (44.6%, P = 0.028) throughout 5 years. The authors concluded that in-stent NA is more common among patients with angiographic and clinical evidence of native atherosclerosis progression suggesting similar pathophysiological mechanisms. QCA did not demonstrate any degree of in-stent restenosis in our case in the three stented segments, but we do not have any OCT data to exclude some degree of neoatherosclerosis, which though did not result in any angiographically apparent restenosis.

Over several years, it has been commonplace practice to advise LDL lowering with use of a statin to levels <100 mg/dl and more recently to <70 mg/dl in order to slow or halt the progression of atherosclerosis in patients with CAD.[7, 8] Statins also have several pleiotropic protective effects that limit the progression of atherosclerosis.[9] Our patient had been on statin therapy and had kept his LDL cholesterol < 100 mg/dl; whether keeping it < 70 mg/dl would have had a better outcome remains a moot point. However, current data support LDL cholesterol lowering to <70 mg/dl in patients after an acute coronary syndrome. This seems achievable with use of a high-intensity statin, with the addition of ezetimibe, if needed, while the newer hypolipidemic agents (PCSK9 inhibitors) may merit consideration in some cases. [10]

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