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ORIGINAL ARTICLE

Clinical outcomes and optimal treatment for stent fracture after drug-eluting stent implantation

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Summary
Background: Many studies have suggested that in the era of drug-eluting stents (DES) one of the causes of in-stent restenosis is stent fracture (SF). Yet there have been few studies of the major adverse cardiac events and treatment of DES SF.
Methods and results: From September 2003 to May 2008, 3365 patients received successful stent implantation with DES, of whom 1009 patients underwent a follow-up coronary angiography irrespective of symptoms. Seventeen SFs were detected in 15/1009 patients (1.5%). All SF patients were continued on medication with combination antiplatelet therapy, regardless of angina symptoms. If in-stent restenosis at the fractured site was significant, we performed coronary interventions even in patients without ischemic symptoms. Patients were treated with heterogenous DES for restenosis lesions (5/8 patients), and the rest were treated with either homogenous DES (2 patients), or plain old balloon angioplasty (1 patient) or medical treatment (7 patients). None of the SF patients suffered from cardiac death during a follow-up period of 20.4 ± 12.3 months.
Conclusion: If patients with SF were continued on combination antiplatelet therapy irrespective of ischemic symptoms, there would occur a low rate of major adverse cardiac events, especially cardiac death associated with SF.

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Introduction

Drug-eluting stents (DES) have dramatically reduced in-stent restenosis compared to bare-metal stents (BMS) [1], but post-DES restenosis remains a problem. Many studies have suggested that one of the causes of post-DES restenosis is stent fracture (SF) [2,3]. The SF was usually detected at a routine follow-up coronary angiography incidentally, but some cases were related to in-stent restenosis or presented with late stent thrombosis [4—7]. Thus, in the era of DES, coronary SF rarely develops, but is one of the important problems.

There are few studies about the major adverse cardiac events after treatment of DES SF. The objective of the present study was to define clinical outcomes, optimal treatment, and major adverse cardiac events of DES SF.

Methods

Subjects

Three thousand three hundred sixty five patients underwent successful implantation with DES from September 2003 to May 2008 at Chonnam National University Hospital, Gwang-ju, Korea, of whom 1009 patients underwent a follow-up coronary angiography irrespective of symptoms. The SF was easily detected on fluoroscopy or angiography, but some cases were difficult to detect unless investigated by careful angiography review or intravascular ultrasound (IVUS) (Fig. 1). We retrospectively enrolled the patients for study analysis after reviewing the initial angiography and medical records.

Stent fracture

A SF was defined as the complete/incomplete separation of the stent strut by a fluoroscopic image and/or the absence of a stent strut on at least one slice of IVUS image. We classified SF into the following four types: type I, a single strut fracture only; type II, multiple strut fractures at different sites; type III, complete transverse SF without displacement of fractured fragments more than 1 mm during the cardiac cycle; type IV, complete transverse linear type III fracture with stent displacement (Fig. 2) [11,12].

Procedure and antiplatelet treatment

Percutaneous coronary intervention (PCI) was performed according to standard interventional methods. The choice of DES was at the discretion of the operator. All patients who underwent PCI were treated with aspirin (100—300 mg daily) and clopidogrel (75 mg daily for at least 6 months). A triple antiplatelet regimen including cilostazol was used in some patients at the operator's discretion.

Follow-up

The follow-up coronary angiography was performed at 6—9 months or earlier if they had clinical symptoms or evidence of myocardial ischemia after PCI.

Angiographic analysis and definitions

We compared follow-up coronary angiogram with angiogram at the index procedure side by side by two independent interventional cardiologists. The lesion type was classified morphologically according to American Heart American/Association College of Cardiology (ACC/AHA) classification. We measured angulation degree of the vessel at the systolic frame by a protractor. Right coronary artery was measured at the left anterior oblique view, and left coronary artery at the right anterior oblique view. The severity of the angulation degree was divided into mild ($<45^\circ$), moderate (45°—90°), or severe ($>90^\circ$). In-stent restenosis (ISR) at repeat angiography was defined as a diameter stenosis >70% within the stented segment, or a gap between the stent strut formed by a SF. Target lesion revascularization was defined as treatment for recurrent angina and signs of ischemia and a >70% diameter stenosis at the target lesion on follow-up angiography. Major adverse cardiac events were defined as death, myocardial infarction, and target lesion revascularization during the hospital stay or at follow-up.

Statistical analysis

Categorical variables are expressed as number and percentages of patients. Continuous variables were presented as mean $\pm$ SD or median and range values.

Results

In the follow-up coronary angiography in 1009 patients, 17 SFs were detected in 15 patients. Two patients had two SFs in one stent. The mean times from stent implantation to detection of fracture at repeat angiography was 15.6 ± 11.6 months. The SF was verified by coronary fluoroscopy in 13 patients, and detected only by IVUS in 2 patients. The individual data of SF patients are described in Table 1.

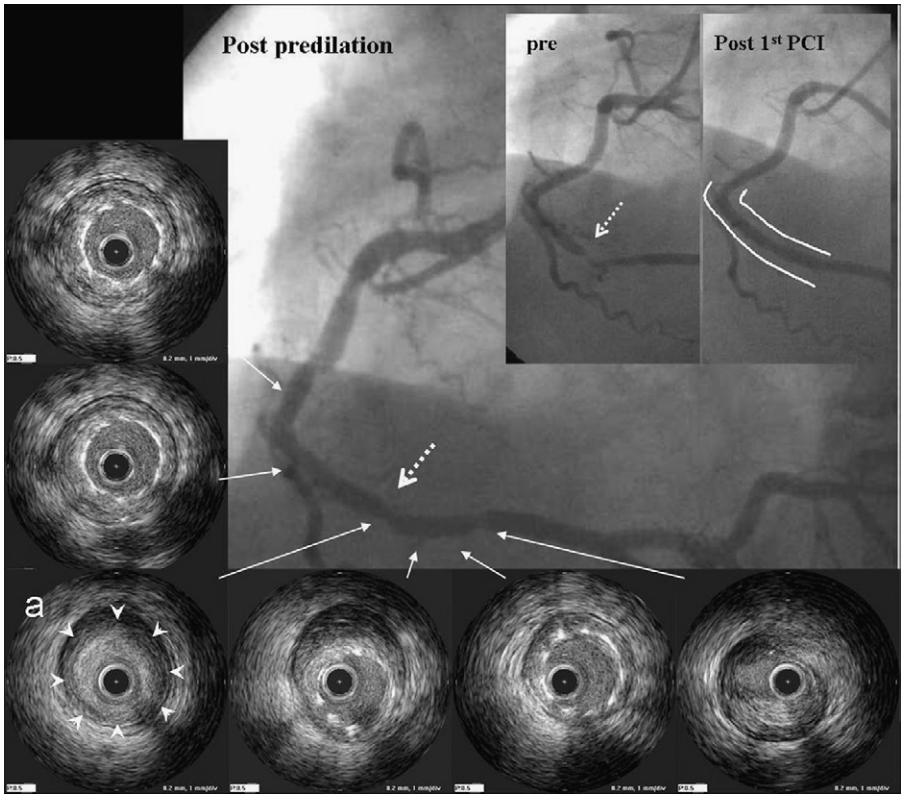

Figure 1 After predilation of right coronary artery (RCA), intravascular ultrasound showed significant neointimal formation and complete stent strut fracture at the point of the angiographic stenosis in the distal RCA. Dotted arrow indicates the stent fracture site. This case was difficult to detect unless investigated by IVUS. (a) A strut-free slice in the stented segment (*arrow heads*). Right side of the inserts shows angiogram of the RCA at first post-stenting and the line represents a schematic diagram of the stent.

Clinical characteristics of patients

The mean age was 59.5 ± 9.1 years. Number of male patients was 10 (10/15 patients, 66.7%). Seven patients had underlying hypertension and 6 had diabetes (46.6%, 40%, respectively). At admission, their diagnoses were old myocardial infarction (1 patients, 6.7%), acute myocardial infarction (5 patients, 33.3%), and angina pectoris (9 patients, 60%).

Procedural and angiographic characteristics

The site of SF was most common in right coronary artery (RCA) (7 patients, 46.6%, 7 lesions, 41.2%), with a similar number in left anterior descending artery (LAD) (6 patients, 40%, 7 lesions, 41.2%), then, left circumflex artery (LCx) (2 patients, 13.3%, 2 lesions, 11.8%). The SF pattern was type III (10 of 17 fractures) and IV (7 of 17 fractures). Most of the fractured stents were sirolimus-eluting stents (SES) (13 patients, 86.7%, 15 lesions, 88.2%), the other were paclitaxel-eluting stents (PES) (2 patients, 13.3%). Mean diameter of fractured stents was 3.0 ± 0.2 mm and length was 33.0 ± 0.2 mm. The mean angulation degree of fractured site was $37.8 \pm 18.3^{\circ}$, over moderate degree ($>45^{\circ}$) was 6 patients, 8 lesions. The restenosis at the site of fracture was associated with majority of SF patients, with significant stenosis (>70%) at the fractured site in 8 patients (53.3%), 10 lesions (58.8%). The restenosis type was mostly focal (9 lesions, 52.9%), only one case was diffuse type (1 lesion, 5.8%). Restenosis rate according to SF type occurred in 7/10 lesions (70%) in SF type III, 3/7 lesions (42.9%) in type IV. There was overlapping stent in 4 patients (26.7%).

Treatment of DES stent fracture and clinical follow-up

Many SF patients in our study had no angina symptoms (8/15 patients, 53.3%), and thus were incidentally detected on the routine follow-up coronary angiography. One patient presented with very late stent thrombosis in the fracture site because he stopped medication for 7 days. If in-stent restenosis at the fractured site was significant, we performed coronary interventions even in patients without ischemic symptoms. In contrast,

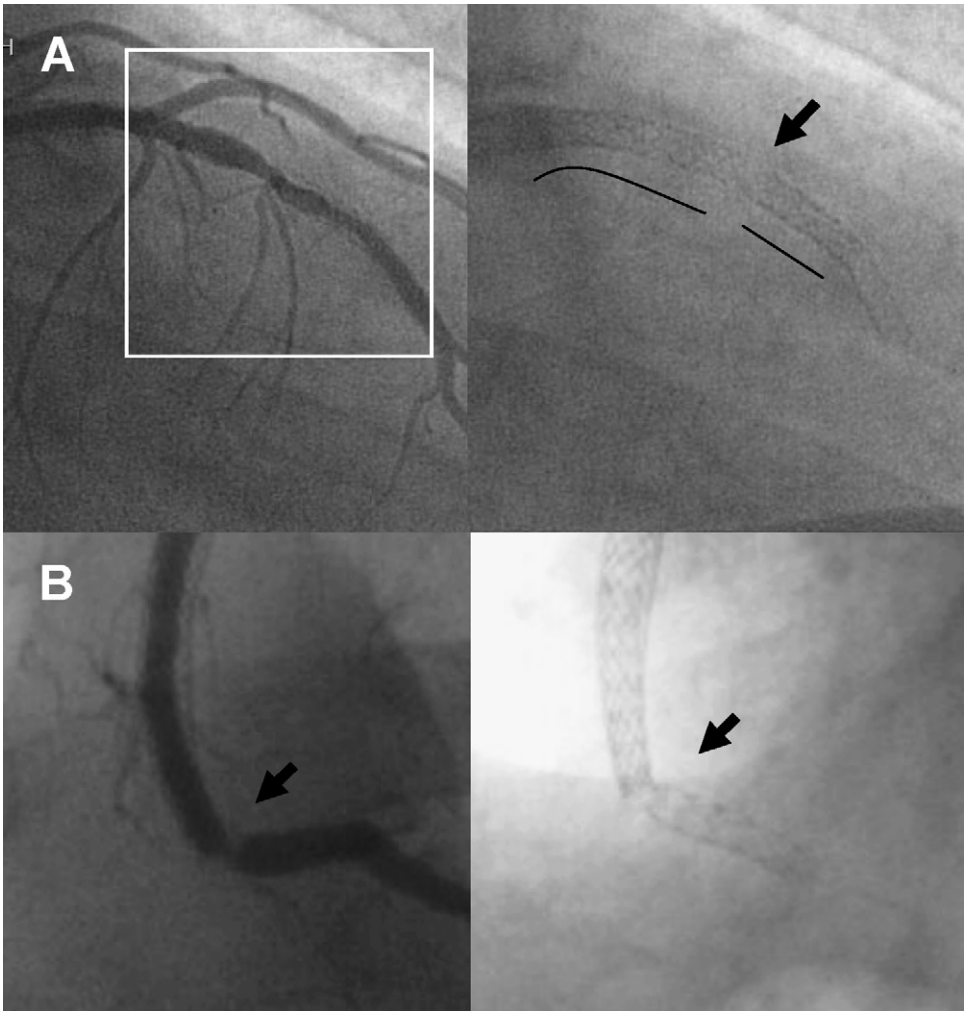

Figure 2 Examples of two different types of stent fracture. (A) Type III defined complete transverse stent fracture (*between black line*) without displacement of fractured fragments more than 1 mm during the cardiac cycle (*black arrow*). (B) Type IV defined complete transverse linear type III fracture with stent displacement (*black arrow*).

even though some patients complained of angina during our clinic follow-up, if there was no significant restenosis at the fractured site, these patients were continued on intensive medical treatment including combination antiplatelet agents. Patients were treated with heterogenous DES for the binary restenosis lesion (5/8 patients), and the rest were treated with either homogenous DES (1 SES, 1 PES) or plain old balloon angioplasty (POBA) (1 patient) or medical treatment (Fig. 3). All SF patients were continued on medication with dual antiplatelet therapy (10/15 patients) or triple antiplatelet therapy (5 patients) regardless of angina symptoms.

Prognosis

Six patients underwent follow-up coronary angiography after detecting SF. Of these, 3 patients continued on medication alone, and 3 patients had a stent deployed in the fractured site. In the follow-up angiography, none of the patients with medication alone showed significant change, nor more aggravated restenosis in the SF lesion compared with previous coronary angiography (Fig. 4). In 1 patient with stent implantation, there was in-stent restenosis, but no recurrent fracture. None of the SF patients suffered from cardiac death during a follow-up period of 20.4 ± 12.3 months after detection of SF.

Discussion

Our study demonstrates the occurrence rate of SF was about 1.5% in the DES. In other reports, the incidence was various (0.84%, 2.6% or 7.7%) in the SES [8—10]. Little is known about the exact incidence in the ''real-world'' since repeat angiography was

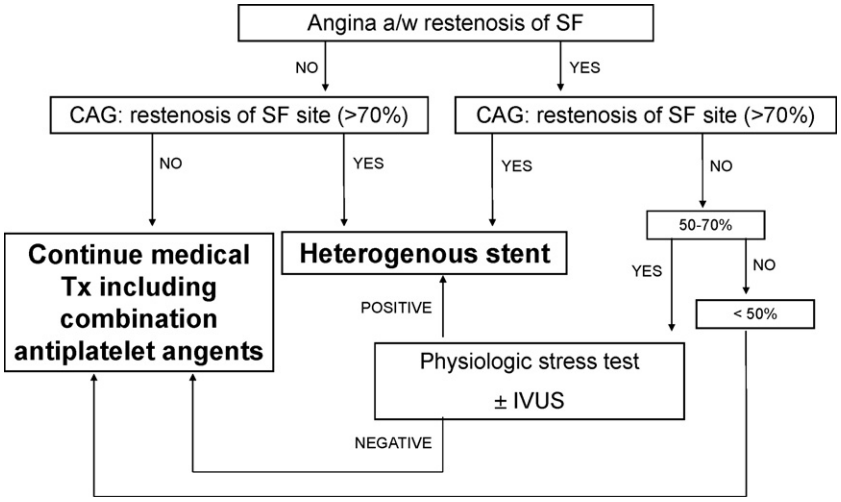

Figure 3 Algorithm for evaluation and optimal treatment of patients having coronary stent fracture. a/w, associated with; SF, stent fracture; CAG, coronary angiography; Tx, treatment; IVUS, intravascular ultrasound.

not performed to all patients who underwent DES implantation, and in some SF, it is difficult to diagnose unless investigated by careful angiography review, or incidentally identified by only IVUS. In our study, the SF was limited to type III/IV. This fact shows that the identification of SF was relatively difficult in the situation of type I/II [11,12]. Therefore, we recommend careful angiography review and/or IVUS at the ISR of DES. In addition, multicenter trials should be further undertaken.

In the present study, SF occurred mostly in SES, with only 2 patients in PES, and it was associated with in-stent restenosis and focal restenosis. These results are similar to previous studies. Even though the PES is an open cell design, the SES is a closed cell design with links connecting the cells, playing an important role in distribution. However, the links are thinner than the frame of the cell and the links are thought to be vulnerable to fracture if the stent receives excessive stress [1]. However, two SFs were observed in PES patients. Both fractures were developed in distal RCA, but the stent lengths were 64 mm and 24 mm, with no significant differences in other factors compared with SES fractures. In our opinion, PES fracture occurred due to the location receiving strong motion such as occurs in distal RCA. SF may represent a potential mechanism for restenosis in DES: local under-dosage due to the SF in combination with mechanical irritation is the most probable cause of focal restenosis associated with SF [2,3]. Similarly, our results showed association with in-stent restenosis. But even though the majority of fractures related to restenosis at the fractured site, the restenosis was

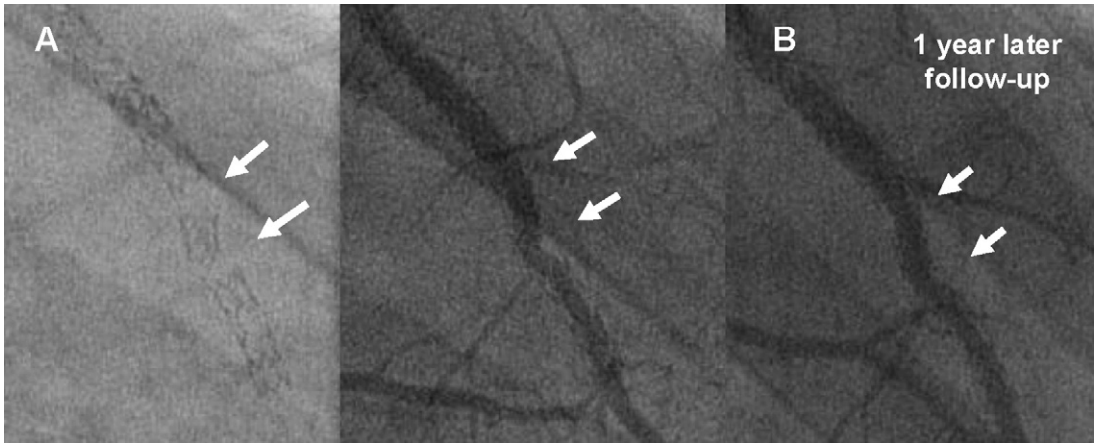

Figure 4 (A) Two type IV stent fractures in one stent (*white arrow*), but there was no significant stenosis. (B) In the follow-up angiography 1 year later, there was no significant change, nor more aggravated restenosis in the stent fracture site (*white arrow*) compared with previous coronary angiography.

Table 1 The individual data of stent fracture patients.

Patient no.	Clinical characteristics							Angiographic, procedural characteristics of index procedure						Follow-up angiography, treatment				
	Age (years)	Sex	DM	HTN	HL	Clinical diagnosis	LVEF (%)	Treated vessel	Lesion type	Maximal angle (degree)	Stent type	Stent diameter (mm)	Stent length (mm)	Presentation	Time interval (days)	SF type	ISR	Treatment	Antiplatelet agents
1	58	F	YES	YES	NO	SA	72	pRCA	B1	55	SES	3.0, 3.0	33, 18	No Angina	231	III	(+)	SES	Dual
2	65	M	NO	NO	NO	OMI	53	pRCA	C	23	SES	3.0	33	No Angina	279	III	(+)	PES	Triple
3	49	M	NO	NO	YES	UA	85	pRCA	C	51	SES	3.0, 3.5	18, 33	No Angina	184	IV	(−)	NA	Dual
4	45	M	YES	YES	NO	AMI	60	mLAD	B2	16	SES	3.0	33	AMI	702	III	(+)	PES	Triple
5	65	M	NO	NO	NO	SA	71	pRCA	C	58	SES	3.0, 3.5	33, 33	No Angina	224	IV	(+)	PES	Triple
6	61	M	YES	YES	NO	AMI	56	dLAD	C	29	SES	3.0, 3.0	28, 33	UA	1033	IV	(−)	NA	Dual
7	43	F	NO	NO	NO	AMI	70	dLAD	B1	52, 47	SES	2.75	33	NO Angina	231	III, IV	(+)	PES	Dual
8	77	F	YES	NO	NO	UA	63	osLCx	B1	60, 68	SES	3.0, 3.5, 3.5	18, 33, 23	UA	894	III, IV	(+), (−)	PES	Dual
9	66	F	NO	YES	NO	AMI	24	pLCx	B2	31	SES	3.0	18	SA	491	IV	(−)	NA	Dual
10	66	F	NO	YES	NO	UA	58	dLAD	B1	11	SES	3.0	23	SA	148	III	(−)	NA	Dual
11	58	M	NO	NO	NO	SA	67	dRCA	C	36	PES	2.75,3.0,3.0	32, 32, 28	SA	292	IV	(−)	NA	Dual
12	60	F	NO	YES	YES	UA	63	pLAD	B1	36	SES	3.5	33	SA	1283	III	(−)	NA	Dual
13	55	M	NO	NO	NO	UA	58	mRCA	B2	12	SES	3.5, 3.0, 2.5	18, 18, 18	SA	665	III	(+)	POBA	Dual
14	56	M	YES	YES	NO	UA	57	mRCA	C	51	PES	3.0	24	SA	212	III	(+)	PES	Triple
15	69	M	YES	NO	NO	AMI	62	mLAD	B2	35	SES	3.5, 3.5	33, 28	SA	180	III	(−)	NA	Dual
Total	59.5 ± 9.1	M: 66%	40.0%	46.6%	13.3%		61.3 ± 13.2			39.6 ± 18.0	SES: 86.7%	3.0 ± 0.2	33.0 ± 0.2		469.9 ± 349.1	III: 58.8%	53.3%		

M, male; F, female; DM, diabetes mellitus; HTN, hypertension; HL, hyperlipidemia; LVEF, left ventricle ejection fraction; pRCA, proximal right coronary artery; mLAD, mid-left anterior descending artery; d-, distal; os-, ostium; LCx, left circumflex artery; SES, sirolimus-eluting stent; PES, paclitaxel-eluting stent; AMI, acute myocardial infarction; UA, unstable angina; SA, stable angina; SF, stent fracture; ISR, in-stent restenosis; (+), significant restenosis; POBA, plain old balloon angioplasty; NA, not applicable.

not always significant. We thought that SF with severe displacement would be more associated with severe restenotic lesions. Interestingly, significant restenosis occurred more in SF type III [7/10 lesions (70.0%)] than type IV [3/7 lesions (42.9%)]. Insignificant restenosis lesions were not treated with any intervention. Even though SF type IV was worse morphology than type III, target lesion revascularization and binary restenosis more frequently occurred in type III.

In some case reports, late stent thrombosis developed in the site of SF and/or coronary aneurysm [4—7]. Previous studies have postulated that exposure of a free metal strut protruding into the vessel lumen clearly could trigger platelet activation and resultant stent thrombosis. SF could involve partial or complete breakage of the stent, the latter event may cause immediate flow obstruction, thrombosis, and myocardial infarction [5]. In the present study, 1 patient presented with very late stent thrombosis in the fracture site because the patient stopped medication for 7 days. Except for this patient with poor medication compliance, there was no patient with stent thrombosis. So we could carefully suggest that if SF patients were continued on medication with dual or triple antiplatelet agents, there would be a very low rate of major adverse cardiac events (post-detection of stent fracture) including stent thrombosis associated with SF. But continued medication with combination antiplatelet agents is very hard during whole life in the real-world. The appropriate duration of combination antiplatelet therapy is needed following SF. In the aspect of DES SF treatment, if in-stent restenosis at the fractured site was significant, we performed coronary interventions even in patients without ischemic symptoms. And we implanted mostly heterogenous stent, performed plain old balloon angioplasty in one case. In the clinical follow-up, there was no cardiac symptom or event during 20.4 ± 12.3 months. However, optimal and detailed strategies should be investigated for SF.

Study limitations

First, this was a retrospective single-center study, so is subject to limitations inherent in this type of clinical investigation. Second, the number of patients was small. Thus, some selection bias cannot be excluded entirely. Third, because follow-up angiographic data were not available in every patient who underwent DES implantation, an accurate frequency of DES fracture could not be obtained.

Conclusions

Of the patients with SF, coronary intervention was performed only when the binary restenosis lesion was significant. During follow-up, patients with SF have continued on combination antiplatelet therapy. There is a very low rate of major adverse cardiac events (post-detection of SF), especially cardiac death associated with SF.

Acknowledgments

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