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CASE REPORT

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A tale of two in stent restenosis in same patient: Surprising findings from optical coherence tomography

Akshyaya Pradhan[1] | **Shubhajeet Roy**[2] | **Gaurav Chaudhary**[1] | **Pravesh Vishwakarma**[1] | **Sharad Chandra**[1] | **Md. Al Hasibuzzaman**[3,4]

[1]Department of Cardiology, King George's Medical University, Lucknow, India

[2]Faculty of Medical Sciences, King George's Medical University, Lucknow, India

[3]The First Affiliated hospital of Ningbo University, Ningbo, China

[4]Institute of Nutrition and Food Science, University of Dhaka, Dhaka, Bangladesh

Correspondence
Md. Al Hasibuzzaman, Institute of Nutrition and Food Science, University of Dhaka, Suhrawardi Udyan Rd, Dhaka 1000, Bangladesh.
Email: al.hasibuzzaman.hasib@gmail.com

Key Clinical Message

The morphology of in-stent restenosis (ISR) in drug eluting stents varies greatly from that of bare metal stents. Optical coherence tomography (OCT) is a useful aid for identifying the nature of ISR and planning the treatment accordingly, which may be by intravascular lithotripsy, cutting balloon or Rotablator, which can be used upfront if OCT shows calcified neoatherosclerosis.

Abstract

Restenosis is the decrease in the diameter of the vessel lumen after the performance of percutaneous intervention (PCI), which may or may not involve the implantation of a stent. The morphology of in-stent restenosis (ISR) in drug eluting stents (DES) vary greatly from that of bare metal stents (BMS). We present the case of a 60-years-old lady, who was a follow up case of PCI of the left anterior descending artery with DES and left circumflex artery using BMS 16 years ago. Optical coherence tomography (OCT) revealed both neoatherosclerosis and neointimal hyperplasia in both DES as well as BMS. The morphology of ISR in DES differed from that of BMS. PCI and pharmacological strategies form the main stream of management in case of neointimal hyperplasia. Detection of pattern of ISR on OCT can direct the management of a particular patient, which may be by the use of adjunct devices like intravascular lithotripsy, cutting balloon and Rotablator, which can be used upfront if OCT shows calcified neoatherosclerosis.

KEYWORDS

bare metal stents, drug eluting stents, in-stent restenosis, percutaneous intervention

1 | INTRODUCTION

In-stent restenosis (ISR) has worried the interventional cardiologists since the age of evolution of bare-metal stents (BMS). The morphology of ISR in drug eluting stents (DES) varies greatly from that of BMS, with it being focal in the former while proliferative in the latter. The difference is due to the underlying pathophysiology, which is mostly neointimal hyperplasia in BMS-ISR and neoatherosclerosis in DES-ISR. Neoatherosclerosis occurs earlier in DES-ISR and has a faster progression.[1] We present the case of a 60-years-old lady, who was a follow-up case of

percutaneous intervention (PCI) of the left anterior descending artery (LAD) with DES and left circumflex artery (LCX) using BMS 16 years ago. Optical coherence tomography (OCT) revealed both neoatherosclerosis and neointimal hyperplasia in both DES as well as BMS. The morphology of ISR in DES differed from that of BMS.

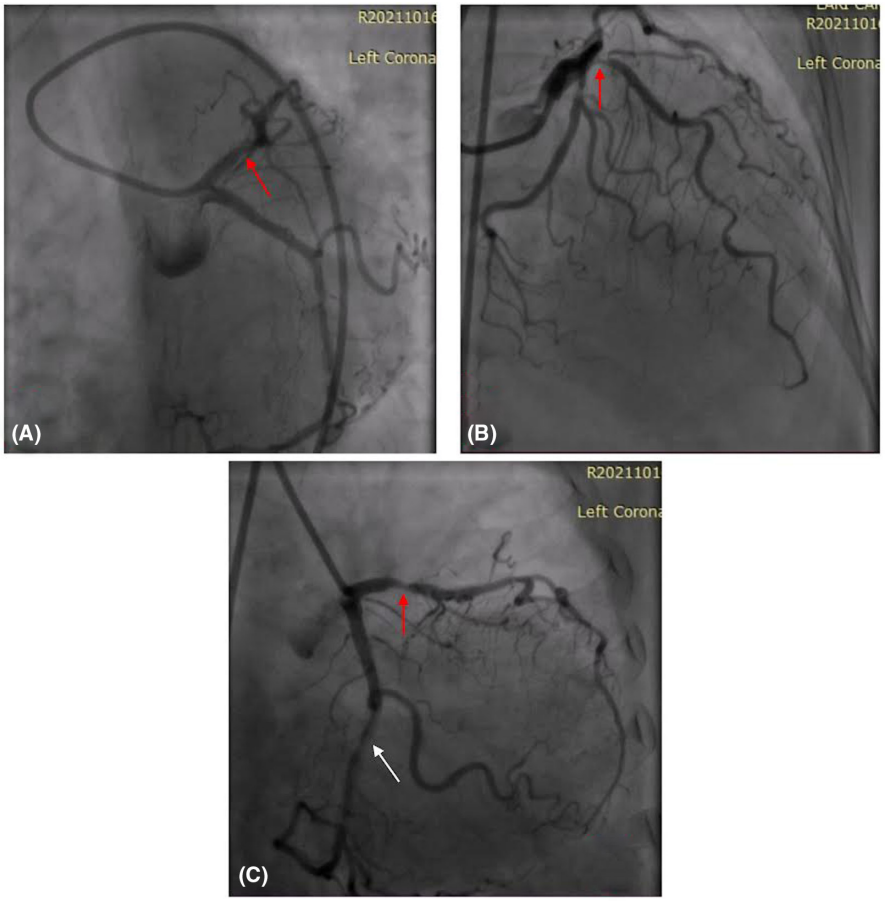

FIGURE 1 Coronary angiography: (A) Left anterior oblique view showing stenosis of the proximal part of left anterior descending artery (LAD) (in red arrow), (B) Anterioposterior cranial view showing stenosis of the proximal part of LAD artery (in red arrow), and (C) Right anterior oblique caudal view showing stenosis of the proximal part of LAD artery (in red arrow) and that of left circumflex artery (in white arrow).

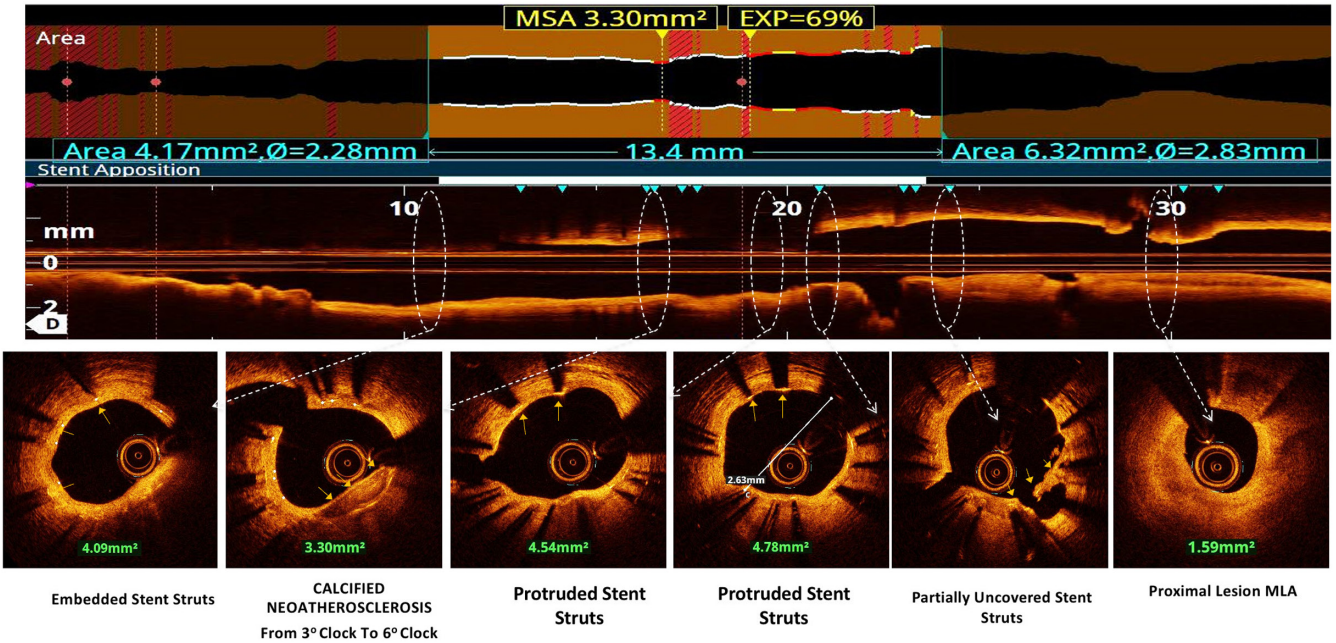

FIGURE 2 Pre percutaneous intervention optical coherence tomography of left anterior descending artery, showing embedded stent struts, calcified neoatherosclerosis, protruded stent struts, partially uncovered stent struts and proximal lesion with minimal lumen area.

2 | CASE PRESENTATION

A 60-years-old lady presented with angina on exertion and resting chest pain associated with diaphoresis for 1 month. She was a follow-up case of acute coronary syndrome and 16 years ago, she had undergone PCI of the LAD artery using CIPHER (Cordis, Santa Clara, California, US) 3×13 mm first generation DES, and of the LCX artery using Medtronic (Driver) 3×18 mm cobalt-chromium alloy coronary stent system. She was a proven case of hypertension and was not known to be diabetic. On examination, she had bilaterally clear chest and stable vitals. She had no other significant findings.

ECG revealed a normal sinus rhythm, and the ejection fraction was found to be normal (60%) upon performing a 2-D echocardiography. Coronary angiography was done, which was suggestive of a left dominant circulation. The proximal part of LAD, before stent placement had 80–90% occlusion and ISR was 50% (Figure 1A). In the LCX, before stent placement, there was 80% occlusion, and its ISR was 90% (Figure 1B). The non-dominant right coronary artery had no visible occlusions (Figure 1C).

The patient was planned for imaging guided PCI to the LAD and LCX arteries. OCT was performed before going for PCI. Within the LAD, it revealed the presence of embedded stent struts, calcified neoatherosclerosis, protruded stent struts, partially uncovered stent struts and proximal lesion with minimal lumen area (Figure 2). PCI was performed to the LAD (Figure 3), after it was predilated with a 2.5×10 mm non-compliant balloon at 16 atm pressure. Following this, a 3×26 mm overlapping everolimus eluting stent (EES) was used. Thrombolysis in myocardial infarction (TIMI) three flow was achieved post-dilation with a non-compliant balloon 3.5×10 mm at 22 atm pressure. The OCT view post PCI of the LAD artery can be seen in Figure 4. OCT performed in the LCX artery, before going for PCI, revealed the presence of lipid neoatherosclerosis, neointimal hyperplasia, calcified neoatherosclerosis, and stent underexpansion due to calcium (Figure 5). PCI was performed to the LCX artery after predilating it with a 2.5×10 mm non-compliant balloon at 16 atm pressure. A 3×40 mm EES was deployed, and TIMI 3 flow was achieved through post-dilation with a 3.5×10 mm non-compliant balloon at 20 atm pressure (Figure 6). The OCT view post PCI of the LCX artery can be seen in Figure 7.

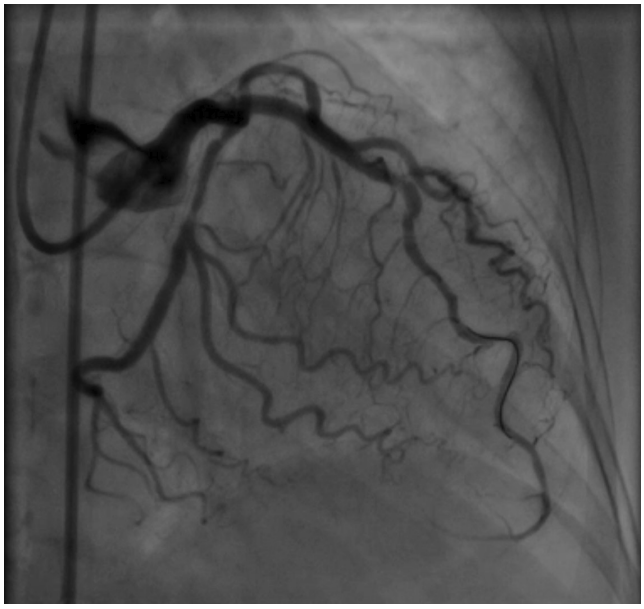

FIGURE 3 Coronary angiography showing percutaneous intervention performed to left anterior descending artery.

3 | DISCUSSION

Restenosis is the decrease in the diameter of the vessel lumen after the performance of PCI, which may or may

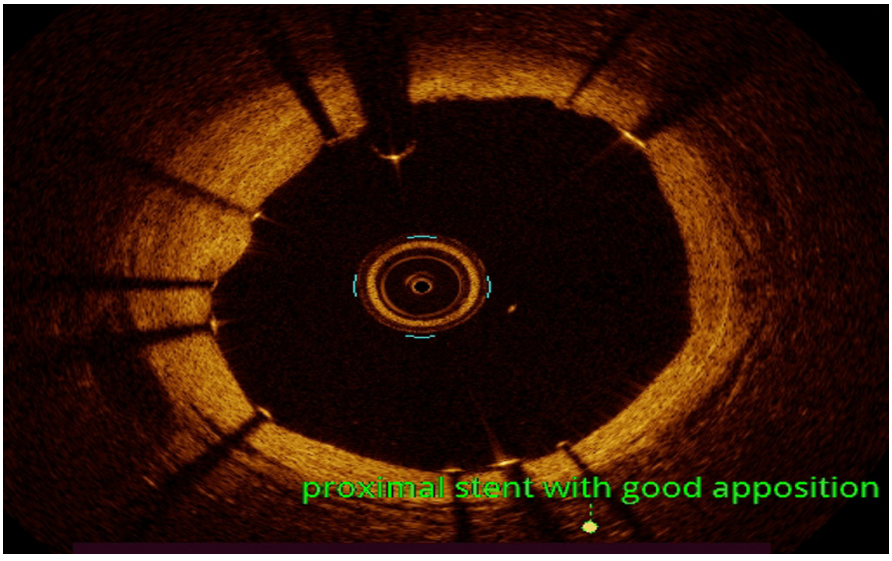

FIGURE 4 Post percutaneous intervention optical coherence tomography of left anterior descending artery, showing proximal stent with good apposition.

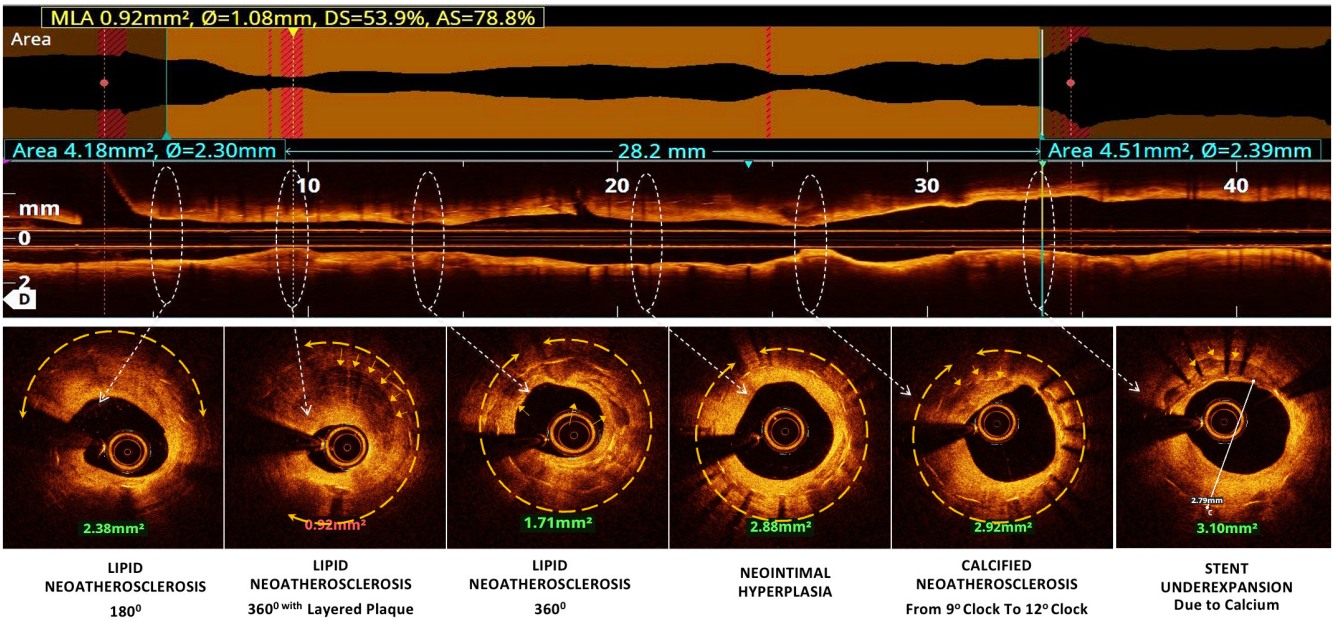

FIGURE 5 Pre percutaneous intervention optical coherence tomography of left circumflex artery, showing lipid neoatherosclerosis, neointimal hyperplasia, calcified neoatherosclerosis and stent underexpansion due to calcium.

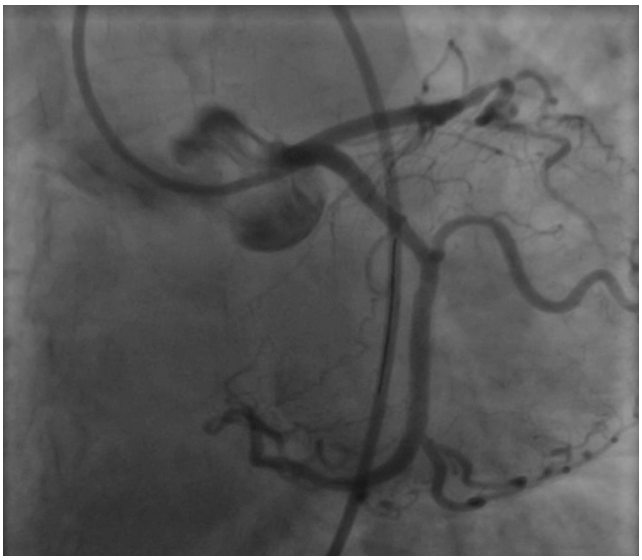

FIGURE 6 Coronary angiography showing percutaneous intervention performed to left circumflex artery.

not involve the implantation of a stent. In case of ISR, it is assessed by an excessive tissue proliferation in the lumen of the vessel, and is referred to as neointimal proliferation, or by a newly happening atherosclerotic process, or better known as neoatherosclerosis.[2] ISR has been the biggest hurdle in the path of intervention cardiologists for quite some time now. Hence, modifications in the manufacturing of stent have been a constant process, including newer generation BMS, DES, and drug-coated balloons (DCB).[3]

The advent of BMS three and a half decades back, was a revolution without doubt. But soon it was realized that ISR was a nagging trouble associated with these stents, which meant repeated revascularization, and which in turn meant increased rates of mortality and morbidity in these patients. So, stent modification efforts, which included—design and alloy manipulations, reduction of the strut thickness and addition of a polymer to elute an anti-proliferative drug.[4] Small vessel size and stent length have been found to be the most important predictors of ISR, regardless of stent type.[5] The use of DES has significantly reduced the incidence of severe neointimal proliferation, the most common cause of ISR, but what cannot be denied is the fact that the rates of ISR are still quite high in both BMS and DES. In a study by Cassese S et al., the incidence of ISR has been reported to be 30.1%, 14.6%, and 12.2% for BMS, first-generation DES, and second-generation DES, respectively.[5]

In a pooled analysis by Alfonso et al.(2014) of the RIBS V (restenosis intra-stent of bare metal stents: Paclitaxel-eluting balloon vs. Everolimus-eluting stent) and RIBS IV (restenosis intra-stent of drug-eluting stents: Paclitaxel-eluting balloon vs. Everolimus-eluting stent) multicenter randomized controlled trials, in which a comparative analysis was done of the efficacy of EES when compared to paclitaxel-eluting balloon in patients in whom BMS-ISR and DES-ISR had been used. It was seen that the outcome of the patients with DES restenosis was worse in terms of the angiographic indices (i.e., lumen diameter just after PCI and at 1 year follow-up). At 1 year clinical follow-up, the DES-ISR group treated with EES had mortality and requirement for target vessel revascularization more, as compared to the BMS-ISR group.[6–8] Most other studies also report higher rate of restenosis, earlier

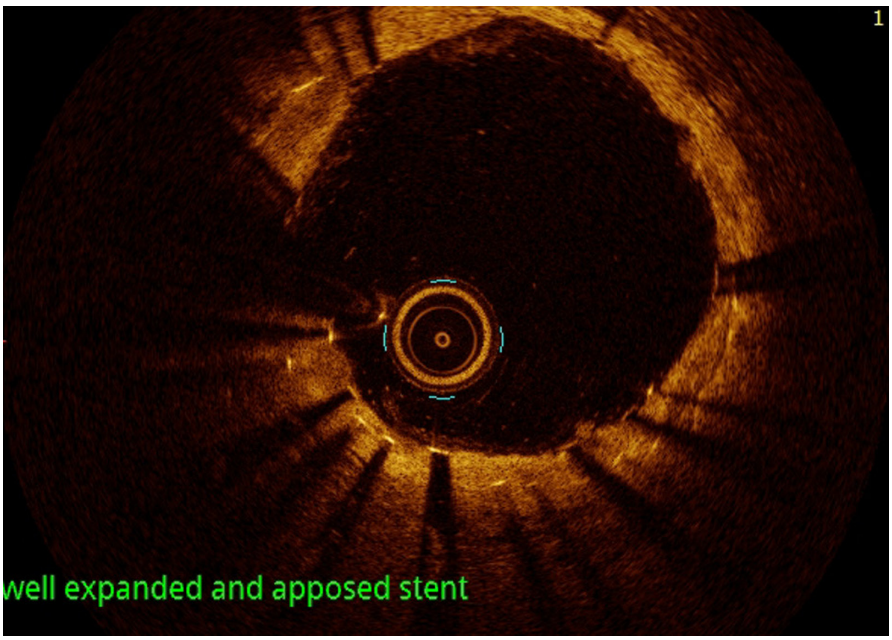

FIGURE 7 Post percutaneous intervention optical coherence tomography of left anterior descending artery, showing well expanded and apposed stent.

TABLE 1 Comparison of the OCT findings of BMS-ISR and DES-ISR, adapted from a study by Nakamura D et al.[10]

Parameter	BMS-ISR	First generation DES-ISR	Second generation DES-ISR
Minimum lumen area	Least	Maximum	Between BMS and first generation DES
Minimum stent area	Maximum	Between BMS and second generation DES	Least
Neointima thickness*	Maximum	Between BMS and second generation DES	Least
Neoatherosclerosis*	Least	Maximum	Between BMS and first generation DES
Fibrous cap thickness*	Least	Between BMS and second generation DES	Maximum
Longitudinal extension of neoatherosclerosis*	Maximum	Between BMS and second generation DES	Least

Abbreviations: BMS, bare metal stents; DES, drug eluting stents; ISR, in-stent restenosis; OCT, optical coherence tomography.
*Statistically significant difference.

presentation, and a more diffuse pattern in patients with BMS, as compared to those with DES. The reasons for the respective stent failures are very different, though. In DES, it is because of hypersensitivity to the drug or the polymer, which does not come into the scene while a BMS is in use. But another aspect which is quite notable here is the fact that treatment outcomes in BMS-ISR is more successful than that of DES-ISR. BMS-ISR can be quite successfully treated with DES or DCB, but DES-ISR shows relatively less responsiveness to another additional drug or even to radiation. The reason cited behind this, is due to the initial failure of the original drug in the DES or the inflammation already occurred due to the polymer of the failed DES. Understanding the pathology of DES-ISR is more important before managing it.[9] Table 1 shows the comparison of OCT characteristics between BMS-ISR and DES-ICR, taken from a study by Nakamura D et al. (2019).[10]

In this particular case, OCT revealed both neoatherosclerosis and neointimal hyperplasia in both DES as well as BMS. The morphology of ISR in DES differed from that of BMS.

The management of neo-atherosclerosis leading to ISR can be done by two approaches, i.e., pharmacological and device based. Pharmacological treatment includes lipid lowering strategies, antiplatelet therapy, glucagon-like peptide-1 analogues, dipeptidyl peptidase IV inhibitors, and anti-inflammatory drugs like methotrexate, colchicine, and IL-1 receptor inhibitors. Device based strategies include drug eluting balloons, DES, debulking strategies, and bioabsorbable vascular scaffolds.[11] Management of NIH includes aspirin, P2Y12, glycoprotein IIb/IIIa inhibitors, heparin, hirudin, probucol, local NO-based perivascular powder therapy and poly (diol-co-citrate) elastomeric vascular wraps, paclitaxel or EES, genetic

therapy targeting SMC migration, proliferation, and NO production, and beta vascular brachytherapy[12]

4 | CONCLUSION

OCT is a viable and effective tool for determining the nature of ISR and guiding treatment. Detection of pattern of ISR on OCT can direct the management of a particular patient, which may be by the use of adjunct devices like intravascular lithotripsy (IVL), cutting balloon and rotablator, which can be used upfront if OCT shows calcified neoatherosclerosis.

AUTHOR CONTRIBUTIONS

Akshyaya Pradhan: Investigation; visualization; writing – original draft. **Shubhajeet Roy:** Resources; software. **Gaurav Chaudhary:** Writing – original draft; writing – review and editing. **Pravesh Vishwakarma:** Formal analysis; funding acquisition. **Sharad Chandra:** Resources; writing – original draft. **Md. Al Hasibuzzaman:** Conceptualization; data curation; software; supervision.

FUNDING INFORMATION

None.

DATA AVAILABILITY STATEMENT

Not applicable.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Md. Al Hasibuzzaman https://orcid.org/0000-0003-0548-4836

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