

Coronary Stent Fracture: How Frequent It Is? Does It Matter?

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Drug-eluting stents (DES) have dramatically reduced in-stent restenosis compared to bare metal stents (BMS). However, the occurrence of late complications such as stent thrombosis has raised concern over DES use. In addition, there has been increasing awareness of stent fracture (SF) as a potential complication following DES implantation. SF is recognized as one of the contributors to in-stent restenosis¹⁻³ and possibly stent thrombosis.^{4,5} Thus, in the DES era, coronary SF is one of the most intriguing issues.⁶ The objective of this article is to analyze controversial issues that concern the incidence and clinical implications of SF.

How frequent is it?

The reported SF incidence varies widely between different studies. Major factors responsible for this variability are the definition of SF, the method used for SF detection, the type of stent and the population studied. The definition of SF varies from study to study and various morphologic classification schemes have been used. Some studies discriminate between isolated strut fractures and SF,⁷ some include both complete and partial types of fractures,⁸ while others only include severe fractures with complete separation of stent segments.^{1,3}

Methods used for detection: angiography/ intravascular ultrasound

The most commonly used method for SF detection is coronary angiography,² or even plain fluoroscopy without contrast injection.⁸ High resolution X-ray equipment is thought to add accuracy.⁹ Most authors advocate the use of intravascular ultrasound (IVUS) as being of additional help in SF detection, since it detects cases missed by angiography.¹⁰⁻¹³ In contrast, Shaikh et al³ supported high magnification cine-angiography as the best method to diagnose SF and found no additive value for IVUS. In other studies IVUS has been used simply for confirmation of an SF diagnosis suggested by angiography.^{1,14,15} The most important studies of SF incidence using angiography and/or IVUS are listed in Table 1. In a study of 530 patients with clinically driven angiographic follow up, a 1.9% incidence of SF was found in 2728 patients treated with 3636 Cypher (Cordis, Miami Lakes FL, USA) and 1162 Taxus (Boston Scientific Corp., Natick MA, USA) stents.² Popma et al,⁷ in 305 patients with moderately severe coronary artery disease treated with Cypher stents and scheduled for routine angiographic follow up in the SIRIUS study, described isolated strut fractures in 4 patients (1.3%: 1.0% type 1, 0.3% type 2), but no SF according to the definitions used. Kim et al¹⁶ reported an SF incidence

of 1.7% in 415 patients with complete angiographic follow up, who were enrolled in the Long-DES-II study, with lesions ≥ 25 mm, randomly treated with sirolimus-eluting stents (SES) or paclitaxel-eluting stents (PES). In some studies, IVUS was used occasionally for confirmation of an SF diagnosis suggested by angiography. In a retrospective analysis of clinical records and angiographic films of 479 patients with 686 SES who received follow-up coronary angiography, Yang et al¹⁵ described 27 SFs in 22 (3.2%) stents in 18 patients, 16 SFs being documented with IVUS. Chung et al,¹⁴ in a large retrospective study of 6190 Cypher and 1990 Taxus stents with angiographic follow up in 50% and 55% of patients, respectively, described 35 patients (0.84%) with SF in 37 stents. IVUS was used to diagnose SF in 16 lesions (43%). Ino et al,⁸ in 273 consecutive patients (364 lesions) with SES implantation and 6-9 months' scheduled follow up, reported a 4.9% incidence of SF. However, follow-up IVUS was performed in only 8.1% of patients. The use of IVUS increased the rate of SF detection in several reports. Lemos et al,¹⁰ in 192 patients treated with Cypher stents with angiographic follow up in 121 and IVUS in only 11 patients, reported 2 cases of SF. Both fractures were not evident on angiography, but were diagnosed by IVUS. Lee SH et al,¹¹ in a prospective study of 868 patients receiving Cypher stents, observed 10 fractures in 27 patients with in-stent restenosis, with 3 of these fractures detected by IVUS alone. Lee SE et al¹³ described 17 SFs in 1009 patients (1.5%), with 2 of them detected only by IVUS. Only a few studies have a high rate of IVUS use, apart from the angiographic follow up. In 280 patients prospectively studied by Aoki et al,¹ with 91.4% angiographic follow up and 67.1% IVUS study, SF, defined as complete separation of the stent, was observed in 8 out of 307 lesions (2.6%) and 8 out of 256 patients (3.1%). All suspected SF cases were confirmed by IVUS. Okumura et al¹⁷ reported 4 SFs (2.4%) in 169 Cypher-stented lesions, with angiographic and IVUS follow up in 91% and 62%, respectively, while Yamada et al,¹² in a prospective study of 102 Cypher stents with 100% angiographic and IVUS follow up, observed 3 SFs (3%), all detected with IVUS but not observed on angiography. However, lesions in the left main, ostium, or those with excessive tortuosity or angulation were excluded from this study. A much higher incidence of SF was reported by Umeda et al¹⁸ in 422 patients treated with Cypher stents who had a high rate of angiographic follow up (90.5%) and use of IVUS (90.2%). SF was found in

33 out of 430 lesions (7.7%), with complete separation occurring in half of the fractures. It seems that as the rate of IVUS use increases, the incidence of SF detected increases as well, and if IVUS evaluation is not routinely performed during follow up of either symptomatic or asymptomatic individuals, SF is likely to be under-diagnosed. Overall, the reported rate of SF ranges between 0.8% and 7.7%. However, standard angiography and IVUS have been criticized as being of limited ability to visualize stent struts and their integrity over time, leading to underestimation of the true SF incidence.¹⁹

Newer imaging methods

New methods of digital subtraction imaging in the catheterization lab have been developed to enhance the details of stents at the time of implantation. The stent boost (StentBoost Subtract, Philips Healthcare, Best, the Netherlands) is such a method, which sums imaging frames around fixed markers on the balloon catheters delivering the stents and can help in the detection of SF missed by angiography.¹⁹ This technique is, however, invasive, as it requires the insertion of a balloon with markers. More recently, cases of SF detected by multi-detector computed tomography (MDCT) have been reported.²⁰⁻²² In a retrospective evaluation, 64-slice MDCT angiography of 371 patients with 545 stents identified 24 SFs, of which 6 were not detected on conventional angiograms at the initial readings.²³ An *in vitro* comparison of 64-slice MDCT, conventional cine-angiography, and IVUS revealed that CT had high accuracy for the evaluation of coronary SF.²⁴ Recently, Hecht et al²⁵ described the retrospective evaluation of stent gaps in 292 patients with 613 stents who underwent CT angiography. Correlations with coronary angiography were available in 143 patients with 384 stents. Stent gaps representing either SF or stent overlap failure were noted in 16.9% by CT angiography and in 1.0% by coronary angiography. In-stent restenosis was noted by coronary angiography in 46.1% of the stent gaps, and stent gaps by CT angiography accounted for 27.8% of the total in-stent restenosis. According to the authors, stent gaps most likely represent SF in the setting of a single stent, and may represent SF or overlap failure in overlapping stents.

Optical coherence tomography (OCT), with its excellent resolution of 10-15 μm , has been described as confirming the SF diagnosis,^{4,26,27} or even detecting cases missed by angiography.²⁸ Excessive intimal hyper-

plasia, altered stent geometry and complete fracture of the stents with lack of circumferential struts at the fracture site are depicted dramatically on OCT. Finally, at the end of the road is the pathologic assessment of SF. During a review of high-contrast film-based radiographs of 177 consecutive lesions from a DES autopsy registry, SF was documented in 51 (29%).⁵ A high rate of adverse pathologic findings was observed in lesions with grade V (i.e. complete separation) SF. However, this incidence is not likely to be representative of what occurs in living patients, since the study population was from an autopsy study and therefore might have had a higher incidence of DES failures, with stent thrombosis and restenosis rates considerably higher than those reported in clinical settings.

The type of stent studied is of particular significance. Very few, sporadic SFs have been reported with BMS, mostly in saphenous vein grafts.²⁹⁻³¹ In a graft, the mechanical stresses can be very high, depending on the curvature of the graft, the presence of peri-graft fibrosis and the intrathoracic space available. In addition, BMS stenting is not common in diffused long lesions with severe angulation – particularly prone to SF – due to the high risk of restenosis. Also, SF might be overlooked and masked due to the diffuse tissue overgrowth within the BMS, in contrast to DES where the more intense neointimal hyperplasia suppression may make SF more obvious. A late BMS fracture has been detected by MDCT,³² as has a

BMS fracture in a right coronary artery causing acute coronary syndrome.³³ SFs have been reported mostly in Cypher stents, but also in Taxus stents^{13,16,34} and in the newer Zotarolimus^{9,35} and Nobori²⁷ stents. In studies involving both Cypher and Taxus stents, 68 and 3 SFs have been reported, respectively (Table 1). It is apparent that stent visibility for Cypher is better than for Taxus and thus there is an inherent bias against Cypher in the detection of SF. The Cypher is a closed-cell design stent with thin links connecting the cells, playing an important role in even drug distribution. In contrast, the Taxus is an open-cell design stent, and thus the external side of the angled lesion may be opened, but its structure is hard to break.

A significant factor affecting SF incidence is the population studied and the completeness of follow-up angiography.⁸ If SF is looked for in patients with in-stent restenosis a very high incidence is expected. In a retrospective study of 188 consecutive patients with DES in-stent restenosis, Shaikh et al³ reported that 18.6% of patients had “severe” SF with complete separation of stent segments, documented by high resolution cine-angiography during repeat coronary intervention. IVUS was used in 10/35 SFs. Finally, the occurrence of predisposing factors – such as saphenous vein graft stents, right coronary artery location, post dilatation with a larger balloon, vessel geometry, a hinge motion and metal overlap – can be expected to alter the frequency of SF.^{1,3,6,15}

Table 1. Incidence of fracture in drug-eluting stents.

Authors	Type of study	IVUS	No of pts	No of angio F/U	No of lesions	No of SF	Cypher/Taxus	Incidence
Angio/sporadic IVUS:								
Lee MS et al ²	Retrospective	No	2728	530	unknown	10	10/0	1.9%
Popma et al ⁷	Retrospective	No	305	305	305	4	4/NA	1.3%
Kim et al ¹⁶	Randomized	No	415	415	415	7	6/1	1.7%
Yang et al ¹⁵	Retrospective	16	479	479	686	27	22/NA	3.2%
Chung et al ¹⁴	Retrospective	16	8180	4189	4189	37	37/0	0.84%
Ino et al ⁸	Retrospective	22	273	273	364	18	18/NA	4.9%
IVUS additive value:								
Lemos et al ¹⁰	Prospective	11	192	121	221	2	2/NA	1.7%
Lee SH et al ¹¹	Prospective	14	868/26ISR	366	1109	10	10/NA	2.7%
Lee SE et al ¹³	Retrospective	2	3365	1009	unknown	17	15/2	1.5%
High rate of IVUS follow up:								
Aoki et al ¹	Prospective	67.1%	280	256	307	8	8/NA	3.1%
Okumura et al ¹⁷	Prospective	62.4%	151	138	169	4	4/NA	2.4%
Yamada et al ¹²	Prospective	100%	56	56	83	3	3/NA	3.1%
Umeda et al ¹⁸	Prospective	90.2%	422	382	430	33	33/NA	7.7%

F/U – follow up; ISR – in-stent restenosis; IVUS – intravascular ultrasound; NA – not applicable; SF – stent fracture.

Does it matter?

It is well recognized that not all SFs are associated with clinical sequelae. Widespread and slow tissue overgrowth inside the stent may mask SF, making it 'silent' and frequently an incidental finding in asymptomatic patients.^{5,6,13} Symptomatic SF can present as clinical restenosis, stent thrombosis,⁴ recurrent angina, myocardial infarction,^{36,37} and even sudden death.³⁸ Maldistribution of the drug due to stent architecture malfunction following SF is implicated in restenosis. Stent thrombosis may result in death prior to hospitalization, so it is possible that some cases of sudden death following DES implantation may result from unrecognized SF. Stent thrombosis and binary restenosis were reported in 1 (10%) and 6 (60%) patients with SF, respectively, after clinically driven repeat angiography, at a median time of 226 days after DES implantation.² On routine follow-up coronary angiography, at a mean time of 15.6 months after DES implantation, restenosis occurred in 8 (53.3%) patients with SF (limited to type III and IV), mostly focal (52.9% of lesions). Eight (53.3%) of the patients were asymptomatic and no patient suffered from cardiac death during a 20.4 month follow-up period.¹³ Similarly, on routine follow-up coronary angiography 6-9 months after SES implantation, Ino et al⁸ reported 33% in-stent binary restenosis, 28% target lesion revascularization (TLR), and 0% stent thrombosis rates in SF lesions. All patients with SF had an additional follow up for 24 months, but no major adverse coronary events were observed. In patients presenting with clinically reported SFs 9.7 months after SES implantation, in-stent binary restenosis, total occlusion and aneurysm formation were observed in 47.4%, 7.9% and 13.2%, respectively. TLR was required in 52.6% of cases, with a positive linear relationship between TLR rate and SF grade. An analysis of the clinical impact of 37 SFs revealed focal in-stent restenosis in 65% and TLR was required in 30% of the cases.¹⁴ Aoki et al reported 4/8 (50%) SFs requiring TLR, compared with only 11% of those without SF.¹ However, a much lower TLR requirement (9% of SF cases) was reported by Umeda et al.¹⁸ A reason for the aforementioned variable TLR rates is that there continues to be no uniform consensus regarding the best treatment methods for SFs. Stenting even without angiographic evidence of restenosis has been reported.⁷ Repeat stent placement in the region of the stent fracture appears to provide immediate symptom relief.⁶ At 450 days, the cumulative

rate of major adverse cardiac events was not significantly different between lesions with and without SF (9.4% vs. 7.7%). Chhatrwalla et al,³⁹ in a literature review, discovered a total of 289 SFs with available clinical information regarding patient presentation. Patients presented with ST-elevation myocardial infarction (STEMI) or stent thrombosis in 30 (10.4%) cases, and with non-STEMI or unstable angina in 76 (26.3%) cases. Nakazawa et al,⁵ in a study that aimed to assess the incidence and pathologic findings of SF at autopsy, observed 5 (9.8%) and 1 (2%) cases of stent thrombosis and restenosis, respectively, in lesions with documented SF (all grade V). The total rates of adverse pathologic findings, irrespective of fracture severity, were similar between lesions with and without fracture, indicating that low grade SF usually remains clinically silent.

The long-term clinical outcome of patients with documented SF remains unclear and longer follow-up duration is needed. Routine follow up after DES implantation (with high-resolution cine-angiography or IVUS) has been suggested in order to avoid SF underreporting and to assess its clinical consequences.⁴⁰ Additionally, various reports^{4,26-28} advocate the use of OCT for SF detection and possibly better risk stratification and optimal treatment of these patients (including the appropriate duration of dual antiplatelet therapy), as the presence of uncovered and/or misaligned struts at the SF level could lead to more aggressive clinical decisions.

Conclusions

As many SFs remain undetected, albeit without any clinical sequelae, their incidence is most likely underestimated. Large-scale prospective studies of different type of stents, with routine follow up and using a high accuracy imaging modality, are needed to elucidate the exact spectrum of this entity and its clinical impact.

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