Serial Observations of In-Stent Restenosis Treated With Drug-Coated Balloon Angioplasty by Optical Coherence Tomography and Coronary Angioscopy

A Case Series

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SUMMARY

The drug-coated balloon (DCB) is a device that is used to reduce the risk of stent re-implantation in patients with in-stent restenosis (ISR). However, imaging findings of the drug covering the neointimal plaque immediately after treatment of ISR by DCB, and during follow-up, have only been discussed in a few reports. Herein, we describe the use of optical coherence tomography (OCT) and angioscopy to evaluate ISR before and after treatment with DCB, and during the follow-up period in 3 patients. The patients developed critical ISR during the follow-up period after drug-eluting stent (DES) implantation. The patients included a 70-year-old woman, a 70-year-old man, and an 80-year-old man. These imaging modalities provided data about the various etiologies of ISR, and about the efficacy of DCB angioplasty. Based on the findings of the intracoronary images in these 3 cases, we concluded that DCB might not only inhibit neointimal proliferation, but also reduce neointimal volume and lead to changes in in-stent neointimal morphology. (Int Heart J 2017; 58: 134-139)

Key words: High intensity coverage, Spotty bright lesion, Neointima volume reduction

T he drug-coated balloon (DCB) is a device that is used to reduce the risk of stent re-implantation in patients with in-stent restenosis (ISR). However, imaging findings of the drug covering the neointimal plaque immediately after treatment of ISR by DCB, and during follow-up, have only been described in a few reports. Herein, we report the use of coronary angioscopy and OCT to confirm drug coating of neointimal plaque at the ISR lesion after paclitaxel DCB angioplasty at baseline and during follow-up.

CASE REPORTS

Case 1: A 70-year-old woman underwent implantation of a drug-eluting stent (DES) (PROMUS element 3.0/32 mm, Boston Scientific Corp, Marlborough, USA) in the proximal left anterior descending artery (LAD). After 1 year, she had recurrent angina pectoris, and coronary angiography was performed, which revealed critical ISR of the proximal LAD. The target lesion was dilated with a scoring balloon at 10 atm (Scoreflex 3.0/15 mm, Orbus Neich Medical K.K., Hong Kong, China), following which the balloon was dilated with a 3.0/30 mm DCB system (SeQuent Please, B. Braun, Melsungen, Germany) at 8 atm. Eight-month follow-up coronary angiography demonstrated no ISR after DCB treatment (Figure 1A). OCT imaging before PCI revealed homogenous neointimal restenosis, with a minimum lumen area (MLA) of 0.57 mm². OCT imaging after DCB treatment demonstrated disruption after plain old balloon angioplasty (POBA) and high-intensity spotty coverage; the MLA was enlarged to 4.61 mm². Coronary angioscopy imaging after DCB demonstrated grade 3 neointimal coverage and a spotty bright lesion. OCT imaging at follow-up revealed homogenous neointimal and late lumen enlargement (MLA = 5.32 mm²), and coronary angioscopy imaging demonstrated grade 3 neointimal coverage and disappearance of the spotty bright lesion (Figures 1B, 1C).

Case 2: A 70-year-old man underwent implantation of a DES (PROMUS element 3.0/20 mm, Boston Scientific Corp, Marlborough, USA) in the proximal right coronary artery (RCA). Nine-month follow-up coronary angiography demonstrated critical ISR in the proximal RCA. The target lesion was dilated with a non-compliant balloon at 14 atm (NC Quantum apex 3.5/12 mm, Boston Scientific Corp) and then dilated with a 3.5/15 mm DCB system at 8 atm (SeQuent Please, B. Braun, Melsungen, Germany and NIPRO Corporation, Osaka, Japan). Nine-month follow-up coronary angiography demonstrated critical ISR in the proximal RCA. The target lesion was dilated with a non-compliant balloon at 14 atm (NC Quantum apex 3.5/12 mm, Boston Scientific Corp) and then dilated with a 3.5/15 mm DCB system at 8 atm (SeQuent Please, B. Braun, Melsungen, Germany and NIPRO Corporation, Osaka, Japan). Nine-month follow-up coronary angiography demonstrated no ISR (Figure 2A). OCT imaging before PCI revealed layered neointimal restenosis with an MLA of 1.28 mm². OCT imaging after DCB treatment demonstrated disruption after POBA and high-intensity spotty coverage; the MLA was enlarged to...
Figure 1. Coronary angiography and intravascular imaging findings in case 1. A: Coronary angiography showed in-stent (drug eluting stent) restenosis (ISR) at the proximal left anterior descending artery before drug-coated balloon (DCB) angioplasty. Follow-up coronary angiography demonstrated no ISR after DCB angioplasty. B: Optical coherence tomography (OCT) images of coronary in-stent restenosis with a drug-coated balloon (DCB) angioplasty. Pre DCB angioplasty, OCT revealed a homogenous neointima. After DCB angioplasty, OCT demonstrated disruption and high-intensity spotty coverage. Follow-up OCT revealed a homogenous neointima and sufficient lumen area, and high-intensity spotty coverage were disappeared. C: Coronary angioscopy imaging after drug-coated balloon (DCB) angioplasty demonstrated grade 3 neointimal coverage and a spotty bright lesion. Follow-up coronary angioscopy imaging demonstrated grade 3 neointimal coverage and disappearance of the spotty bright lesion.
Figure 2. Coronary angiography and intravascular imaging findings in case 2. A: Coronary angiography showed in-stent (drug eluting stent) restenosis (ISR) at the proximal right coronary artery before drug coated balloon (DCB) angioplasty. Follow-up coronary angiography demonstrated no ISR after DCB angioplasty. B: Optical coherence tomography (OCT) images of coronary in-stent restenosis with a drug-coated balloon (DCB) angioplasty. Pre DCB angioplasty, OCT revealed a layered neointima. After DCB angioplasty, OCT demonstrated disruption and high-intensity spotty coverage. Follow-up OCT revealed a homogenous neointima and sufficient lumen area, and high-intensity spotty coverage were disappeared. C: Coronary angioscopy imaging after drug-coated balloon (DCB) angioplasty demonstrated grade 3 neointimal coverage and a spotty bright lesion. Follow-up coronary angioscopy imaging demonstrated grade 2 neointimal coverage and disappearance of the spotty bright lesion.
**Figure 3.** Coronary angiography and intravascular imaging findings in case 3. A: Coronary angiography showed in-stent (drug eluting stent) restenosis (ISR) at the proximal right coronary artery before drug coated balloon (DCB) angioplasty. Follow-up coronary angiography demonstrated no ISR after DCB angioplasty. B: Optical coherence tomography (OCT) images of coronary in-stent restenosis with a drug-coated balloon (DCB) angioplasty. Pre DCB angioplasty, OCT revealed a heterogeneous neointima. After DCB angioplasty, OCT demonstrated disruption and high-intensity spotty coverage. Follow-up OCT revealed a homogenous neointima and sufficient lumen area, and high-intensity spotty coverage were disappeared. C: Coronary angioscopy imaging after drug-coated balloon (DCB) angioplasty demonstrated grade 3 neointimal coverage and a spotty bright lesion. Follow-up coronary angioscopy imaging demonstrated grade 3 neointimal coverage and disappearance of the spotty bright lesion.
5.02 mm². Coronary angiography imaging after DCB demonstrated grade 3 neointimal coverage and a spotty bright lesion. OCT imaging at follow-up revealed a homogenous neointima with an MLA of 4.65 mm², and coronary angiography imaging demonstrated grade 2 neointimal coverage and disappearance of the spotty bright lesion (Figures 2B, 2C).

Case 3: An 80-year-old man underwent implantation of a DES (PROMUS element 3.0/24 mm, Boston Scientific Corp, Marlborough, USA) in the proximal RCA. One-year follow-up coronary angiography demonstrated critical ISR in the proximal RCA. The target lesion was dilated with a scoring balloon at 14 atm (Lacrosse NSE 3.5/13 mm, Goodman Company, Ltd., Nagoya, Japan). After that, it was dilated with a 3.5/26 mm DCB system (SeQuent Please, B. Braun, Melsungen, Germany) at 7 atm. Seven-month follow-up coronary angiography demonstrated no ISR after DCB treatment (Figure 3A). OCT imaging before PCI revealed heterogeneous neointimal restenosis with MLA of 0.76 mm². OCT imaging after DCB treatment demonstrated disruption at follow-up and high-intensity spotty coverage, and MLA was enlarged to 5.14 mm². Coronary angiography imaging after DCB demonstrated grade 3 neointimal coverage and a spotty bright lesion. OCT imaging at follow-up revealed homogenous neointimal and late lumen enlargement (MLA = 5.68 mm²), and coronary angiography imaging demonstrated grade 3 neointimal coverage and disappearance of the spotty bright lesion. (Figures 3B, 3C).

In these 3 cases, OCT (Dragonfly JP image catheter, St. Jude Medical, Westford, MA, USA) was performed to evaluate ISR before and after DCB and during follow-up. Angioscopy was performed with VISIBLE Fiber (FT-203F; Fiber Tech Co. Ltd., Tokyo), a fiber imaging system, and a console (Inter-ttec Medicals Co. Ltd., Osaka, Japan) to evaluate ISR after DCB, and at follow-up.

Discussion
Our case series showed neointimal plaque volume reduction after DCB angioplasty for ISR lesions. Recent case studies reported OCT and angioscopic findings before and after DCB, however, serial imaging has not been reported. To the best of our knowledge, this is the first report of post DCB assessment by both OCT and angioscopy in the immediate postoperative period and during follow-up.

OCT imaging before PCI revealed various neointimal morphologies, such as homogenous, heterogeneous, and layered patterns. A previous study reported various OCT patterns of the restenotic tissue structure as follows: layered pattern in 52%, homogeneous pattern in 28%, and heterogeneous pattern in 20%. It showed the presence of neointimal materials with different optical properties, suggesting that “restenosis” might be composed of different tissues.40

After DCB, OCT imaging demonstrated high-intensity superficial regions of the intimal tissue, and uncovered lesions due to disruption of the neointimal surface after conventional balloon angioplasty. Sakamoto, et al previously reported similar OCT imaging findings.37 The high-intensity superficial regions are thought to represent an iopromide/paclitaxel mixture. At follow-up, OCT imaging revealed further suppression of neointimal proliferation (MLA in case 1 decreased from 4.61 mm² to 5.32 mm², in case 2 from 5.02 mm² to 4.65 mm², and in case 3 from 5.14 mm² to 5.68 mm²). The uncovered lesions detected by OCT imaging after treatment were not associated with further restenosis after DCB. Furthermore, the morphology of the neointima changed to the homogenous pattern (Figures 1B, 2B, 3B). Previous studies reported OCT-documented late vessel healing and enlargement after DCB angioplasty.1,4 In animal models, paclitaxel-eluting stent exhibited greater neointimal area and medial necrosis, due to a reduction in endothelial and smooth muscle cells, at follow-up.7,8 Similar mechanisms may underlie late vessel healing and enlargement after DCB angioplasty in human coronary arteries. Angioscopic imaging after DCB demonstrated spotty bright lesions without red thrombus. Yoneyama, et al similarly reported visible white granular materials on the covered neointimal plaque.3 At follow-up, angioscopic imaging revealed grade 2-3 neointimal coverage without red thrombus and yellow-colored plaque (Figures 1C, 2C, 3C). The yellow color of the plaque is closely related to degenerated plaque or atheroma and is associated with unstable coronary syndromes.8,9 To the best of our knowledge, no angioscopic findings after DCB angioplasty at follow-up have been reported until now, so this is the first report of angioscopic findings indicating the stabilization of neointima in the chronic period after DCB angioplasty.

To sum up, DCB treatment may suppress neointimal proliferation regardless of incomplete high-intensity coverage, and may lead to changes in neointimal morphology assessed by OCT. On angioscopy, red thrombus and yellow plaques were not found immediately after DCB treatment or during follow-up. Our case series indicated the neointimal volume reduction effect of DCB on ISR lesions. Large clinical trials are required to confirm the findings in our case series.

Conclusion: We observed intracoronary images in 3 patients, and concluded that DCB might not only inhibit proliferation of neointima, but may also reduce neointimal volume and lead to changes in in-stent neointimal morphology.

Disclosure
The authors report no financial relationships or conflicts of interest regarding the content herein.

References

