Drug-eluting stents or balloon angioplasty for drug-eluting stent-associated restenosis:
An observational follow-up study of first-time versus repeated restenosis

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Background: The treatment of patients with repeated drug-eluting stent–in stent restenosis (DES-ISR) remains a challenge and a burdensome clinical problem.

Methods: Over a 3-year period, 130 lesions in 123 patients who underwent target lesion revascularization (TLR) for DES restenosis were included in the study. They were classified into two main groups: the first group having first-time DES-ISR (n = 84), and the second group having rerestenosis of DES-treated DES-ISR (n = 39). Further classification according to the treatment strategy yielded four subgroups: balloon angioplasty (BA) in first-time DES-ISR (n = 66), re-DES in the same group (n = 22), BA in rerestenosis of DES-treated DES-ISR (n = 30), and re-DES in the same group (n = 10). Angiographic follow-up was planned at 1 year, and clinical follow-up for re-TLR up to 2 years later.

Results: The mean duration of clinical follow-up was 24.8 ± 9.7 months. The angiographic follow-up data were obtained for 108 patients (87.8%) at 1 year. Among patients treated for first-time DES-ISR, late lumen loss (0.65 ± 0.83 mm and 1.02 ± 0.52 mm, p = 0.02) and binary restenosis rates (25% and 49.1%, p = 0.05) were significantly less in those undergoing re-DES compared with BA. This benefit was not evident in patients having rerestenosis of DES-treated DES-ISR. Re-TLR at 2 years was significantly less in the re-DES group compared with BA (log rank p = 0.038) in first-time DES-ISR patients, while no significant difference (log rank p = 0.58) was observed in those having rerestenosis of DES-treated DES-ISR.

Conclusion: While a strategy of re-DES would be better than BA in first-time DES-ISR, this could not be extrapolated to rerestenosis cases.

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Keywords: Balloon angioplasty, Drug-eluting stents, In-stent restenosis, Rerestenosis
Introduction

Since its introduction in the late 1970s, one of the major drawbacks of percutaneous coronary intervention (PCI) is restenosis [1]. The introduction of intravascular stents was seen as a solution to this problem; however, rates of restenosis remained significantly high, giving rise to a new dilemma—in-stent restenosis (ISR).

The introduction of drug-eluting stents (DESs) was seen as a solution to this problem, and the various technologies and materials used in their manufacturing have succeeded to considerably reduce the incidence of ISR. However, this early enthusiasm led to increased use of DESs in a diverse range of complex coronary lesions, leading to a resurge in the rates of ISR [2,3]. Furthermore, problems arising from the polymer or the drug-release kinetics, in the early generations, have hampered their antirestenosis efficacy [4].

DES-associated restenosis remains a problematic issue despite the major innovations in the stent design and components. According to the most recent guidelines [5], DESs or drug-coated balloons are recommended for the treatment of DES-associated restenosis.

Nevertheless, data about the treatment of DES-associated restenosis remain sparse and conflicting. Some questions are still to be answered like whether the same or different type of DES should be used in cases of restenosis and what is the best treatment strategy for DES rerestenosis? Does balloon angioplasty (BA) play a role in such cases?

In an attempt to tackle this issue, we present an observational follow-up study comparing DESs with plain BA in the treatment of two groups of patients; those with first-time DES-ISR and the other was a group of patients with rerestenosis of DES-treated DES-ISR.

Materials and methods

Study design

This represents a single-center retrospective observational study according to the institutional protocols adopted at Kokura Memorial Hospital, Kitakyushu, Japan. The data from consecutive patients with DES-ISR were prospectively collected and retrospectively analyzed in the departmental electronic patient information system. The study was performed according to the provisions of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board and Ethics Committee. Informed consent was obtained from all patients.

Study population

Over a 3-year period, 123 consecutive patients with 130 lesions undergoing TLR for DES restenosis were included in the study. Among those, 84 patients (90 lesions) had first-time DES-ISR, while 39 patients (40 lesions) had repeated restenosis of DES used to treat previous DES-ISR, i.e., rerestenosis subtending two layers of DESs (Fig. 1). Follow-up coronary angiography was performed in 108 patients (87.7%) at 1 year, according to the institutional protocols. Clinical follow-up data in the form of subsequent re-TLR was scheduled up to 2 years later.

PCI and procedural management

A bolus of 100 IU/kg of heparin was administered after insertion of the sheath and titrated to maintain an activated clotting time >250 seconds throughout the procedure. PCI was performed either with BA or with restenting by a different DES according to the strategy adopted by Kokura Hospital at that time. The selection of the device to treat ISR was left to the operator’s discretion. All patients received aspirin 100 mg indefinitely, clopidgrel 75 mg/d for at least 12 months, and other cardiac medications according to the clinical condition.

End-points and definitions

Both angiographic follow-up scheduled at 1 year and clinical follow-up for re-TLR at 2 years were end-points for the study. TLR was defined as first-time revascularization involving the target DES-ISR lesions or within 5 mm from the stent edges. Re-TLR refers to a second-time revascularization for DES re-restenosis (i.e., restenosis subtending 2 layers of DESs). Angiographic patterns of restenosis, previously reported by Mehran et al. [6], were used to classify in-stent restenosis into four broad types: (1) focal ISR <10 mm length; (2) diffuse ISR >10 mm within the stent borders; (3) proliferative ISR >10 mm beyond the stent.
Quantitative coronary angiography

Quantitative coronary angiography was performed pre- and postintervention, as well as 1 year after the procedure (latter was available for only 87.7% of patients). Quantitative angiography was performed using a computer-assisted, dedicated software package (CMS-MEDIS Medical Imaging System, Leiden, The Netherlands).

Table 1. Baseline patients’ clinical characteristics.

|                     | First-time DES-ISR | Rerestenosis of DES-treated ISR | p (overall) |
|---------------------|--------------------|---------------------------------|------------|
|                     | BA (n = 62)        | Re-DES (n = 22)                 | p          |
| Age (y)             |                |                                 |            |
| Male                | 70.9 ± 9.8       | 68.1 ± 5.8                      | NS         |
| Hypertension        | 48 (77.4)        | 18 (81.8)                       | NS         |
| Dyslipidemia        | 57 (91.9)        | 20 (90.9)                       | NS         |
| Diabetes mellitus   | 42 (67.7)        | 16 (72.7)                       | NS         |
| DM on insulin       | 40 (64.5)        | 13 (59.1)                       | NS         |
| Current smoking     | 10 (16.1)        | 3 (13.6)                        | NS         |
| Prior MI            | 13 (21)          | 2 (9.1)                         | NS         |
| Prior CABG          | 29 (46.8)        | 10 (45.5)                       | NS         |
| Prior HF            | 4 (6.5)          | 1 (4.5)                         | NS         |
| PVD                 | 9 (14.5)         | 5 (22.7)                        | NS         |
| eGFR < 60           | 17 (27.4)        | 5 (22.7)                        | NS         |
| EF (%)              | 22 (35.5)        | 8 (36.4)                        | NS         |
|                     |                |                                 |            |
|                     | BA (n = 30)      | Re-DES (n = 9)                  | p          |
| Age (y)             |                |                                 |            |
| Male                | 69.7 ± 9.5       | 74.7 ± 6.3                      | NS         |
| Hypertension        | 27 (90)          | 8 (88.9)                        | NS         |
| Dyslipidemia        | 29 (96.7)        | 8 (88.9)                        | NS         |
| Diabetes mellitus   | 22 (73.3)        | 7 (77.8)                        | NS         |
| DM on insulin       | 18 (60)          | 6 (66.7)                        | NS         |
| Current smoking     | 5 (16.7)         | 0 (0)                           | NS         |
| Prior MI            | 7 (23.3)         | 3 (33.3)                        | NS         |
| Prior CABG          | 21 (70)          | 3 (33.3)                        | NS         |
| Prior HF            | 4 (13.3)         | 2 (22.2)                        | NS         |
| PVD                 | 6 (20)           | 1 (11.1)                        | NS         |
| eGFR < 60           | 8 (26.7)         | 4 (44.4)                        | NS         |
| EF (%)              | 16 (53.3)        | 2 (22.2)                        | NS         |
|                     |                |                                 |            |
| Data are presented as n (%) or mean ± standard deviation. BA = balloon angioplasty; CABG = coronary artery bypass graft; DES = drug-eluting stents; DM = diabetes mellitus; EF = ejection fraction; eGFR = estimated glomerular filtration rate; HF = heart failure; ISR = in-stent restenosis; MI = myocardial infarction; PVD = Peripheral vascular disease; NS = nonsignificant. |

Standard qualitative and quantitative definitions and measurements were used [7]. Reference vessel diameter, minimal lumen diameter, diameter of stenosis, and lesion length were measured using a single matched “worst” view. Acute lumen gain was defined as the immediate gain in the lumen size of the target lesion postintervention. Late luminal loss was defined as the difference between the minimal lumen diameter of the target lesion immediately after the procedure and at 1 year after PCI. Net lumen gain was the
difference between acute lumen gain and late lumen loss. Binary restenosis was defined as ≥50% diameter of stenosis at follow-up angiography of a treated lesion. Similarly, rerestenosis was defined as more than 50% diameter of stenosis by quantitative coronary angiography on follow-up.

Table 2. Baseline lesion characteristics.

|                  | First-time DES-ISR | Rerestenosis of DES-treated ISR | p (overall) |
|------------------|--------------------|--------------------------------|-------------|
|                  | BA (n = 66)        | Re-DES (n = 24)                |             |
| ACC/AHA lesion type | NS                 |                                |             |
| A                | 32 (48.5)          | 6 (25)                         |             |
| B1               | 15 (22.7)          | 7 (29.2)                       |             |
| B2               | 11 (16.7)          | 6 (25)                         |             |
| C                | 8 (12.1)           | 5 (20.8)                       |             |
| ISR pattern      | NS                 |                                |             |
| Focal proximal edge | 12 (18.2)      | 8 (33.3)                       |             |
| Focal stent body | 32 (48.4)          | 7 (29.2)                       |             |
| Focal distal edge | 5 (7.6)           | 1 (4.2)                        |             |
| Multifocal       | 5 (7.6)            | 2 (8.3)                        |             |
| Diffuse          | 7 (10.6)           | 1 (4.2)                        |             |
| Occlusive        | 5 (7.6)            | 5 (20.8)                       |             |
| CTO              | 4 (6.1)            | 3 (12.5)                       |             |
| Ostial           | 3 (4.5)            | 1 (4.2)                        |             |
| Bifurcation      | 4 (6.1)            | 6 (25)                         |             |

Data are presented as n (%).

Table 3. Procedural characteristics.

|                  | First-time DES-ISR | Rerestenosis of DES-treated ISR | p (overall) |
|------------------|--------------------|--------------------------------|-------------|
|                  | BA (n = 66)        | Re-DES (n = 22)                |             |
| Approach         | NS                 |                                |             |
| Femoral          | 13 (19.7)          | 8 (33.3)                       |             |
| Brachial         | 32 (48.5)          | 11 (45.8)                      |             |
| Radial           | 21 (31.8)          | 5 (20.9)                       |             |
| Target vessel    | NS                 |                                |             |
| LM               | 2 (3)              | 2 (8.3)                        |             |
| LAD              | 22 (33.3)          | 12 (50)                        |             |
| LCX              | 15 (22.7)          | 2 (8.3)                        |             |
| RI               | 1 (1.5)            | 0 (0)                          |             |
| RCA              | 26 (39.5)          | 7 (29.2)                       |             |
| Graft            | 0 (0)              | 1 (4.2)                        |             |
| IVUS guided      | NS                 |                                |             |
| Balloon type     | NS                 |                                |             |
| Semi complaint   | 19 (28.8)          | 11 (45.8)                      |             |
| Non complaint    | 42 (63.6)          | 12 (50)                        |             |
| Other            | 5 (7.6)            | 1 (4.2)                        |             |
| Balloon diameter | 2.6 ± 0.5          | 2.5 ± 0.6                      |             |
| Inflation pressure | 17.0 ± 4.8     | 14.4 ± 3.4                     |             |
| Stent type       | Cypher             | 8 (33.4)                       |             |
|                  | Taxus              | 15 (62.4)                      |             |
|                  | Cypher & taxus     | 1 (4.2)                        |             |
|                  | Total stent length | 18.7 ± 8.2                     |             |
|                  | Stent diameter     | 2.8 ± 0.3                      |             |
|                  | Inflation pressure | 16.2 ± 3.4                     |             |

Data are presented as n (%) or mean ± standard deviation.

BA = balloon angioplasty; DES = drug-eluting stents; ISR = in-stent restenosis; IVUS = intravascular ultrasound; LAD = left anterior descending artery; LM = left main; LCX = left circumflex artery; NS = nonsignificant; RCA = right coronary artery; RI = ramus intermedius.
Continuous variables were expressed as mean ± standard deviation, and categorical variables as frequency (%). Continuous variables were compared using unpaired Student t test or analysis of variance. Categorical variables were compared with Chi-square test ($\chi^2$) or Fisher’s exact tests. Two-year clinical outcomes were analyzed.
using Kaplan–Meier method and were compared with log-rank test pooled over strata. All tests were two-sided and a \( p \) value <0.05 was considered significant. All analyses were performed with SPSS version 18 (SPSS, Inc., Chicago, IL, USA).

**Results**

One-hundred and twenty-three patients, subtending 130 lesions, were included in the study. Among those, 84 patients (90 lesions) had first-time DES-ISR, while 39 patients (40 lesions) had rerestenosis of DES-treated DES-ISR (Fig. 1). From the first group, 62 patients (66 lesions) were treated by BA, while 22 patients (24 lesions) had re-DES implantation. In the second group, 30 patients (30 lesions) were treated by BA, while nine patients (10 lesions) had re-DES implantation. Table 1 shows the baseline clinical characteristics of the study population. There were no statistically significant differences between both subgroups (BA or re-DES). Of notice, the majority of patients were men, more than 90% were hypertensive, around 70% had dyslipidemia, and almost 60% were diabetic. Tables 2 and 3 represent the angiographic and procedural results. There were no significant differences between the patients’ subgroups (BA vs. re-DES) of each major group (1st-time DES-ISR vs. DES rerestenosis). The majority of lesions were Type A in the first group (1st-time DES-ISR), while the second group (DES rerestenosis) had a majority of Type B1 lesions. The ISR was of focal pattern in most of the lesions. Complex lesions like chronic total occlusions and bifurcation lesions were more frequently treated by re-DES than BA. Almost two-thirds of the patients had the procedure performed through upper extremity, either radial or brachial. The most frequently targeted vessels were the left anterior descending artery and right coronary artery. Intravascular ultrasound-guided PCI was performed more often in re-DES strategy than BA. Noncompliant balloon was used more often than semicompliant balloon, especially in those undergoing BA. Table 4 shows the quantitative angiographic results at: (1) baseline; (2) immediately postintervention; and (3) at 1-year follow-up. Compared with baseline, postintervention minimal lumen diameter and acute lumen gain were significantly larger; the diameter of stenosis was less in the re-DES strategy compared with BA in both groups (1st-time DES-ISR vs. DES rerestenosis). At 1-year angiographic follow-up, quantitative measurements showed that minimal lumen diameter was still significantly larger and the diameter of stenosis was significantly smaller in patients treated with re-DES compared with BA in both patient groups. However, for the late lumen loss and net lumen gain, it was only significantly different in the first-time DES-ISR in favor of patients undergoing re-DES, while there was no significant difference between both treatment strategies among patients with DES rerestenosis. Binary restenosis rates were high in both groups. Of notice, binary restenosis rates were significantly higher in the DES rerestenosis group compared with first-time DES-ISR group. Nevertheless, within the treatment subgroups, binary restenosis rates tended to be significantly higher in patients undergoing BA compared with re-DES only in first-time DES-ISR patients. The majority of rerestenosis was of focal pattern, more often within the stent body and less often at the stent edges (Table 4). Moreover, binary restenosis occurred at the same previous site more often in BA treatment compared with re-DES treatment subgroups, which was statistically significant among the first-time DES-ISR patient group only.

According to the Kaplan–Meier survival curves (Fig. 2), the cumulative incidence of re-TLR among First-time DES-ISR patients was significantly higher in BA-treated patients than those undergoing re-DES. This was not the case with patients having rerestenosis of DES-treated ISR (Fig. 2). Table 5 shows the incidence of re-TLR at 1- and 2-year clinical follow-up. Late catch-up phenomenon, which is the delayed occurrence of clinical restenosis warranting secondary revascularization, was observed in both groups comparing 1- and 2-year follow-ups, with significantly higher rates in the rerestenosis of DES-treated ISR group at 2 years (overall \( p = 0.01 \)).

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**Table 5. Re-target lesion revascularization incidence at 1-year and 2-year follow-up.**

|                          | First-time DES-ISR | Rerestenosis of DES-treated ISR |
|--------------------------|--------------------|---------------------------------|
|                          | BA (n = 66)        | Re-DES (n = 24)                 | p (overall) |
|                          | Re-DES (n = 30)   | re-DES (n = 10)                 | p           |
| 1 y                      | 21 (33.3)         | 3 (12.5)                        | 0.04        |
| 2 y                      | 25 (37.8)         | 4 (16.6)                        | 0.03        |

Data are presented as n (%).
BA = balloon angioplasty; DES = drug-eluting stents; ISR = in-stent restenosis; NS = nonsignificant.
Discussion

In this study, we compared the angiographic and clinical outcomes after BA versus re-DES among two groups of patients. The first group included those with first-time DES-ISR, while the patients in the second group had previous DES-treated ISR of DES who developed restenosis. At 1-year angiographic and up to 2-year clinical follow-up, it was obvious that the binary restenosis and re-TLR rates, respectively, were still relatively high in both patient groups. Among the first group (1st-time DES-ISR), a strategy of re-DES implantation resulted in a lower incidence of angiographic restenosis and re-TLR than BA. However, re-DES had no significant advantage over BA in terms of angiographic restenosis or re-TLR among the second group (rerestenosis in DES-treated ISR).

Despite the different treatment strategies tested, mostly in small retrospective studies, the optimal treatment for DES-ISR remains unsettled. The initial enthusiasm with the use of DES to treat DES-ISR has declined after clinical reports revealing that clinical recurrences after interventions for DES-ISR were two-fold those seen after bare-metal stent-ISR [8], probably related to the different underlying pathophysiological mechanism and the composition of the restenosis tissue [9,10]. This warrants further investigations to unravel this mystery.

Previous large-scale studies have shown that a strategy of re-DES is superior to BA in case of DES-ISR [11–13]. A recent meta-analysis has concluded that the use of BA should be discouraged in patients with DES restenosis, owing to the observation that BA had the lowest efficacy with respect to all angiographic end-points as compared with drug-eluting balloons or repeated DES implantation. However, there was no data on whether this reflects hard clinical outcomes.

Although a small number of patients were tested, this study sheds some light upon an uprising issue that we are currently confronted with in real-world practice, with the wide off-label use of DES.

In accordance to previous studies and reports [14,15], this study showed that DES-ISR patterns were mostly focal. This predominant restenosis pattern extends to second time DES-ISR as shown in this study.

Our results are in agreement with that of Kita-hara et al. [16], which showed that the rates of binary restenosis and TLR were less after adopting a re-DES strategy compared with BA, among patients with sirolimus-eluting stent restenosis. Their study, however, showed that the benefit of re-DES implantation was confined to focal pattern of DES-ISR, and does not hold much benefit compared with BA when the ISR pattern is nonfocal.

To our knowledge, no previous study has tackled the issue of repeated restenosis of DES used to treat previous DES-ISR. This study represents the first angiographic and clinical follow-up study addressing the issue of rerestenosis of DES-treated DES-ISR. We observed no difference between a re-DES strategy and BA among this patient subset in terms of 1-year binary restenosis rates or re-TLR at 2 years. In a recent optical coherence tomography study [17], addressing the mechanisms of lumen gain in reinterventions for DES-ISR, lumen gain equally resulted from a reduction of intrastent lumen volume (tissue compression) and further DES expansion. We assume that probably the effect of the latter is more pronounced in cases of rerestenosis of DES-treated ISR. This might explain why BA exerted the same benefit as re-DES among patients treated for restenosis of DES-treated ISR.

Another previous optical coherence tomography study showed that the morphologic appearance of the restenosis tissue influenced the outcome [18], where BA was more effective for DES-ISR with heterogeneous tissue appearance than that with homogenous/layered tissue. This warrants extensive intravascular imaging research to explore the morphology of restenosis tissue in repeated ISR lesions, and explain why BA might perform as good as re-DES in this patient subset.

In the scope of the relatively low restenosis rates after DES implantation, it is difficult to conduct large-scale trials. Thus, evaluation of optimum treatment of DES-ISR remains a challenge. Rerestenosis rates, although increasingly observed, are still scarce and this adds to the difficulty in exploring this issue and increases the challenge.

This study has some limitations. Data were analyzed in a retrospective and nonrandomized manner. Additionally, the sample size was small and not powered enough to detect clinical endpoints, especially among the second group of patients. However, the angiographic follow-up rate was relatively high, approaching 90%, which was higher than that reported in previous studies from Japanese [16] or non-Japanese hospitals [15,19]. In the present study, the underlying mechanisms of DES restenosis or rerestenosis were not explored. Stent underexpansion, geographic miss, or DES polymer damage [20–22] are possible causes and should have been thoroughly evaluated. Further large-scale studies, sufficiently powered for angiographic and clinical end-points, are warranted to make this issue clear.
Conclusions
The rates of restenosis and re-TLR after treatment of DES-ISR are relatively high. While a strategy of re-DES would be better than BA in first-time DES-ISR, this could not be extrapolated to restenosis cases where no clear benefit could be justified. Until further light is shed upon such an uprising issue, BA could offer a better choice for restenosis cases instead of putting further stents when more than two stent layers are already present in the vessel. Studies addressing this subgroup of patients and exploring other treatment strategies like drug-eluting balloons and cutting balloons are eagerly awaited.

References
[1] Gruntzig AR, Senning A, Siegenthaler WE. Nonoperative dilatation of coronary-artery stenosis: percutaneous transluminal coronary angioplasty. N Engl J Med 1979;301:61–8.
[2] Simsek C, Magro M, Boersma E, Onuma Y, Nauta ST, Gasperz MP, et al. The unrestricted use of sirolimus- and paclitaxel-eluting stents results in better clinical outcomes during 6-year follow-up than bare-metal stents: an analysis of the RESEARCH (Rapamycin-Eluting Stent Evaluated at Rotterdam Cardiology Hospital) and T-SEARCH (Taxus-Stent Evaluated at Rotterdam Cardiology Hospital) registries. JACC Cardiovasc Inter 2010;3:1051–8.
[3] Stolker JM, Kennedy KF, Lindsey JB, Marso SP, Pencina MJ, Cullip DE, et al. Predicting restenosis of drug-eluting stents placed in real-world clinical practice: derivation and validation of a risk model from the EVENT registry. Circ Cardiovasc Inter 2010;3:327–34.
[4] Jukema JW, Ahmed TA, Verschuren JJ, Quax PH. Restenosis after PCI. Part 2: prevention and therapy. Nat Rev Cardiol 2012;9:79–90.
[5] Windecker S, Kolh P, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS guidelines on myocardial revascularization: the task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35:2541–619.
[6] Mehran R, Dangas G, Abizaid AS, Mintz GS, Lansky AJ, Satler LF, et al. Angiographic patterns of in-stent restenosis: classification and implications for long-term outcome. Circulation 1999;100:1872–8.
[7] Popma JJ, Bashore TD. Qualitative and quantitative angiography. In: Topol E, editor. Textbook of interventional cardiology. Philadelphia: W.B. Saunders; 1994. p. 1052–68.
[8] Steinberg DH, Gaglia Jr MA, Pinto Slottow TL, Roy P, Bonello I, de LA, et al. Outcome differences with the use of drug-eluting stents for the treatment of in-stent restenosis of bare-metal stents versus drug-eluting stents. Am J Cardiol 2009;103:491–5.
[9] Alfonso F, Perez-Vizcayno MJ, Cruz A, Garcia J, Jimenez-Quevedo P, Escaned J, et al. Treatment of patients with in-stent restenosis. Eur J Interventional Radiol 2009;5(Suppl 1):D70–8.
[10] Gonzalo N, Serruys PW, Okamura T, van Beusekom HM, Garcia-Garcia HM, van SG, et al. Optical coherence tomography patterns of stent restenosis. Am Heart J 2009;158:284–93.
[11] Alfonso F, Zueco J, Cequier A, Mantilla R, Bethencourt A, Lopez-Minguez JR, et al. A randomized comparison of repeat stenting with balloon angioplasty in patients with in-stent restenosis. J Am Coll Cardiol 2003;4:796–805.
[12] Alfonso F, Perez-Vizcayno MJ, Hernandez R, Bethencourt A, Marti V, Lopez-Minguez JR, et al. A randomized comparison of sirolimus-eluting stent with balloon angioplasty in patients with in-stent restenosis: results of the Restenosis Infrastent: Balloon Angioplasty Versus Elective Sirolimus-Eluting Stenting (RIBS-II) trial. J Am Coll Cardiol 2006;47:2152–60.
[13] Kastrati A, Mehilli J, von BN, Dipa A, Pache J J, et al. Sirolimus-eluting stent or paclitaxel-eluting stent versus balloon angioplasty for prevention of recurrences in patients with coronary in-stent restenosis: a randomized controlled trial. JAMA 2005;293:165–71.
[14] Alfonso F. Treatment of drug-eluting stent restenosis the new pilgrimage: quo vadis? J Am Coll Cardiol 2010;55:2717–20.
[15] Cosgrave J, Melzi G, Biondi-Zoccai GG, Airoldi F, Chieffi A, Sangiorgi GM, et al. Drug-eluting stent restenosis the pattern predicts the outcome. J Am Coll Cardiol 2006;47:2399–404.
[16] Kitahara H, Kobayashi Y, Takebayashi H, Fujimoto Y, Nakamura Y, Kuroda N, et al. Restenosis and target lesion revascularization after treatment of sirolimus-eluting stent restenosis: retrospective analysis of 4 Japanese hospitals. Circ J 2009;73:867–71.
[17] Alfonso F, Sandoval J, Perez-Vizcayno MJ, Cardenas A, Gonzalez N, Jimenez-Quevedo P, et al. Mechanisms of balloon angioplasty and repeat stenting in patients with drug-eluting in-stent restenosis. Int J Cardiol 2015;156:218–20.
[18] Arikawa R, Yamaguchi H, Takaoka Y, Miyamura A, Atsuchi N, Ninomiya T, et al. Simple balloon dilation for drug-eluting stent restenosis of bare-metal stents: results of a randomized comparison of the EXPRESS and EUPHORIA 2006 studies. JACC Cardiovasc Interv 2014;7:866–72.
[19] Aho Y, Vanhala M, Seppala M, Voutilainen M, Aho K, Lehtonen M, et al. A randomized comparison of balloon angioplasty and repeat stenting in patients with drug-eluting in-stent restenosis: the same or a different stent. J Am Coll Cardiol 2014;65:2713–20.
[20] Colombo A, Orlic D, Stankovic G, Corvaja N, Spanos V, Montorfano M, et al. Preliminary observations regarding angiographic pattern of restenosis after rapamycin-eluting stent implantation. Circulation 2003;107:2178–80.
[21] Fujii K, Mintz GS, Kobayashi Y, Carlier SG, Takebayashi H, Yasuda T, et al. Contribution of stent underexpansion to recurrence after sirolimus-eluting stent implantation for in-stent restenosis. Circulation 2004;109:1085–8.
[22] Okumura M, Ozaki Y, Ishii J, Kan S, Naruse H, Matsui S, et al. Restenosis and stent fracture following sirolimus-eluting stent (SES) implantation. J Jpn Circ J 2007;71:1669–77.