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Incidence and predictors of drug-eluting stent fractures in long coronary disease

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Abstract

Background: Stent fractures after drug-eluting stent (DES) implantation have not been evaluated sufficiently in patients with long coronary artery disease.
Methods: This study comprised of 415 patients, who were enrolled in the Long-DES-II study and had a complete serial angiography both before and after procedure and also at follow-up. The lesions were ≥25 mm in length and were randomly treated with sirolimus-eluting stents (SES, 210 lesions) or paclitaxel-eluting stent (205 lesions).
Results: DES fracture was identified in 7 lesions (1.7%): 1 minor, 3 moderate, and 3 severe fractures. Most of the fractures occurred in patients who received SES (85.7%) and in the right coronary artery (RCA) lesions (71.4%). Lesions with fracture had a smaller minimal lumen diameter before procedure than lesions without fracture (0.38±0.55 vs. 0.71±0.46 mm, $p=0.043$). However, acute gain (2.28±0.39 vs. 1.44±0.60 mm, $p=0.001$) and late loss (0.81±0.49 vs. 0.42±0.50 mm, $p=0.033$) in analysis segment were greater in lesions with fracture. By multivariate analysis, the independent predictor of fracture was the RCA lesion (Odds ratio, 7.81; 95% CI, 1.45∼42.04; $p=0.017$). Although one patient had an intermediate angiographic narrowing at the fracture site, there was no adverse cardiac event related with fracture.
Conclusions: The incidence of stent fracture in long DES implantation was not common and was associated with SES implantation or RCA lesions. Fortunately, the clinical prognosis of DES fracture was somewhat benign.

Keywords: Coronary artery disease; Drug-eluting stent; Stent fracture

1. Introduction

In recent years, several cases of drug-eluting stent (DES) fractures have been described and suggested as one of the

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potentially serious complications of coronary intervention with DES [1–6]. Although DES fractures reported frequently in long coronary lesions [1], data about the incidence, predictors, and outcomes of DES fractures were limited in selected patients group with long coronary disease. We evaluated the incidence and predictors of DES fracture in patients treated with long DESs enrolled in the Long-DES-II randomized study [7].

2. Materials and methods

Details of the Long-DES-II Study have been described previously [7]. A total of 500 patients with long coronary lesions (≥25 mm) were randomly treated with long (≥32 mm) sirolimus-eluting stent (SES) or paclitaxel-eluting stent (PES). If the patients had multiple lesions meeting the inclusion and exclusion criteria, only 1 target lesion was pre-determined for enrollment. Of these, 415 target lesions (210 SESs and 205 PESs) which had serial and analyzable angiographic data obtained prior to the procedure, post-procedure, and at 6-month follow-up were selected for this study. Coronary stenting was performed by each institutional standard. To achieve optimal stent expansion, use of intravascular ultrasound, atherectomy, predilation, or post-dilation was decided at the operators' discretion. Eighty five patents enrolled in the long-DES II study were not included in our analysis because of death (2 patients), insufficient clinical follow-up (6 patients), or loss of repeat angiography (77 patients). The 2 deaths were suffered from subacute stent thrombosis and septic shock. The 77 patients who did not undergo repeat angiography were free of ischemic symptoms in all patients.

All angiograms were retrospectively reviewed by independent angiographers using the validated automated edge detection system (CASS II, Pie Medical, the Netherlands). Lesion morphology was observed and defined according to the guidelines of American College of Cardiology-American Heart Association [8]. Discontinuity of the stent strut with identifiable gaps was considered as a finding corresponding to the stent fracture from follow-up, which was not noted after procedure in the fluoroscopy [1]. Stent fractures were classified as minor (single strut fracture), moderate (fracture of >1 strut), and severe (complete separation of stent segments) [9]. Quantitative angiographic measurements of target lesions were obtained for both the stented segment only (in-stent), and the region including the stented segment as well as the margins 5 mm proximal and distal to the stent (in-segment). Angiographic restenosis was defined as ≥50% diameter stenosis at follow-up. Target lesion revascularization was defined as any repeat revascularization for ischemia due to restenosis within the stent or within the adjacent 5-mm edges proximal or distal to stent.

Continuous variables were presented as mean (±SD), and compared using Mann–Whitney *U* test. Categorical variables were presented as frequencies or percentages, and compared using Fisher's exact test. To determine the independent predictors of stent fracture, logistic regression analysis was performed, and variables that were predictive at

Table 1
Characteristics of patients with stent fractures.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Age, year	53	42	48	75	49	79	64
Gender	Male	Male	Male	Male	Male	Female	Female
Clinical diagnosis	ACS	Stable	Stable	ACS	ACS	ACS	ACS
Target vessel	RCA	RCA	RCA	LCX	RCA	LAD	RCA
Lesion length, mm	29.5	30.4	25.5	27.8	25.4	58.0	72.2
Tortuosity	None	Mild	Mild	Severe	None	None	Moderate
Calcification	None	None	Mild	None	None	Mild	None
Type of DES implanted	SES	SES	SES	SES	SES	SES	PES
Number of DES	1	1	1	1	1	2	3
Time to angiographic follow-up, months	6	7	6	7	7	6	6
Fractured DES	1	1	1	1	1	1	2
Nominal diameter, mm	3.5	3.5	3.5	2.5	3.5	3.5	2.75
Length, mm	33	33	33	33	33	33	80
Maximal inflation pressure, atm	14	25	10	14	16	20	9
Location of fracture	Body	Body Hinge point	Body Hinge point	Body Hinge point	Body	Body	Body Hinge point
Fracture grading	Moderate	Minor	Severe	Severe	Moderate	Moderate	Severe
Adjunctive balloon post-stenting	No	No	No	Yes	No	Yes	Yes
Nominal diameter, mm				2.5		4.0	2.75
Maximal inflation pressure, atm				14		20	14
Reference diameter pre-procedure, mm	3.05	2.58	3.07	2.89	2.73	3.10	2.62
Maximal device size, mm	3.64	4.0	3.5	2.7	3.76	4.26	3.01
Diameter stenosis post-procedure, %	21	−8	2	8	−4	28	14
Cardiac event	None	None	None	None	None	None	None

ACS = acute coronary syndrome; DES = drug-eluting stent; LAD = left anterior descending artery; LCX = left circumflex artery; PES = paclitaxel-eluting stent; RCA = right coronary artery; SES = sirolimus-eluting stent.

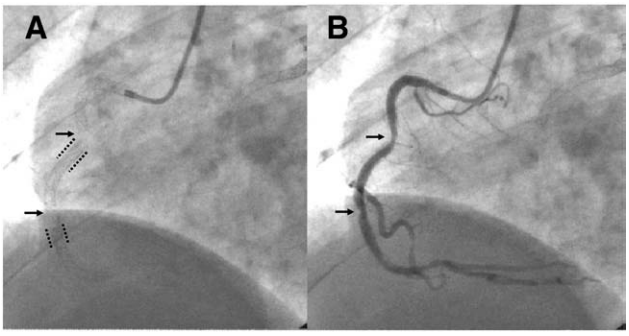

Fig. 1. Angiographic images on two fractures at the right coronary artery in the fluoroscopy (A) and with contrast injection (B). Of the three paclitaxel-eluting stents, there were discontinuity of the stent strut with identifiable gaps at the bodies of the first (proximal arrow, 62% stenosis) and the second (distal arrow, 37% stenosis) stents, which were just proximal to the overlapping site (dashed line).

the 0.2 level by univariate analysis were entered into final multivariate analysis per lesion basis. A p value <0.05 was considered to indicate a significant difference.

3. Results

Stent fracture was identified in 7 from 415 lesions (1.7%) as shown in Table 1. The extent of the stent fractures was graded as 1 minor, 3 moderate, and 3 severe fractures. Most of fractures occurred in patients who received SES (85.7%) and in the right coronary artery (RCA) lesions (71.4%). Fractured stents were initially deployed at 16±5 atmospheres. A post-stent adjunctive dilatation with larger-diameter balloons was used in 3 patients (42.9%). During the clinical follow-up (15±7 months), no death, myocardial infarction or target lesion revascularization occurred in patients with fracture. Although one patient had an intermediate narrowing at the fracture site of PES (Fig. 1), she was discharged without further intervention due to the absence of ischemic symptom or sign.

Tables 2 and 3 depict clinical and angiographic characteristics between patients with and without fractures. SES was more likely to be fractured compared with PES, which did not reach statistical significance (2.9% vs. 0.5%, $p=0.12$). The procedural characteristics, presented by the prevalence of direct stenting, use of adjunctive devices in post-dilation, the number of used stents, and the diameter of used maximal device were not statistically different between the two groups. By quantitative angiographic measurements, lesions with fracture had smaller minimal lumen diameter before procedure than lesions without fracture. However, post-procedure minimal lumen diameter in analysis segment was significantly larger in lesions with fracture due to greater acute lumen gain. At follow-up angiography, late lumen loss was larger in lesions with fracture than lesions without fracture. By multivariate analysis, the following variables were tested: lesion location, types of DES, excessive tortuosity in the proximal segment, pre- and post-procedural minimal lumen diameter in stent, and acute gain. The only independent predictor of fracture was the lesion location of the RCA compared with the non-RCA (Odds ratio, 7.81; 95% CI, 1.45–42.04; $p=0.017$).

Table 2
Baseline and procedural characteristics.

Variable	Fracture (+) ($N=7$)	Fracture (−) ($N=408$)	p value
Age, years	57.3±12.4	60.3±8.9	0.479
Men	5 (71.4%)	227 (55.6%)	1.000
Hypertension	2 (28.6%)	137 (54.8%)	0.251
Diabetes mellitus	3 (42.9%)	139 (34.1%)	0.695
Total cholesterol ≥200 mg/dL	2 (28.6%)	116 (28.4%)	1.000
Current smoker	1 (14.3%)	118 (28.9%)	0.679
Acute coronary syndrome	5 (71.4%)	214 (52.5%)	0.454
Left ventricular ejection fraction, %	59.7±6.9	59.8±8.9	0.684
Target lesion location			
Left anterior descending artery	1 (14.3%)	261 (64.0%)	0.011
Left circumflex artery	1 (14.3%)	44 (10.8%)	0.555
Right coronary artery	5 (71.4%)	103 (25.2%)	0.015
Severe tortuosity	1 (14.3%)	8 (2.0%)	0.143
Severe calcium	0 (0%)	9 (2.2%)	1.000
Thrombus	2 (28.6%)	23 (5.6%)	0.06
Sirolimus-eluting stent	6 (85.7%)	204 (50.0%)	0.12
Direct stenting	0 (0%)	7 (1.7%)	1.000
Number of used stents	1.4±0.8	1.5±0.6	0.568
Use of intravascular ultrasound	4 (57.1%)	176 (43.1%)	0.473
Cutting balloon angioplasty	0 (0%)	6 (1.5%)	1.000
Rotablating atherectomy	0 (0%)	1 (0.2%)	1.000
Debulking atherectomy	1 (14.3%)	15 (3.7%)	0.242
Maximal device diameter, mm	3.55±0.54	3.49±0.41	0.559
Maximal inflation pressure, atm	16.1±4.9	15.5±3.5	0.912
Adjunctive dilatation, post-stenting	3 (43%)	173 (42%)	1.000

Table 3
Quantitative angiographic measurements.

Variable	Fracture (+) ($N=7$)	Fracture (−) ($N=408$)	p value
Reference diameter, mm	2.86±0.21	2.82±0.48	0.633
Lesion length, mm	38.4±18.8	34.6±11.9	0.985
Stent length, mm	42.4±19.0	41.0±13.1	0.928
Minimal lumen diameter, mm			
In-segment			
Before procedure	0.38±0.55	0.71±0.46	0.043
After procedure	2.65±0.39	2.15±0.46	0.008
At follow-up	1.97±0.67	2.00±0.57	0.863
In-stent			
After procedure	2.74±0.35	2.48±0.39	0.102
At follow-up	2.03±0.66	2.20±0.60	0.448
Acute gain, mm			
In-segment	2.28±0.39	1.44±0.60	0.001
In-stent	2.37±0.40	1.78±0.53	0.005
Balloon to artery ratio	1.25±0.20	1.24±0.19	0.834
Late loss, mm			
In-segment	0.81±0.49	0.42±0.50	0.033
In-stent	0.71±0.48	0.26±0.50	0.015
Restenosis			
In-segment	1 (14.3%)	36 (8.8%)	0.482
In-stent	1 (14.3%)	29 (7.1%)	0.411

4. Discussion

The present study demonstrated that DES fracture may not be a common phenomenon in long stent implantation. Use of SES or implantation at the RCA may provide a possible chance toward a higher occurrence of fractures compared with PES or non-RCA lesions, respectively. Despite concerns about potential complication associated with DES fractures, it showed benign outcomes.

Current registries published the incidences of DES fracture ranging from 1.9% to 2.6% [1,2]. However, the incidence in these studies might be under- or over-estimated by limitations that these were retrospective studies with heterogeneous patient characteristics and had low angiographic follow-up rate. To our knowledge, the present study is the first study regarding the phenomenon of DES fracture in a randomized study with mandatory angiographic follow-up. Furthermore, in the present study, all angiograms were retrospectively reviewed by independent angiographers to prevent cases with minor stent fracture being missed during routine angiographic assessment. The incidence of DES fractures in this study was 1.7% with long stented segment, which was comparable to that of unselected registry data [1,2]. This finding implies that long stent implantation, which was considered a potential predictor of stent fracture [1], may not significantly affect on the development of DES fracture. However, in selected lesions treated with long SES, the incidence of fracture was relatively common compared with PES (2.9% vs. 0.5%). This finding led to suggestion about the possible association of stent structure with fracture [2].

The variables that were prone to stent fracture were long stent, vein graft, or the RCA lesion in the previous studies [1–5]. Consistently with these reports, in the present study comprising of long coronary lesions, the lesion location at the RCA increased the risk of fracture by 8-fold compared with non-RCA. In addition, we observed that fracture was prone to the tight lesions where DESs were vigorously expanded. By quantitative angiography, the lesion with fracture had smaller luminal diameter before procedure, but achieved greater acute gain after procedure, than the lesions without fracture. Considering these findings in the present study, mechanical fatigue caused by excessive vessel movement of the RCA during cardiac contraction as well as damaged stent strut by vigorous expansion might predispose DES to fracture [5,6]. In addition, fracture was relatively common at the "hinge" point where the mechanical stress to the DES strut was greatest [10]. Out of seven fractures in this study, four fractures were located at the hinge point which was adjacent to the edge of overlapped stent or the biggest angle in the RCA. In the present study, however, the procedure-related factors were not significantly associated with the occurrence of fracture.

Due to the insufficient delivery of drug, neointimal growth was significantly increased at the fracture site. However, virtually, greater late loss by angiography was not translated to any increase of clinical complication. In the present study, no cardiac event occurred in the patients with fractures. While some studies supported our finding [11,12], others reported that DES fracture was an infrequent cause of repeat revascularization [1,2] or stent thrombosis [3,4]. Different characteristics of study population might be the possible explanation for the discrepancy of outcomes. Our study enrolled patients from the prospective and randomized study in a selected homogeneous population with de novo long coronary lesion. By contrast, database registry studies, that showed conflicting results to the present study, included a broad range of patients with diverse lesion subsets.

The present study had some limitations. First, intravascular ultrasound was not performed in all cases. Therefore, there was a possibility that a few cases with partial DES fracture were not detected by angiographic analysis alone. However, serious fractures which had clinical importance might be thoroughly detected with our careful and comprehensive retrospective review. The angiograms taken at 6 months might underestimate the incidence of DES fractures. Furthermore, while the outcome of fractures was benign, our study was limited to establish the influence of focal stent fracture on long-term clinical prognosis. Therefore, a longer follow-up with angiographic and intravascular ultrasound examination may further reveal the actual incidence and clinical outcomes of DES fracture. Second, this study was still underpowered to assess a significant difference of fracture rates between the two different DESs. Third, although there was an insignificant tendency of higher balloon-to-artery ratio and greater luminal expansion in fracture lesions than in non-fracture lesions, our study might be still underpowered to detect the differences in procedural findings and angiographic consequences of the two groups. Fourth, the follow-up period of 6-month angiography and 1-year clinical observation might not be sufficiently long enough to evaluate the association of DES fracture with long-term clinical outcomes. A recent report showed that a fractured DES with a patent artery progressed to diffuse neointimal hyperplasia 2 years after DES implantation [3]. Therefore, further studies with larger population and longer follow-up are required to overcome our limitations.

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