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Original article

Effect of combination of non-slip element balloon and drug-coating balloon for in-stent restenosis lesions (ELEGANT study)☆

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ABSTRACT

Background: In-stent restenosis (ISR) remains a problematic issue of coronary intervention. The non-slip element balloon (NSE) is a balloon catheter with 3 longitudinal nylon elements which are attached proximally and distally to the balloon component. The expectation is that this design of balloon is able to achieve a larger lumen area due to the elements, as well as reducing balloon slippage. We investigated whether NSE pre-dilatation improves angiographic outcomes compared to a high pressure non-compliant balloon pre-dilatation, followed by a drug-coating balloon (DCB) for treatment of ISR lesions with optical coherence tomographic imaging (OCT).

Methods: Patients were eligible for the study if one or more in-stent restenosis lesions were treated with a paclitaxel-coating balloon. Patients were randomized to NSE pre-dilatation (NSE group) or high pressure non-compliant balloon pre-dilatation (POBA group) in a 1:1 fashion in 17 hospitals. The primary endpoint was in-segment late loss [post minimal lumen diameter (MLD) − follow-up MLD] at 8 months.

Results: One hundred and five patients were allocated to each group. Balloon slippage (7.9% versus 22.9%, $p = 0.002$) and geographical miss (6.9% versus 21.9%, $p = 0.002$) were observed less in the NSE group compared to the POBA group. Acute gain was significantly larger in the NSE group (1.17 ± 0.42 mm versus 1.06 ± 0.35 mm, $p = 0.04$), but post minimum stent lumen area analyzed by OCT was similar between the two groups (3.85 ± 1.67 mm^2 versus 3.81 ± 1.93 mm^2, $p = 0.64$). At 8 months, average lesion length was significantly shorter than the POBA group (5.78 ± 3.26 mm versus 6.97 ± 4.59 mm, $p = 0.04$), but average

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in-segment late loss was similar between the two groups (0.28 ± 0.45 mm versus 0.27 ± 0.38 mm, $p = 0.75$).

Conclusion: Eight-month angiographic outcomes were similar between NSE and non-compliant balloon pre-dilatation with DCB for treatment of ISR lesions. However, NSE pre-dilatation has advantages such as reduction of balloon slippage and geographical miss during the procedure.

Introduction

In-stent restenosis (ISR) remains a problematic issue in the second-generation drug-eluting stent (DES) era [1,2]. Drug-coating balloons (DCB) generally provide excellent angiographic and clinical outcomes in patients with ISR lesions [3]. However, suppression of neointimal growth following DCB treatment varies [4–9]. Some technical issues such as insufficient pre-balloon dilatation, and geographical miss might affect the angiographic outcomes. Non-slip element balloon (NSE) is a balloon catheter with three longitudinal nylon elements which are attached to the proximal and distal balloon segments. This balloon is expected to achieve a larger lumen area due to the focused force of the three elements into tissue, and to reduce geographical miss due to avoiding balloon slippage [10]. We investigated whether NSE dilatation prior to DCB treatment improved angiographic outcomes, compared to high pressure non-compliant balloon pre-dilatation with optical coherence tomographic imaging (OCT) in ISR lesions.

Methods

Study design and population

The ELEGANT study is a multicenter randomized trial. A total of 17 centers across Japan participated in this study. Patients were eligible for the study if one or more ISR lesions were treated with paclitaxel-coating balloons (SeQuent Please, NIPRO, Osaka, Japan). Patients were not eligible for enrollment if they had an evolving myocardial infarction or angiographically visible thrombus within the target lesion. Patients were randomized to NSE pre-dilatation (NSE group) or high pressure non-compliant balloon pre-dilatation (POBA group) in a 1:1 fashion. If NSE or non-compliant balloon was not able to cross the target lesion, a 2-mm standard balloon pre-dilatation was used in order to cross NSE or non-compliant balloon through the lesions. All interventions were performed using standard techniques. The size and pressure of NSE and DCB were chosen according to the physician's discretion. Pre- and post-OCT was recommended in all cases. All patients were advised to continue treatment with dual antiplatelet therapy (aspirin 100 mg/day and clopidogrel 75 mg/day) for 12 months after percutaneous coronary intervention, as well as lifelong daily use of aspirin. Randomization was performed before percutaneous coronary intervention procedure by using a computer-generated randomization code. The medical ethics committees of all sites approved the study protocol, and written informed consent was obtained from every patient.

Data collection and follow-up

Clinical data were collected and documented in an electronic case report form at the following time points: baseline, post-procedure, 8 months, and 2 years. Pre-specified clinical events were adjudicated by an independent clinical event committee consisting of cardiologists. Follow-up angiography was planned in all patients at 8 months. Qualitative and quantitative coronary analysis (QCA) and OCT analyses were performed by an independent core laboratory (Cardiocore Japan, Tokyo, Japan) with QAngio®XA7.1 and QIvus® version 3.0 (Medis medical imaging systems BV, Leiden, The Netherlands).

Study endpoints and definitions

In this study, definitions of coronary risk factors were decided by each participating hospital. All deaths were considered as cardiac death unless an unequivocal non-cardiac cause was established. Myocardial infarction (MI) was defined as development of new, pathological Q waves on electrocardiogram, or elevation of creatinine kinase (CK) levels greater than or equal to two times the upper limit of normal with elevated CK-MB in the absence of new pathological Q waves. Target vessel revascularization (TVR) was defined as any repeat percutaneous intervention or surgical bypass for any segment in the target vessel. Target vessel failure (TVF) was defined as the composite of cardiac death, target vessel MI, and TVR. Stent thrombosis was defined as definite and probable, according to the Academic Research Consortium definition [11]. The primary endpoint was in-segment late loss [post minimal lumen diameter (MLD) – follow-up MLD]. The secondary endpoints were follow-up MLD, post minimal lumen stent area, post neointimal area, incidence of pre-balloon slipping, incidence of unplanned stenting, and TVF at 8 months or 2 years. Balloon slippage was visually defined as more than 3 mm slippage during balloon dilatation, and geographical miss was visually defined when the DCB was not fully covering the pre-dilated lesions [12,13]. Both analyses were performed by an independent core laboratory. Pre-specified sub-analysis was conducted following parameters [bare-metal stent (BMS) versus DES, hemodialysis versus non-hemodialysis, diabetes versus non-diabetes, stent size $\leq$2.5 mm versus $>$2.5 mm, and first ISR or repeat ISR].

Statistics

Statistical analysis was performed using SAS software (version 9.3; SAS Institute; Cary, NC, USA). With the assumption of 0.11? mm in-segment late loss after NSE dilatation and 0.19 mm in-segment late loss after non-compliant balloon dilatation with a level of 2-sided alpha level of 0.05 and power of 80%, we estimated that a total of 180 patients were required [14]. A total of 210 patients were to be enrolled considering possible dropout . Continuous variables were expressed as mean value ± standard deviation and were compared by use of Student *t* test. For binary variables, Pearson's chi-squared test or Fisher's exact test was performed when appropriate. Odds ratios and 95% confidence intervals (CI) for binary restenosis were analyzed by logistic regression analysis.

Results

Baseline and procedural characteristics

From August 2015 to April 2017, a total of 105 patients were enrolled in each group. After excluding 7 patients without

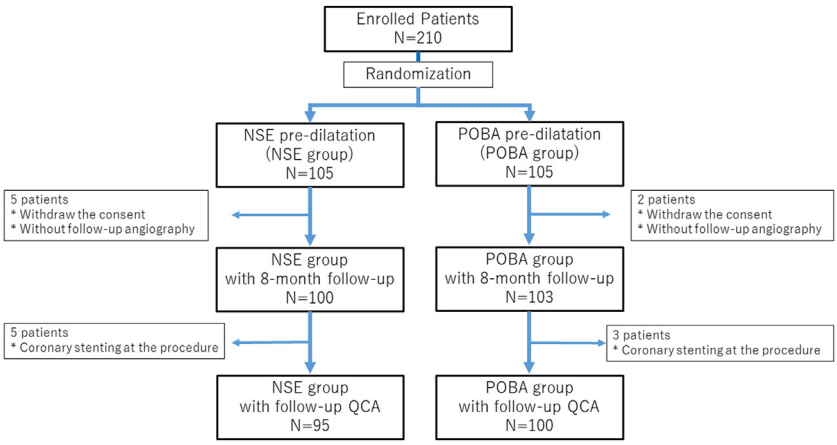

Fig. 1. Flow chart of the present study.
NSE, non-slip element balloon; POBA, high pressure non-compliant balloon; QCA, quantitative coronary analysis.

Table 1
Patient characteristics.

	NSE $N = 105$	POBA $N = 105$	p-Value
Age (years)	70.0 ± 8.3	68.9 ± 10.0	$p = 0.40$
Gender, male (*N*, %)	91 (86.7%)	91 (86.7%)	$p = 1.00$
Diabetes (*N*, %)	54 (51.4%)	50 (47.6%)	$p = 0.58$
Insulin requiring (*N*, %)	18 (17.1%)	10 (9.5%)	$p = 0.10$
Dyslipidemia (*N*, %)	85 (81.0%)	87 (82.9%)	$p = 0.72$
Current smoker (*N*, %)	8 (7.6%)	15 (14.3%)	$p = 0.12$
Family history (*N*, %)	10 (9.5%)	17 (16.2%)	$p = 0.15$
CKD (*N*, %)	21 (20.0%)	22 (21.0%)	$p = 0.86$
Hemodialysis (*N*, %)	18 (17.1%)	18 (17.1%)	$p = 1.00$
Acute coronary syndrome (*N*, %)	4 (3.8%)	4 (3.8%)	$p = 1.00$
Prior MI (*N*, %)	48 (5.7%)	50 (47.6%)	$p = 0.78$
Prior CABG (*N*, %)	10 (9.5%)	10 (9.5%)	$p = 1.00$

CKD, chronic kidney disease; MI, myocardial infarction; CABG, coronary artery bypass grafting; NSE, non-slip element balloon; POBA, high pressure non-compliant balloon.

follow-up coronary angiography and 8 patients with coronary stenting at the procedure, follow-up coronary angiographies were analyzed in 195 patients (Fig. 1). Patient and lesion characteristics are summarized in Tables 1 and 2. The two groups were well matched. The prevalence of DES restenosis was similar between the two groups (76.9% in the NSE group, and 78.9% in the POBA group, $p = 0.72$). Approximately half of the lesions were diffuse ISR lesions (56.5% in the NSE group, and 54.1% in the POBA group, $p = 0.73$). The average stent diameter was also similar between the two groups (3.00 ± 0.46 mm in the NSE group, and 2.95 ± 0.44 mm in the POBA group, $p = 0.73$). Pre-dilatation prior to cross NSE or non-compliant balloon was performed in 28 lesions (25.9%) in the NSE group and 10 lesions (9.2%) in the POBA group ($p = 0.002$), respectively. Finally, NSE was not able to pass the target lesion in 7 (6.5%) lesions. The average NSE diameter was 2.95 ± 0.47 mm and average maximum pressure was 14.4 ± 3.7 atm (Table 3). In the POBA group, average balloon diameter was 3.00 ± 0.71 mm and average maximum pressure was 17.8 ± 4.3 atm (Table 2). Unplanned coronary stenting was performed in 5 (4.6%) lesions in the NSE group and 3 lesions (2.8%) in the POBA group ($p = 0.46$).

Angiographic, OCT, and clinical outcomes

Angiographic outcomes are summarized in Table 3. There were no significant differences in pre-QCA parameters between the NSE and POBA group. During the procedure, NSE significantly reduced geographical miss (6.9% in the NSE group, and 21.9% in the POBA group, $p = 0.002$) due to avoiding balloon slippage (7.9% in the NSE group, and 22.9% in the POBA group, $p = 0.002$). In addition, acute gain was significantly larger in the NSE group compared to the POBA group (1.17 ± 0.42 mm versus 1.06 ± 0.35 mm, $p = 0.04$). However, there were no significant differences in in-segment late loss between the NSE and POBA group (0.28 ± 0.45 mm versus 0.27 ± 0.38 mm, $p = 0.75$), and binary restenosis rate (12.9% in the NSE group, and 15.2% in the POBA group, $p = 0.63$). Pre- and post-OCT imaging was also analyzed (Table 4). There were no significant differences in OCT analyses including post minimum stent lumen area and post neointimal average area between the NSE and POBA group. Cumulative distribution curves almost overlapped for in-segment late loss, follow-up MLD, and post minimum stent lumen area except acute gain between the two groups (Fig. 2). Table 5 shows the 8-month clinical outcomes. There were no significant differences in clinical outcomes including TVF between the two groups (7.0% in the NSE group, and 9.7% in the POBA group, $p = 0.49$). In the per-lesion analysis, TLR rate was also similar between the two groups (5.7% in the NSE group, and 7.4% in the POBA group, $p = 0.61$).

Pre specified sub-analysis

Cumulative distribution curves for in segment late loss are depicted in Fig. 3. Although baseline characteristics such as prevalence of hemodialysis (21% in the DES ISR versus 4.2% in the BMS ISR, $p = 0.04$), stented length (25.1 ± 8.0 mm in the DES ISR versus 19.1 ± 5.3 mm in the BMS ISR, $p < 0.0001$), and stented diameter (2.90 ± 0.43 mm in the DES ISR versus 3.26 ± 0.42 mm in the BMS ISR, $p < 0.0001$) were significantly different between the DES and BMS restenosis lesions, average in-segment late loss was significantly larger in the DES restenosis lesions, compared to BMS restenosis lesions. In addition, average in-segment late loss was also significantly larger in hemodialysis, compared to non-hemodialysis patients. Odds ratios and 95% confidence intervals (CI) for binary restenosis were analyzed in pre-specified parameters. DES versus BMS was not analyzed, since no binary restenosis was observed in the BMS restenosis lesions. Only hemodialysis was

Table 2
Lesion and procedural characteristics.

	NSE N = 108	POBA N = 109	p-Value
Lesion characteristics			
Previous stent, DES (N, %)	83 (76.9%)	86 (78.9%)	p = 0.72
Average stented length (mm)	23.7 ± 8.0	24.1 ± 7.9	p = 0.75
Average stent diameter (mm)	3.00± 0.46	2.95 ± 0.44	p = 0.45
First ISR (N, %)	88 (81.5%)	88 (80.7%)	p = 0.89
Treated vessel			
LAD (N, %)	60 (55.6%)	55 (50.5%)	p = 0.45
LCX (N, %)	10 (9.3%)	15 (13.8%)	p = 0.30
RCA (N, %)	36 (33.3%)	37 (33.9%)	p = 0.92
LMCA (N, %)	1 (0.9%)	1 (0.9%)	p = 0.99
Artery graft (N, %)	1 (0.9%)	0 (0.0%)	p = 0.31
Vein graft (N, %)	0 (0.0%)	1 (0.9%)	p = 0.32
Mehran classification			
1A (N, %)	0 (0.0%)	0 (0.0%)	p = N/A
1B (N, %)	3 (2.8%)	6 (5.5%)	p = 0.31
1C (N, %)	39 (36.1%)	39 (35.8%)	p = 0.96
1D (N, %)	2 (1.9%)	2 (1.8%)	p = 0.99
Diffuse (N, %)	61 (56.5%)	59 (54.1%)	p = 0.73
Proliferative (N, %)	3 (2.8%)	2 (1.8%)	p = 0.64
Occlusive (N, %)	0 (0.0%)	1 (0.9%)	p = 0.32
Fracture, all (N, %)	1 (0.9%)	3 (2.8%)	p = 0.32
PSS (N, %)	0 (0.0%)	0 (0.0%)	p = N/A
Bifurcation (N, %)	18 (16.7%)	22 (20.2%)	p = 0.50
Ostium (N, %)	7 (6.5%)	9 (8.3%)	p = 0.62
Procedural characteristics			
Use of NC balloon (N, %)	28 (25.9%)	109 (100.0%)	p < 0.0001
Average maximum diameter (mm)	2.23 ± 0.34	2.91 ± 0.53	p < 0.0001
Average maximum pressure (atm)	14.1 ± 5.2	17.8 ± 4.3	p = 0.0002
Use of NSE (N, %)	101 (93.5%)	2 (1.8%)	p < 0.0001
Average maximum diameter (mm)	2.95 ± 0.47	3.00 ± 0.71	p = 0.88
Average maximum pressure (atm)	14.4 ± 3.7	12.0 ± 2.8	p = 0.37
DCB			
Average maximum diameter (mm)	3.02 ± 0.50	3.04 ± 0.47	p = 0.82
Average maximum pressure (atm)	10.7 ± 2.8	10.7 ± 3.2	p = 0.95
Total length (mm)	21.6 ± 8.1	21.8 ± 8.6	p = 0.95
Use of stent (N, %)	5 (4.6%)	3 (2.8%)	p = 0.46
Average stent diameter (mm)	2.90 ± 0.52	3.38 ± 0.18	p = 0.24
Total stented length (mm)	13.6 ± 3.6	24.0 ± 12.7	p = 0.09
Use of OCT (N, %)			
Pre (N, %)	93 (86.1%)	100 (91.7%)	p = 0.19
Post (N, %)	97 (89.8%)	100 (91.7%)	p = 0.62

DES, drug-eluting stents; ISR, in-stent restenosis; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; LMCA, left main coronary artery; PSS, peri-stent staining; CTO, chronic total occlusion; N/A, not available; NC, non-compliant; NSE, non-slip element balloon; DCB, drug-coating balloon; OCT, optical coherence tomography; POBA, high pressure non-compliant balloon.

Table 3
Qualitative and quantitative coronary analyses.

	NSE	POBA	p-Value
Pre-procedure			
Reference vessel diameter (mm)	2.56 ± 0.54	2.54 ± 0.55	p = 0.76
Minimum lumen diameter (mm)	0.93 ± 0.31	0.91 ± 0.32	p = 0.57
% Diameter stenosis (%)	63.4 ± 9.8	64.1 ± 9.9	p = 0.60
Lesion length (mm)	13.77 ± 7.72	13.25 ± 7.67	p = 0.47
Post-procedure			
Reference vessel diameter (mm)	2.62 ± 0.47	2.56 ± 0.53	p = 0.37
Minimum lumen diameter (mm)	2.10 ± 0.45	1.98 ± 0.42	p = 0.05
% Diameter stenosis (%)	20.1 ± 8.8	22.3 ± 9.1	p = 0.08
Lesion length (mm)	4.97 ± 2.52	5.21 ± 3.00	p = 0.93
Acute gain (mm)	1.17 ± 0.42	1.06 ± 0.35	p = 0.04
Balloon slip more than 3 mm (%)	8 (7.9%)	24 (22.9%)	p = 0.002
Geographic miss	7 (6.9%)	23 (21.9%)	p = 0.002
Geographic miss proximal	6 (5.9%)	13 (12.4%)	p = 0.11
Geographic miss distal	2 (2.0%)	17 (16.2%)	p = 0.0004
Follow-up			
Reference vessel diameter (mm)	2.62 ± 0.49	2.57 ± 0.56	p = 0.54
Minimum lumen diameter (mm)	1.82 ± 0.61	1.71 ± 0.55	p = 0.19
% Diameter stenosis (%)	30.4 ± 18.7	33.1 ± 17.7	p = 0.15
Lesion length (mm)	5.78 ± 3.26	6.97 ± 4.59	p = 0.04
Binary restenosis rate (%)	13 (12.9%)	16 (15.2%)	p = 0.63
Late loss (mm)	0.28 ± 0.45	0.27 ± 0.38	p = 0.75

NSE, non-slip element balloon; POBA, high pressure non-compliant balloon.

a significant predictor for binary restenosis (odds ratio: 2.74, 95% CI: 1.14–6.55, $p = 0.02$).

Discussion

Major findings of the present study were: (1) NSE pre-dilatation significantly reduced balloon slippage and geographical miss in the DCB-treated ISR lesions compared to high pressure NC-balloon pre-dilatation. (2) NSE pre-dilatation was associated with larger acute gain compared to high pressure NC-balloon pre-dilatation. (3) Using OCT imaging, NSE and high-pressure NC balloon pre-dilatation had similar late loss at 8-month follow-up. Both treatments were associated with acceptable low binary restenosis rates and TLR rates at 8 months. (4) DES restenosis and hemodialysis were associated with larger late loss using NSE or high-pressure NC balloon with OCT imaging compared to BMS restenosis or non-hemodialysis patients, respectively.

In the present study, the procedural and acute results were significantly better in the NSE group. Three longitudinal nylon elements are able to incise the neointimal tissue up to the metallic stent cage scoring into the fibrotic tissue. This might be related to the better acute gain after NSE dilatation. In addition, balloon slippage and geographical miss were significantly less in the NSE group. Conventional balloons tend to move forward or backward during inflation into the larger segments with lower resistance from the smooth, slippery ISR lesions [15]. Theoretically, balloon slippage induces geographical miss and unnecessary vascular injury. This is prevented by the nylon elements which anchor the balloon to the plaque during balloon inflation. Although the procedural and acute results were significantly better after NSE pre-dilatation, late angiographic outcomes were not improved after NSE pre-dilatation. Nylon elements are able to cut the neointimal tissue and create cracks. Paclitaxel easily penetrates into these cracks and anti-proliferative effect is theoretically enhanced after NSE pre-dilatation compared to normal balloon pre-dilatation. However, this effect was not observed in the present study. Neointima is composed of several tissues. Proteoglycan mainly constitutes neointimal tissue. This tissue is compressed by balloon, and nylon elements might be not able to create effective cracks. NSE pre-dilatation might be effective in solid tissue such as fibrotic or calcified ISR lesions.

In the ISAR-DESIRE4 trial, neointimal modification with scoring balloon pre-dilatation before DCB therapy improved the anti-restenotic efficacy of DCB in ISR lesions [16]. Although late loss was not significantly different (0.31 ± 0.59 mm versus 0.41 ± 0.74 mm, $p = 0.27$), in-segment percent stent diameter stenosis was significantly lower after scoring balloon pre-dilatation compared to normal therapy (35.0 ± 16.8% versus 40.4 ± 21.4%, $p = 0.047$). In the present study, late loss (0.276 ± 0.445 mm versus 0.273 ± 0.375 mm, $p = 0.75$) and in-segment percent stent diameter stenosis (30.4 ± 18.7% versus 33.1 ± 17.7%, $p = 0.15$) were similar between NSE pre-dilatation and high-pressure NC balloon pre-

Table 4
Optical coherence tomography analyses.

	NSE	POBA	*p*-Value
Pre-procedure			
Stent lumen area minimum (mm^2)	1.53 ± 0.91	1.44 ± 0.82	*p* = 0.41
Stent lumen area average (mm^2)	4.73 ± 1.77	4.56 ± 2.04	*p* = 0.29
Stent lumen area volume (mm^3)	151.74 ± 94.57	128.98 ± 72.74	*p* = 0.23
Stent area minimum (mm^2)	5.50 ± 2.49	5.59 ± 2.57	*p* = 0.83
Stent area average (mm^2)	7.30 ± 2.65	7.20 ± 2.70	*p* = 0.86
Stent volume (mm^3)	224.76 ± 133.70	200.32 ± 96.09	*p* = 0.49
Neointimal area average (mm^2)	2.45 ± 1.53	2.59 ± 1.54	*p* = 0.46
Neointimal volume (mm^3)	79.37 ± 60.01	77.31 ± 50.50	*p* = 0.82
% stent obstruction (%)	37.00 ± 15.89	40.56 ± 19.84	*p* = 0.30
Post-procedure			
Stent lumen area minimum (mm^2)	3.85 ± 1.67	3.81 ± 1.93	*p* = 0.64
Stent lumen area average (mm^2)	5.87 ± 1.90	5.70 ± 2.26	*p* = 0.23
Stent lumen area volume (mm^3)	182.02 ± 100.63	161.09 ± 72.50	*p* = 0.42
Stent area minimum (mm^2)	6.09 ± 2.68	6.11 ± 2.81	*p* = 0.89
Stent area average (mm^2)	8.18 ± 2.85	7.93 ± 3.00	*p* = 0.53
Stent volume (mm^3)	248.05 ± 144.09	223.75 ± 99.68	*p* = 0.61
Neointimal area average (mm^2)	2.26 ± 1.28	2.24 ± 1.33	*p* = 0.85
Neointimal volume (mm^3)	72.07 ± 56.11	69.97 ± 46.39	*p* = 0.93
% stent obstruction (%)	29.02 ± 10.94	31.73 ± 14.12	*p* = 0.27
Serial (post–pre)			
Stent lumen area minimum (mm^2)	2.36 ± 1.54	2.45 ± 1.85	*p* = 0.95
Stent lumen area average (mm^2)	1.20 ± 1.02	1.13 ± 1.20	*p* = 0.37
Stent lumen area volume (mm^3)	33.01 ± 34.79	30.26 ± 34.81	*p* = 0.54
Stent area minimum (mm^2)	0.66 ± 1.07	0.51 ± 1.07	*p* = 0.36
Stent area average (mm^2)	0.88 ± 0.92	0.75 ± 1.17	*p* = 0.10
Stent volume (mm^3)	24.08 ± 36.46	21.52 ± 35.85	*p* = 0.66
Neointimal area average (mm^2)	−0.26 ± 0.52	−0.36 ± 0.56	*p* = 0.32
Neointimal volume (mm^3)	−9.46 ± 16.18	−8.79 ± 15.90	*p* = 0.96

Neointimal area average = stent area average − stent lumen area average.
Neointimal volume = stent volume − stent lumen volume.
% Stent obstruction = neointimal volume/stent volume × 100.
NSE, non-slip element balloon; POBA, high pressure non-compliant balloon.

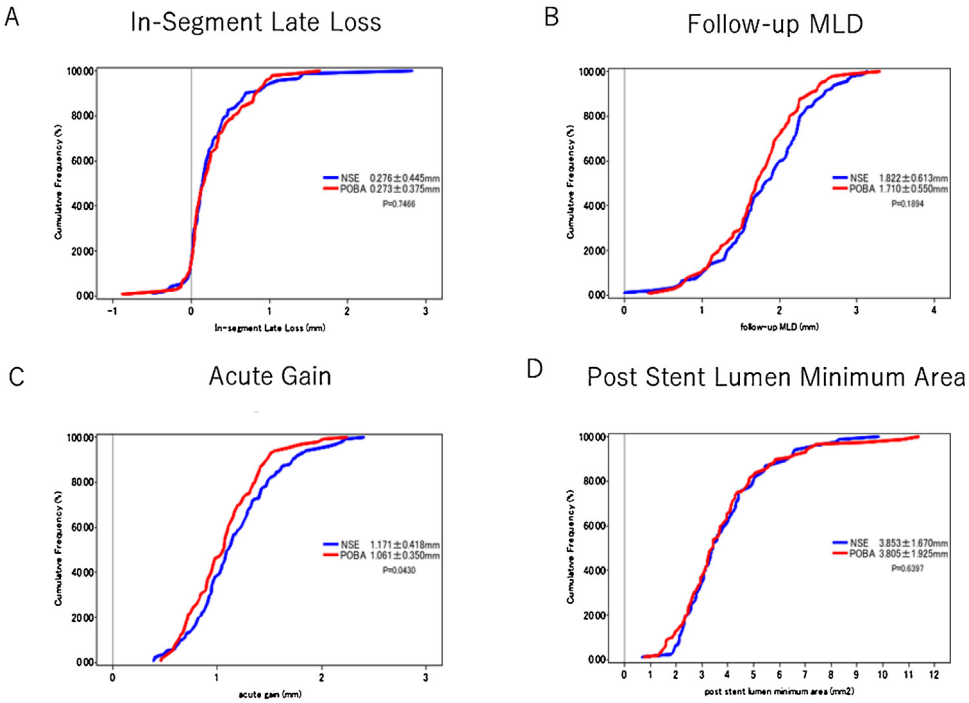

Fig. 2. Cumulative distribution curves for in-segment late loss (A), follow-up MLD (B), acute gain (C), and post minimum stent lumen area (D) between the NSE and POBA groups.
MLD, minimal lumen diameter; NSE, non-slip element balloon; POBA, high pressure non-compliant balloon.

Table 5
Eight-month clinical outcomes.

	NSE $N=100$	POBA $N=103$	p-Value
Death (*N*, %)	1 (1.0%)	4 (3.9%)	$p=0.19$
Cardiac death (*N*, %)	0 (0.0%)	0 (0.0%)	$p=$N/A
Myocardial infarction (*N*, %)	0 (0.0%)	2 (1.9%)	$p=0.16$
Q-wave (*N*, %)	0 (0.0%)	0 (0.0%)	$p=$N/A
Non Q-wave (*N*, %)	0 (0.0%)	0 (0.0%)	$p=$N/A
TLR (*N*, %)	6 (6.0%)	8 (7.8%)	$p=0.62$
TVR (*N*, %)	7 (7.0%)	10 (9.7%)	$p=0.49$
Stent thrombosis (*N*, %)	0 (0.0%)	0 (0.0%)	$p=$N/A
TVF (*N*, %)	7 (7.0%)	10 (9.7%)	$p=0.49$

NSE, non-slip element balloon; POBA, high pressure non-compliant balloon; TLR, target lesion revascularization; TVR, target vessel revascularization; TVF (cardiac death, TV-myocardial infarction, TVR), target vessel failure; N/A, not available.

dilatation. This difference might be explained by the better angiographic outcomes in the control arm in the present study, compared to the control arm in the ISAR-DESIRE 4 study. In the present study, OCT was used in more than 90% of cases. OCT provides precise measurements of coronary dimensions, accurate detection of stent under expansion, incomplete stent apposition, and stent dissection [17–19]. Use of OCT might be associated with better angiographic outcomes. In addition, non-compliant high-pressure balloons were used in the control arm of the present study. The average of maximum pressure was 17.8 atm in the present study, whereas it was 14.2 atm in the ISAR-DESIRE 4 study. These differences might be also associated with the better anti-restenotic efficacy in the control group in this study.

This study also highlights the comparison between DES and BMS ISR. Several studies showed worse angiographic or clinical outcomes in DES ISR lesions compared to BMS ISR lesions [20–22]. The present study further confirms this result. In-segment late loss was significantly higher in the DES restenosis lesions compared to BMS restenosis lesions. DES restenosis is already a failure of inhibition of neointimal growth by local anti-proliferative drug therapy, whereas BMS restenosis does not utilize anti-proliferative drug therapy to suppress neointimal growth and this might explain the difference in outcomes between DES and BMS ISR lesions. In addition, higher prevalence of hemodialysis, longer stented length, and smaller stented diameter might be associated with poor angiographic outcomes in the DES-ISR group compared to the BMS-ISR group.

ISR lesions in hemodialysis patients were associated with worse angiographic outcomes compared to patients without hemodialysis. Patients with hemodialysis tend to have multi-vessel, diffuse, and calcified coronary artery disease. A rigid calcified vessel is associated with stent under-expansion, which is one of the main risk factors for stent restenosis and might affect the incidence of re-restenosis [23–26]. In addition, severe endothelial dysfunction, enhanced platelet activation, and poor response to antiplatelet drugs contribute to the poor outcomes after coronary intervention in hemodialysis patients [23,27,28]. Although DCB significantly improved patency compared to balloon therapy in arteriovenous hemodialysis access, the application of DCB for coronary artery disease including ISR lesions has been not reported in hemodialysis patients [29]. A high prevalence of hemodialysis might counteract the better angiographic outcomes in the NSE group, and affect the similar 8-month late loss between the two groups. Further study is warranted to evaluate the revascularization approach in hemodialysis patients with ISR lesions.

Limitations

The study sample size was not sufficient for evaluating clinical outcomes. Additionally, long-term follow-up was not available, and follow-up OCT image was not evaluated. Furthermore, number of OCT pull backs during the procedure, number of times of

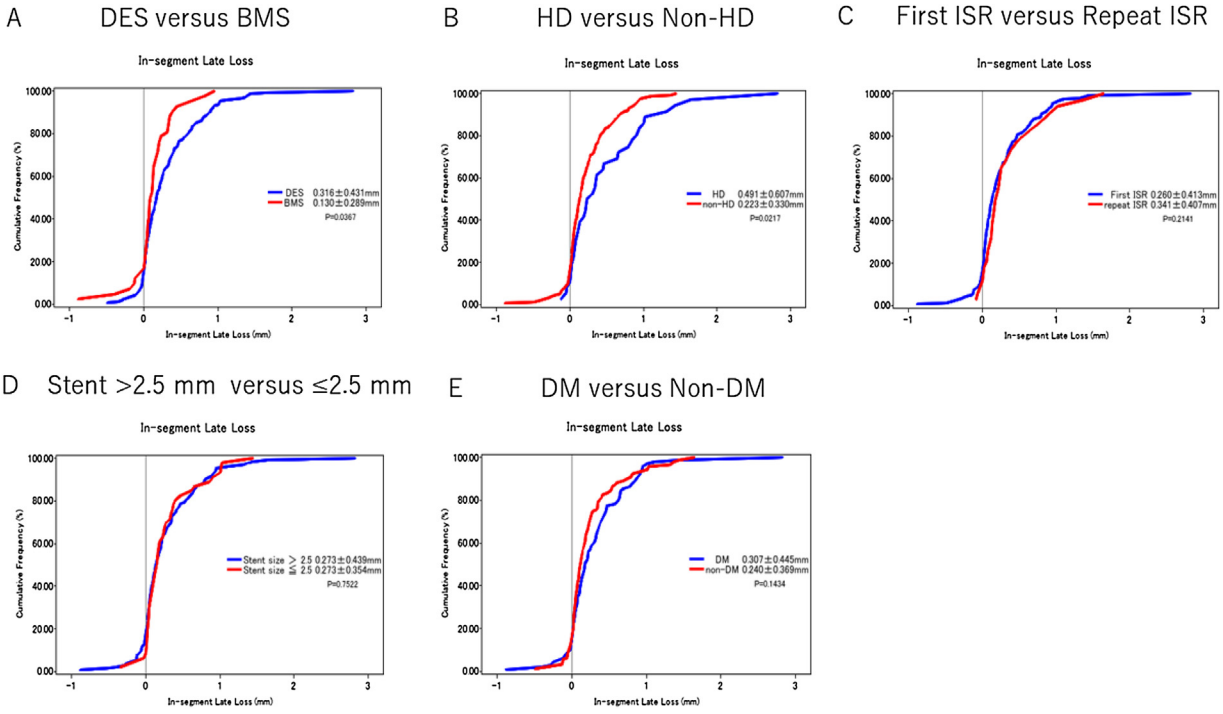

Fig. 3. Cumulative distribution curves for in segment late loss according to the pre-specified subsets.
DES, drug-eluting stent; BMS, bare metal stent; HD, hemodialysis; ISR, in-stent restenosis; DM, diabetes mellitus.

pre-dilatation, and the details of DCB manipulation such as balloon inflation and deflation time were not collected. Finally, potential influence of OCT on lesion preparation strategies was not assessed.

Conclusions

NSE pre-dilatation and high-pressure non-compliance balloon pre-dilatation achieved similar good angiographic and clinical outcomes in the DCB-treated ISR lesions under OCT imaging. However, NSE pre-dilatation was associated with some advantages such as better acute angiographic outcomes and a lower incidence of balloon slippage and geographical miss during the procedure.

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