Predictors and Prognosis of Stent Fracture After Sirolimus-Eluting Stent Implantation

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Background: Stent fracture is a cause of in-stent restenosis (ISR) after sirolimus-eluting stent (SES) implantation, so this study investigated the incidence, predictors and prognosis of stent fracture.

Methods and Results: The 273 consecutive patients (364 lesions) after SES implantation and who had 6–9 month’ scheduled follow-up coronary angiography (CAG) were divided into groups with and without stent fracture. Δangle was defined as the difference in the angle in the target lesion between diastole and systole before the procedure. The incidence of stent fracture was 4.9% (18 of 364 lesions). Δangle in the target lesion was larger in the fracture group (28.3±11.5° vs 12.3±9.0°, P<0.0001). Independent predictors of stent fracture were Δangle and total stent length. The rates of binary restenosis and target lesion revascularization (TLR) were higher in the fracture group (33% vs 4.0%, P=0.0002 and 28% vs 3.5%, P=0.0007, respectively). There were no major adverse cardiac events (MACE) in the fracture group during a mean 24-month follow-up after follow-up CAG.

Conclusions: Predictors of stent fracture were Δangle and total stent length. Although stent fracture was associated with ISR and TLR, it was not associated with MACE during long-term follow-up. (Circ J 2009; 73: 2036–2041)

Key Words: Prognosis; Restenosis; Sirolimus-eluting stent; Stent fracture
Figure 1. Representative case of complete stent fracture. (A) Left coronary angiography shows 75% stenosis in the mid-portion of the left anterior descending artery (LAD) (white arrow). (B) New stenosis after sirolimus-eluting stent (SES) (2.5*18 mm) implantation (white arrow). (C) LAD stenosis treated completely after another SES (2.5*18 mm) deployed from the distal edge of the first stent without a gap (black line, proximal stent; white line, distal stent). (D) Angiography at 9-month follow-up shows mild stenosis with stent fracture (white arrow). (E) Complete fracture on plain fluoroscopy (white arrow, fracture site; black line, proximal stent; white line, distal stent).

Figure 2. Representative case of partial stent fracture. (A) Left coronary angiography shows chronic total occlusion in the proximal portion of the left anterior descending artery (LAD) (white arrow). (B) Sirolimus-eluting stent (SES) (2.5*23 mm) deployed in the mid-portion of the LAD. (C) Another SES (3.0*28 mm) is deployed in the proximal site without a gap using the kissing balloon technique. (D) Final angiography after stent deployment. (E) Angiography at 8-month follow-up shows mild stenosis with stent fracture (white arrow). (F) Partial fracture on plain fluoroscopy (white arrow, fracture site; black line, proximal stent; white line, distal stent). (G) Partial absence of struts on intravascular ultrasound (white arrow). (H) Progression of stenosis at the stent fracture site cannot be seen on second follow-up angiography (24 months after percutaneous coronary intervention) (white arrow).
systole in the angle (Δangle) in the target lesion before PCI (Figure 3). Angiographic images were obtained and the views in which the angle in the target lesion was maximal were selected for the analyses.

With the guiding catheter for magnification calibration and an online system (QCA-CMS version 5.0, Goodman), the minimal luminal diameter (MLD) of the lesion and the diameters of the reference segments were measured before and after stenting, and at the 6–9-month follow-up.

Definition of Major Adverse Cardiac Events (MACE) and Clinical Follow-up

Long-term clinical follow-up data were obtained from outpatient records or telephone interviews. Stent thrombosis was defined as the angiographic confirmation of thrombotic occlusion with at least 1 of the following: (1) continuous chest pain for ≥20 min, (2) ischemic ECG changes, and (3) typical rise and fall of cardiac biomarkers, according to the definitions of the Academic Research Consortium. TLR was defined as repeat percutaneous or surgical intervention of the stented lesion. MACE after scheduled follow-up CAG were defined as death of cardiac origin, late (or very late) stent thrombosis, and TLR because of late restenosis. All patients were followed for a minimum of 8 months (range 8–38 months) after the 6–9-month scheduled follow-up CAG.

Statistical Analysis

Statistical analysis was performed with Stat View 5.0 software (SAS Institute, Cary, NC, USA). Categorical data are presented as frequencies and compared with χ² statistics or Fisher’s exact test. Continuous variables are presented as the mean±SD and compared with the unpaired Student’s t-test or the Mann-Whitney U test. Multiple logistic regression analysis was performed to determine independent predictors of stent fracture. The following variables were tested (all variables except 1 with P<0.1 in univariate analysis): right coronary artery (RCA) location, chronic total occlusion lesion, total stent length, stent overlap, pre-intervention MLD on quantitative CAG (QCA), pre-intervention QCA % diameter stenosis (DS), Δangle and maximal angle in target lesion before PCI. The RCA location was entered into this model, despite P>0.1 on univariate analysis, because several studies have reported that it was an independent predictor of stent fracture. A P value <0.05 was considered significant.

Results

Clinical, Angiographic and Procedural Characteristics

Stent fracture was documented in 18 of the 364 lesions (4.9%: 14 lesions with the complete type, 4 lesions with the partial type). There were no significant differences in the baseline clinical characteristics of the 2 groups (Table 1). Angiographic and procedural characteristics of both groups are shown in Table 2. There were significant differences in the rate of type C lesions (P=0.0006), chronic total occlusion lesion (P=0.019), total stent length (P<0.0001), number of stents per lesion (P=0.0001), rate of stent overlap lesions (P=0.0001), pre-MLD (P=0.004), and pre-% DS (P=0.013). Maximal angle and Δangle in the target lesion were larger in the fracture group than in the non-fracture group (P=0.002 and P<0.0001, respectively).

Table 1. Baseline Clinical Characteristics of the Stent Fracture and Non-Fracture Groups

<table>
<thead>
<tr>
<th></th>
<th>Fracture group (n=18)</th>
<th>Non-fracture group (n=255)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>67±10</td>
<td>67±10</td>
<td>0.924</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>16 (89)</td>
<td>198 (78)</td>
<td>0.379</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>17 (94)</td>
<td>201 (79)</td>
<td>0.136</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>11 (61)</td>
<td>173 (68)</td>
<td>0.556</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>11 (61)</td>
<td>114 (45)</td>
<td>0.177</td>
</tr>
<tr>
<td>Cigarette smoking, n (%)</td>
<td>10 (56)</td>
<td>121 (47)</td>
<td>0.506</td>
</tr>
<tr>
<td>Prior MI, n (%)</td>
<td>7 (39)</td>
<td>112 (44)</td>
<td>0.677</td>
</tr>
<tr>
<td>Prior PCI, n (%)</td>
<td>7 (39)</td>
<td>125 (49)</td>
<td>0.406</td>
</tr>
<tr>
<td>Prior CAGB, n (%)</td>
<td>2 (11)</td>
<td>28 (11)</td>
<td>1</td>
</tr>
<tr>
<td>ACS, n (%)</td>
<td>3 (17)</td>
<td>67 (26)</td>
<td>0.576</td>
</tr>
<tr>
<td>No. of diseased vessels, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>7 (39)</td>
<td>146 (57)</td>
<td>0.129</td>
</tr>
<tr>
<td>2</td>
<td>10 (56)</td>
<td>93 (36)</td>
<td>0.106</td>
</tr>
<tr>
<td>3</td>
<td>1 (6)</td>
<td>16 (6)</td>
<td>1</td>
</tr>
<tr>
<td>Multivessel disease, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>11 (61)</td>
<td>109 (43)</td>
<td>0.129</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>59±11</td>
<td>58±12</td>
<td>0.849</td>
</tr>
</tbody>
</table>

MI, myocardial infarction; PCI, percutaneous coronary intervention; CAGB, coronary artery bypass grafting; ACS, acute coronary syndrome; LVEF, left ventricular ejection fraction.
Independent Predictors of Stent Fracture
By multivariate logistic regression analysis, \( \Delta \) angle (per 1° increase; odds ratio (OR) = 1.183, 95% confidence interval (CI) = 1.087–1.286, \( P < 0.0001 \)) and total stent length (per 1.0-mm increase; OR = 1.059, 95% CI = 1.001–1.121, \( P = 0.045 \)) were identified as independent predictors of stent fracture.

Follow-up CAG and Long-Term Follow-up
Follow-up CAG findings and long-term follow-up results are shown in Table 3. In-stent DS was larger in the fracture group than in the non-fracture group (\( P < 0.0001 \)), and the rates of binary restenosis and TLR were higher in the fracture group (\( P = 0.0002 \) and \( P = 0.0007 \), respectively). In all restenosis lesions with stent fracture, restenosis was observed at the fracture site, and the angiographic pattern of restenosis was focal. Of 5 patients who underwent TLR in the fracture group, 2 had an additional SES implanted, 2 were implanted with paclitaxel-eluting stents, and 1 was treated with balloon angioplasty. One of the patients with an additional SES implanted and the 1 patient undergoing balloon angioplasty had recurrent restenosis with clinical symptoms, and both patients underwent paclitaxel-eluting stent implantation. Another 3 patients with re-implantation of a drug-eluting stent had no recurrent restenosis at follow-up CAG.

In the non-fracture group, 2 patients died of cardiac failure.
at 8 and 16 months, respectively, after the 6–9-month follow-up CAG. 2 patients underwent TLR because of late restenosis at 11 and 36 months, respectively, after the follow-up CAG, and another patient underwent TLR because of very late stent thrombosis at 7 months after the follow-up CAG. In that patient, ticlopidine was discontinued at 9 months after SES implantation and only aspirin was continued.

In the fracture group, except for 3 patients who underwent PCI because of a new lesion of the non-target vessel, there were no MACE during a mean 24-month follow-up after the 6–9–month follow-up CAG. Of 13 patients without TLR in the fracture group, 10 underwent a second follow-up CAG (19.8±4.9 months after PCI), and none had late restenosis because of the late catch-up phenomenon. There was no significant difference between the 2 groups in the incidence of MACE after the follow-up CAG (0% vs 1.4%, P=0.99).

Discussion

The important findings in the present study are that (1) the incidence of stent fracture after SES implantation was 4.9%; (2) independent predictors of stent fracture were the angle in target lesion and total stent length; (3) the rate of in-stent binary restenosis and TLR in fracture lesions was 33% and 28%, respectively; and (4) among cases of stent fracture, none of the patients suffered stent thrombosis, late restenosis or death of cardiac origin during long-term follow-up.

Although previous studies have reported that the incidence of stent fracture after SES implantation is 1.9–3.2%, 9–12 it was higher in the present study, which may be explained as follows. Firstly, the definition of stent fracture in the present study included both complete and partial types. Secondly, 6 stent fracture lesions, which could not be seen on angiography, were detected only on plain fluoroscopy without contrast injection, so it is possible that the incidence of stent fracture in previous studies might have been underestimated because there was no restenosis or obvious stent fracture on angiography. Thirdly, follow-up CAG was not performed in all patients who underwent SES implantation, so the incidence in the present study might be overestimated.

Several studies have suggested that stent implantation in the RCA or saphenous vein graft, overlap stenting, and the presence of a hinge motion are related to stent fracture after SES implantation. 7,9–12,14,15 The present study showed that hinge motion lesions and/or long stenting lesions with stent overlap are high risks for stent fracture, similar to the previous studies. Halkin et al reported that the mechanism of stent fracture might be related to mechanical factors such as strut stretching at the time of deployment followed by repetitive kinking of the stent during the cardiac cycle. 17 Sianos et al reported that overlap stenting might increase the likelihood of stent fracture because of increased axial stiffness at the overlap stenting segment acting as a fulcrum for stent deformation and fracture from vessel movement. 7 Okumura et al reported that a combination of aggressive movement during the cardiac cycle, the angulations at the hinge points, and overstretching and overlapping of stents might play a role in stent fracture. 11 In the present study, stent fractures were more often seen in hinge motion lesions with overlap stenting, and the fracture points of overlap stenting lesions were all located at the border of metal overlap sites. Therefore, stent fracture might be related because differences in stent rigidity often increase at the border of overlapping sites, and because metal fatigue following repetitive kinking of the stent during the cardiac cycle often occurs at the hinge point.

Several case reports have suggested that post dilatation with a larger balloon was related to stent fracture after SES implantation. 17,18 The lesions in those cases were located in the large RCA, and it was necessary to perform post-dilatation to prevent malapposition in the lesions. In the present study, post-dilatation with a balloon ≥4.0 mm was performed in only 4 of 18 lesions. Among the fracture lesions in the present study, 6 were located in the mid-portion of the left anterior descending artery (LAD), and 5 of 8 in the RCA were small to moderate in size. The reference vessel size of these lesions was 2.5–3.0 mm, so post-dilatation with a balloon ≥4.0 mm was not necessary.

It is reported that the rate of binary restenosis in cases of stent fracture after SES implantation is 21–100%, and it has been suggested that neo-intimal hyperplasia resulted from a decrease in local drug delivery at the fracture site. 9–12,15 Halkin et al reported stent fracture in RCA lesion without restenosis and suggested that stent fracture might occur long enough after PCI that the sirolimus effect was not compromised. 17 Min et al reported stent fracture in LAD lesion without restenosis and suggested that the degree of restenosis in fracture cases might be related with the timing of the fracture. 19 In the present study, in-stent binary restenosis in fracture lesions occurred in 6 of 18 lesions (33%), and TLR in 5 lesions (28%). The lower rates of these events in the present study may be explained as follows. Firstly, we carefully analyzed not only lesions with restenosis but also those without restenosis to identify stent fracture by plain fluoroscopy without contrast injection or IVUS use, so our rate of fracture lesions without restenosis might be higher. Secondly, 6 of 18 lesions with stent fracture were located in the LAD, and restenosis occurred in only 1 LAD lesion. Within the fracture cases in the present study, the degree of hinge motion (Δangle) was smaller in the LAD lesion than in the RCA or LCX lesions (22.8±4.9° vs 31.0±13.1°). Metal fatigue in LAD lesions might be less because of the smaller Δangle, and the timing of stent fracture might be late, so most LAD lesions with stent fracture might not result in ISR. Late restenosis related to the late catch-up phenomenon after drug-eluting stent implantation 20–26 and late stent thrombosis at the stent fracture site 10,27 have been reported. Although these events did not occur in the fracture group during long-term follow-up in the present study, close follow-up should be performed in cases of stent fracture.

Study Limitations

Firstly, not every patient underwent follow-up CAG. Furthermore, because follow-up IVUS was not performed in all cases (22 of 273 patients; 8.1%), small stent fractures, such as a single strut fracture, were difficult to detect with fluoroscopy and therefore, the incidence of stent fracture might not be precise. However, the rate of follow-up CAG was high (90%), and the diagnosis of stent fracture required the consensus agreement of 2 independent reviewers. Secondly, we excluded patients who did not undergo follow-up CAG, so cardiac events related to stent fracture and/or thrombosis in the early phase (before follow-up CAG) might have been missed. Thirdly, analysis of the angle in the target lesion was not 3 dimensional, so analysis error within
the tolerance might have occurred. However, angiographic images were obtained in several projections, and images with the maximal angle in target lesions were selected to reduce analysis error. Finally, this was a retrospective, observational analysis from a single center, and the number of patients with stent fracture was small, so the results should be viewed as preliminary and await confirmation by larger clinical trials.

Conclusions

Stent fracture occurs in 4.9% of lesions after SES implantation. The predictors of stent fracture in the present study were larger lesion and total stent length. Stent fracture was associated with ISR and TLR. However, stent fracture was not associated with any MACE in the present study population during a 24-month follow-up subsequent to the scheduled follow-up CAG.

References