Editors' Choice

ORIGINAL PAPER

Nagoya J. Med. Sci. **84**. 352–365, 2022
doi:10.18999/nagjms.84.2.352

Very long-term clinical outcomes after percutaneous coronary intervention for complex vs non-complex lesions: 10-year outcomes following sirolimus-eluting stent implantation

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ABSTRACT

Few studies have reported the long-term outcomes (>10 years) following first-generation drug-eluting stent implantation. In this single-center retrospective study, we investigated the very long-term clinical outcomes after first-generation sirolimus-eluting stent (SES) implantation in patients with complex lesions. The study included 383 consecutive patients who underwent initial SES implantation between July 2004 and January 2006; 84 and 299 of these patients reported a history of percutaneous coronary intervention (PCI) for complex and noncomplex lesions, respectively. Complex PCI was defined as having at least one of the following features: left main trunk PCI, implantation of ≥3 stents, bifurcation lesions with implantation of 2 stents, total stent length >60 mm, or chronic total occlusion. The target lesion revascularization (TLR) rate was significantly higher in the complex PCI than in the noncomplex PCI group (29.4% vs 13.0%, P=0.001), and we observed a significant intergroup difference in the late TLR (>1 year) rates (21.6% vs 9.5%, P=0.008). Late TLR continued over 10 years at a rate of 2.4%/year in the complex PCI and 1.1%/year in the noncomplex PCI group. Cox regression analysis revealed that complex PCI was related to TLR both over 10 years (hazard ratio 2.29, P=0.003) and beyond 1 year (hazard ratio 2.32, P=0.01). Cardiac death was more common in the complex PCI than in the noncomplex PCI group, particularly 4 years after PCI (15.8% vs 7.5%, P=0.031). Sudden death was the major cause of cardiac death beyond 4 years in the complex PCI group. These data indicate that long-term careful follow-up is essential for patients implanted with SES, especially those treated for complex lesions.

Keywords: first-generation drug-eluting stent, complex PCI, very-long-term outcomes, coronary artery disease

Abbreviations:
ACS: acute coronary syndrome
DES: drug-eluting stent
PCI: percutaneous coronary intervention
SES: sirolimus-eluting stent
TLR: target lesion revascularization
TVR: target vessel revascularization

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INTRODUCTION

Compared with bare-metal stents, first-generation drug-eluting stents (DES) significantly reduce the incidence of restenosis and the need for revascularization.[1,2] Since their introduction, DES are widely used in clinical practice to treat various lesions, including those that are complex in nature.[3-6] However, in contrast to the clinical course after bare-metal stent implantation, implantation of sirolimus-eluting stents (SES), which represent the most widely used first-generation DES, is known to be associated with late adverse events, such as late target lesion revascularization (TLR) and very late stent thrombosis (even >1 year after implantation).[7-10] Despite ongoing concerns regarding DES-induced late adverse events, there is lack of data on the long-term safety and effectiveness of DES implantation in patients with complex lesions.

In this study, we compared the very long-term clinical outcomes (>10 years [median]) after SES implantation between patients with complex and noncomplex lesions.

MATERIALS AND METHODS

Study population

We retrospectively investigated 493 consecutive patients who underwent initial SES (CypherTM, Cordis Corp., Johnson&Johnson, Miami Lakes, FL, USA) implantation at Handa City Hospital between July 2004 and January 2006. All procedures were performed based on standard procedural guidelines. The duration of maintenance dual-antiplatelet therapy was at the discretion of the treating physician. Following were the exclusion criteria for this study: a history of bypass graft percutaneous coronary intervention (PCI) (n=8), a history of in-stent lesion PCI (n=11), and unavailability of complete follow-up data (n=91); therefore, 383 patients were enrolled in the study. The study was approved by the local research ethics committee and was performed in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all patients before the PCI procedure.

Complex lesions

Complex lesion PCI was defined as PCI performed in patients who met at least one of the following criteria: left main trunk PCI, implantation of ≥3 stents, bifurcation lesions with implantation of 2 stents, total stent length >60 mm, or chronic total occlusion.[11,12] Left main trunk PCI was defined as PCI performed for left main trunk lesions without patent coronary artery bypass grafts in the left anterior descending or the left circumflex artery. Chronic total occlusion was defined as a totally occluded lesion with complete interruption of antegrade flow (Thrombolysis in Myocardial Infarction flow grade 0) observed for at least 3 months.

Endpoints

The primary endpoints in the study were all-cause and cardiac death, myocardial infarction, stent thrombosis, any coronary revascularization, TLR, and target vessel revascularization (TVR). Cardiac death was defined as a composite of death attributable to acute coronary syndrome (ACS), heart failure, arrhythmia, and sudden death. Stent thrombosis was diagnosed based on the Academic Research Consortium definition.[13] TLR was defined as either PCI or coronary artery bypass grafting necessitated by restenosis or thrombosis of the target lesion along the

proximal and distal edge segments. Late TLR was defined as TLR observed beyond 1 year post-procedure. TVR was defined as repeat revascularization of the target vessel, and any coronary revascularization was defined as revascularization of the target or nontarget vessel. Follow-up data were obtained from patients' medical records.

Statistical analysis

Continuous variables are expressed as means±standard deviations and categorical variables as percentages. Continuous variables were compared using the unpaired Student's t-test or the Mann–Whitney U test based on data distribution, and categorical variables were compared using the chi-square or the Fisher's exact test. Kaplan–Meier analysis was used to estimate the cumulative incidence, and differences were evaluated using the log-rank test. The median duration of follow-up was 3654 days (interquartile range, 1972–4582 days). Landmark analysis was performed at the 1-year landmark point to investigate late events (>1 year); we excluded patients who showed individual endpoint events before the completion of 1 year. The Cox proportional hazards model was used to determine related factors of TVR. All statistical analyses were performed using the SPSS for Windows software, version 18.0 (SPSS, Inc., Chicago, IL, USA). P value <0.05 was considered statistically significant.

RESULTS

Baseline characteristics

Based on the aforementioned definitions, the enrolled patients were categorized into the complex PCI (n=84) and the noncomplex PCI group (n=299). In the complex PCI group, 27 patients (7.0%) underwent PCI of the left main trunk, 51 (13.3%) underwent implantation of ≥3 stents, 14 (3.7%) underwent PCI for coronary bifurcation lesions with implantation of 2 stents, 41 (10.7%) had a total stent length >60 mm, and 20 (5.2%) underwent PCI for chronic total occlusion. The mean age of the entire cohort was 66.3±10.6 years; 289 (75.5%) were men and 192 (50.1%) had diabetes mellitus. Overall, 143 (37.3%) patients underwent primary PCI for ACS.

Table 1 shows the clinical and angiographic characteristics of the study groups. We observed no significant intergroup difference in clinical presentation, except with regard to the prevalence of ACS and previous coronary revascularization. The most common culprit vessel was the left main stem and the left anterior descending coronary artery in the complex and non-complex PCI groups, respectively. Stent lengths were longer and stent diameters smaller in patients in the complex PCI group than in those in the noncomplex PCI group.

Table 1 Baseline characteristics according to PCI complexity

	Complex PCI n=84	**Non-complex PCI n=299**	**P value**
Clinical presentation and history			
Men	63 (75.0%)	226 (75.6%)	1.00
Age (years)	66.3±10.2	66.3±11.0	0.99
Body mass index (kg/m²)	23.4±3.3	23.7±3.7	0.64
Hypertension	60 (71.4%)	207 (69.2%)	0.58
Diabetes	42 (50.0%)	150 (50.2%)	1.00
Dyslipidemia	53 (63.1%)	184 (61.5%)	0.70

Current smoking	18 (21.4%)	87 (29.1%)	0.26
Hemodialysis	3 (3.6%)	8 (2.7%)	0.71
Acute coronary syndrome	23 (27.4%)	120 (40.1%)	0.041
Previous myocardial infarction	17 (20.2%)	28 (9.4%)	0.008
Previous PCI	19 (22.6%)	37 (12.4%)	0.023
Previous CABG	9 (10.7%)	8 (2.7%)	0.004
Angiographic and procedural characteristics			
Number of stents	2.6±0.9	1.3±0.5	<0.001
Total stent length, mm	58.0±24.9	28.4±11.3	<0.001
Minimal stent size<3.0mm	54 (64.3%)	93 (31.1%)	<0.001
Target of LMT	27 (32.1%)	0 (0%)	<0.001
Target of LAD	26 (31.0%)	154 (51.5%)	0.001
Target of LCX	16 (19.0%)	61 (20.4%)	0.88
Target of RCA	31 (36.9%)	99 (33.1%)	0.60

Data are expressed as number (percentages) or as means ± SD.
PCI: percutaneous coronary intervention
CABG: coronary artery bypass graft
LMT: left main trunk
LAD: left ascending artery
LCX: left circumflex artery
RCA: right coronary artery

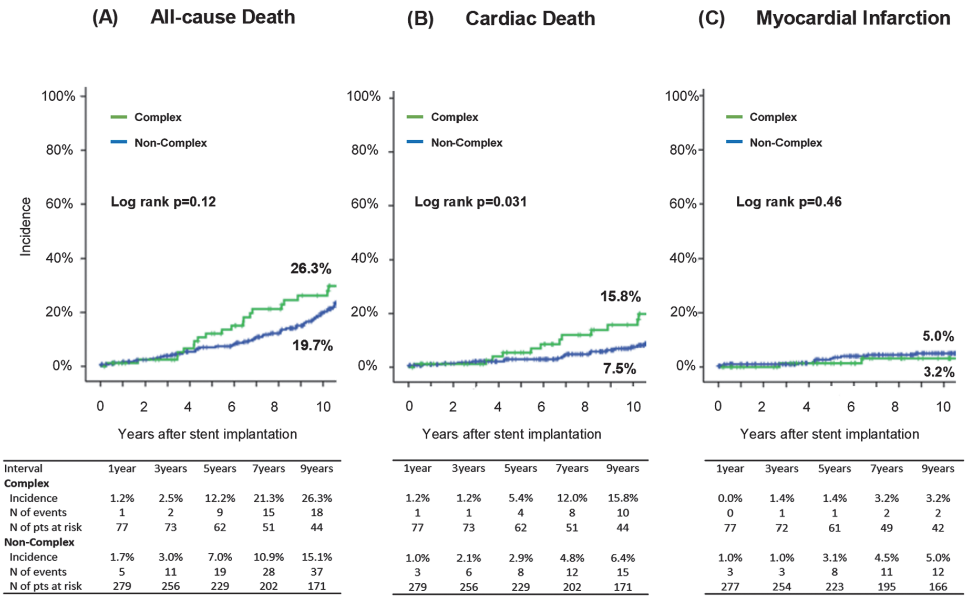
Clinical outcomes

The median follow-up duration was 3654 days (interquartile range 1972–4582 days). Table 2 shows data regarding clinical outcomes observed in this study. The cumulative incidence of cardiac death was significantly higher in the complex PCI than in the noncomplex PCI group (15.8% vs 7.5%, P=0.031). However, no significant intergroup differences were observed in the rates of all-cause death (26.3% vs 19.7%, P=0.12) and myocardial infarction (5.0% vs 3.2%, P=0.46). Kaplan-Meier analysis indicated a higher incidence of all-cause and cardiac death beyond 4 years in the complex PCI group (Figure 1). The increase in the all-cause death rates beyond 4 years was largely attributable to an increase in the cardiac death rates. No intergroup difference was observed in non-cardiac death rates. Supplemental Table 1 shows the specific causes of cardiac and non-cardiac death beyond 4 years. The TLR (29.4% vs 13.0%, P=0.001), TVR (33.6% vs 16.5%, P=0.003), and any coronary revascularization (52.8% vs 33.5%, P=0.001) rates were significantly higher in the complex PCI than in the noncomplex PCI group (Figure 2). Landmark analysis showed a significantly higher rate of late TLR in the complex PCI than in the noncomplex PCI group (21.6% vs 10.1%, P=0.001). Additionally, we observed that late TLR occurred over 10 years at a rate of 2.4%/year in the complex PCI group and 1.1%/year in the noncomplex PCI group. A similar trend was observed with regard to the incidence of TVR beyond 1 year (2.9%/year vs 1.3%/year, P=0.013, Figure 3). As shown in Table 3, Cox regression analysis suggested that complex PCI was a related factor for both TLR through 10 years (hazard ratio 2.29, 95% confidence interval 1.34–3.92, P=0.003) and TLR beyond 1 year (hazard ratio 2.32, 95% confidence interval 1.22–4.40, P=0.01). Complex PCI was also a related factor for both TVR throughout 10 years (hazard ratio 1.889, 95% confidence interval 1.15–3.12, P=0.013) and TVR beyond 1 year (hazard ratio 2.14, 95% confidence interval 1.18–3.87, P=0.012)

(Supplemental Table 2). Among patients with ACS, no intergroup differences were observed in any clinical outcomes, whereas TLR, TVR and any coronary revascularization more frequently occurred in noncomplex PCI group among patients without ACS (Supplemental Figure 1 [patients with ACS], Supplemental Figure 2 [patients without ACS]).

Table 2 Clinical event rates in the complex PCI group and non-complex PCI group through 10 years

	Complex PCI n=84	**Non-complex PCI n=299**
Median follow-up period (days)	3102±1583	3218±1567
All-cause death	25 (29.8%)	66 (22.1%)
Cardiac death	13 (15.5%)	24 (8.0%)
Cardiovascular death	14 (16.7%)	30 (10.0%)
Non-cardiac death	12 (14.3%)	42 (14.0%)
Myocardial infarction	2 (2.4%)	12 (4.0%)
Stent thrombosis(definite/probable)	2 (2.4%)	5 (1.7%)
Target lesion revascularization	21 (25%)	32 (10.7%)
Target vessel revascularization	22 (26.2%)	41 (13.7%)
Any coronary revascularization	36 (42.3%)	83 (27.8%)
Heart failure	4 (4.8%)	37 (12.4%)

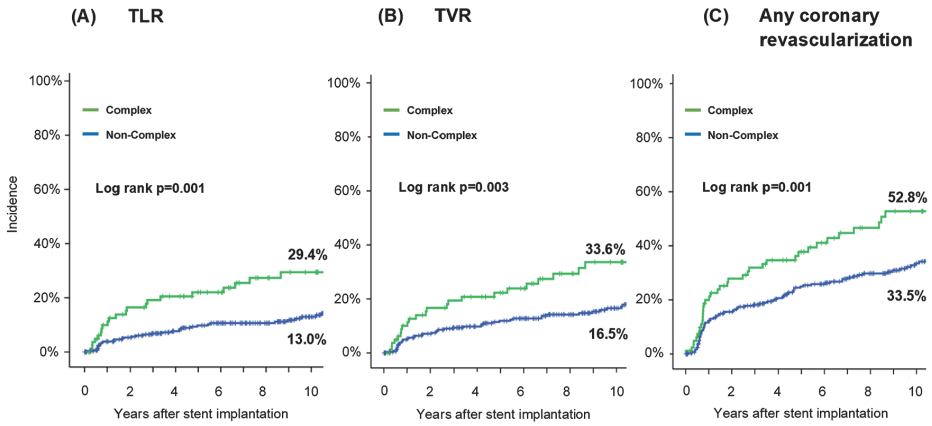


Interval	1year	3years	5years	7years	9years
Complex					
Incidence	1.2%	2.5%	12.2%	21.3%	26.3%
N of events	1	2	9	15	18
N of pts at risk	77	73	62	51	44
Non-Complex					
Incidence	1.7%	3.0%	7.0%	10.9%	15.1%
N of events	5	11	19	28	37
N of pts at risk	279	256	229	202	171

	1year	3years	5years	7years	9years
Incidence	1.2%	1.2%	5.4%	12.0%	15.8%
N of events	1	1	4	8	10
N of pts at risk	77	73	62	51	44
Incidence	1.0%	2.1%	2.9%	4.8%	6.4%
N of events	3	6	8	12	15
N of pts at risk	279	256	229	202	171

	1year	3years	5years	7years	9years
Incidence	0.0%	1.4%	1.4%	3.2%	3.2%
N of events	0	1	1	2	2
N of pts at risk	77	72	61	49	42
Incidence	1.0%	1.0%	3.1%	4.5%	5.0%
N of events	3	3	8	11	12
N of pts at risk	277	254	223	195	166

Fig. 1 Cumulative incidences of all-cause death, cardiac death and myocardial infarction
Fig. 1A: All-cause death
Fig. 1B: Cardiac death
Fig. 1C: Myocardial infarction



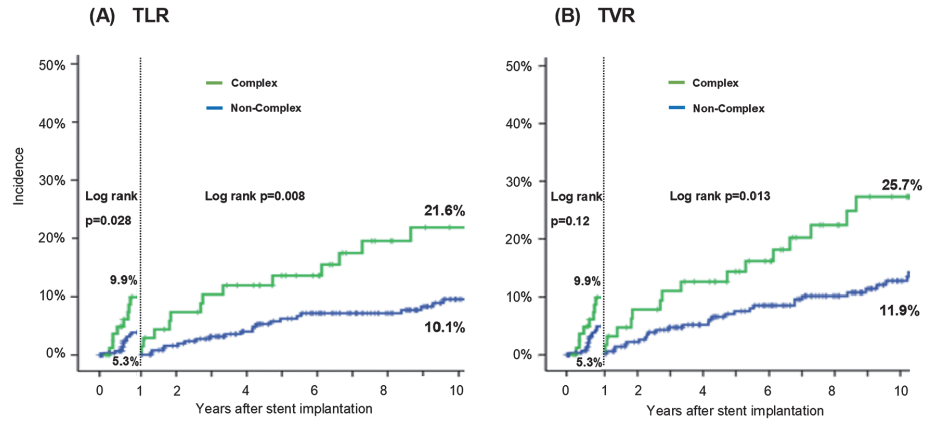
Interval	1year	3years	5years	7years	9years
Complex					
Incidence	9.9%	19.2%	22.0%	25.5%	29.4%
N of events	8	15	17	19	21
N of pts at risk	70	60	51	40	34
Non-Complex					
Incidence	3.9%	6.8%	9.8%	10.7%	11.8%
N of events	11	19	26	28	30
N of pts at risk	269	239	207	184	155

1year	3years	5years	7years	9years
10.1%	19.4%	22.3%	27.4%	33.6%
8	15	17	20	23
69	59	50	38	31
5.3%	9.4%	11.9%	13.7%	15.3%
15	26	32	36	39
265	233	202	177	147

1year	3years	5years	7years	9years
20.0%	31.9%	37.8%	44.7%	52.8%
16	25	29	33	37
62	50	39	29	23
12.3%	18.2%	25.0%	27.7%	30.9%
35	51	67	73	79
246	210	171	147	117

Fig. 2 Cumulative incidences of TLR, TVR and any coronary revascularization

Fig. 2A: TLR
Fig. 2B: TVR
Fig. 2C: Any coronary revascularization
TLR: target lesion revascularization
TVR: target vessel revascularization



Interval	0day	1year	2years	4years	6years	8years	10years
Complex							
Incidence		9.9%	7.3%	11.7%	13.4%	19.3%	21.6%
N of events		8	5	8	9	12	13
N of pts at risk	84	70	63	57	48	37	32
Non-Complex							
Incidence		3.9%	1.5%	3.9%	7.1%	7.1%	9.5%
N of events		11	4	10	17	17	21
N of pts at risk	299	269	255	222	197	174	135

0day	1year	2years	4years	6years	8years	10years
	9.9%	7.3%	11.7%	15.1%	21.1%	25.7%
	5	5	8	10	13	15
84	70	63	57	47	36	30
	5.3%	1.9%	4.7%	7.9%	9.4%	11.9%
	15	5	12	19	22	26
299	265	250	217	192	164	128

Fig. 3 Results of landmark analysis of the incidences of TLR and TVR

Fig. 3A: TLR
Fig. 3B: TVR
TLR: target lesion revascularization
TVR: target vessel revascularization

Table 3 Univariate and multivariate analysis for prediction of TLR through 10 years

	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Men	1.04	0.58–1.90	0.89			
Age	0.98	0.96–1.00	0.065	0.98	0.96–1.01	0.11
Body mass index	1.02	0.95–1.10	0.62			
Hypertension	0.63	0.38–1.08	0.09	0.64	0.37–1.09	0.10
Diabetes	1.17	0.70–1.95	0.55			
Dyslipidemia	1.01	0.59–1.72	0.99			
Current smoking	0.97	0.55–1.70	0.91			
Hemodialysis	3.64	1.32–10.1	0.013	2.59	0.91–7.39	0.075
ACS	0.91	0.54–1.54	0.73			
Complex PCI	2.42	1.44–4.06	0.001	2.29	1.34–3.92	0.003

Multivariate model includes all variables at baseline with $p < 0.10$ by univariate analysis.

Univariate and multivariate analysis for prediction of TLR beyond 1 year

	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Men	2.96	1.06–8.29	0.04	2.76	0.97–7.83	0.057
Age	0.98	0.95–1.00	0.071	0.98	0.95–1.01	0.21
Body mass index	1.0	0.92–1.09	0.99			
Hypertension	0.61	0.33–1.13	0.12			
Diabetes	0.89	0.49–1.63	0.71			
Dyslipidemia	1.01	0.53–1.92	0.97			
Current smoking	1.17	0.62–2.23	0.63			
Hemodialysis	4.29	1.32–13.9	0.015	2.87	0.84–9.73	0.092
ACS	0.87	0.46–1.64	0.66			
Complex PCI	2.31	1.23–4.34	0.010	2.32	1.22–4.40	0.010

Multivariate model includes all variables at baseline with $p < 0.10$ by univariate analysis.
CI: confidence interval
TLR: target lesion revascularization
ACS: acute coronary syndrome
PCI: percutaneous coronary intervention

DISCUSSION

This study highlights that repeat coronary revascularization (represented by late TLR) occurred beyond 1 year after SES implantation, and the incidence of adverse cardiac events over 10 years was significantly higher in the complex PCI than in the noncomplex PCI group.

Owing to rapid technological advances and the availability of novel PCI devices, the number of patients who undergo PCI for coronary lesions of high anatomical complexity has been progressively increasing in recent years.[14,15] Nevertheless, the long-term outcomes of PCI remain inferior to those of coronary artery bypass grafting in patients with lesions of high anatomical complexity compared with those who show lesions of low-to-moderate anatomical complexity.[16-18]

In the present study, the increase in the incidence of TVR from 10.1% at 1 year to 33.6% at 10 years represents a very long-term outcome after SES implantation for complex de novo lesions.

To date, only a few studies have discussed the very long-term outcomes of SES implantation over 10-year follow-up, and these authors observed an increase in the incidence of adverse cardiovascular events at a constant rate over 10 years.[19-22] In the current study, the 10-year incidence rates of cardiac death and repeat coronary revascularization were similar to those reported by previous studies, with the same trend observed beyond 1 year. Interestingly, our study showed a significant increase in the cardiac death rate beyond 4 years. Most cardiac deaths beyond 4 years were attributable to sudden death in the complex PCI group and to congestive heart failure, followed by sudden death and myocardial infarction in the noncomplex PCI group. In view of the relatively low incidence of myocardial infarction observed in the complex PCI group, it is possible that stent thrombosis may manifest as sudden death. Furthermore, we observed that the 10-year cumulative incidence of adverse cardiac events was significantly higher in the complex PCI than in the noncomplex PCI group (classified based on the aforementioned five complex PCI components). Despite poor clinical outcomes observed in some patients in real-world clinical practice, recent guidelines suggest that routine cardiovascular screening tests, such as single-photon emission computed tomography are not useful for cardiovascular risk stratification in patients with asymptomatic coronary artery disease, with a history of PCI.[23] Our findings suggest that risk stratification is useful and necessary for accurate identification of patients at a high risk of adverse cardiovascular events and prompt initiation of appropriate preventive measures. In a study with the longest follow-up after bare-metal stent implantation,[24] the 10-year cumulative incidence of any coronary revascularization was reportedly 53%. Additionally, cardiovascular events observed during follow-up were attributable to both recurrence at the culprit (36%) and non-culprit lesions (34%). Interestingly, the incidence of TLR beyond 1 year was only 0.9%/year. In our study, the 10-year cumulative incidence of any coronary revascularization (52.8%) and TLR rates (29.4%) in the complex PCI group were largely similar to the findings of previous reports; however, the incidence of TLR beyond 1 year remained high at 2.4%/year. Therefore, close long-term follow-up is necessary for the management of patients who undergo complex PCI with SES implantation.

The SYNTAX score is a well-established angiographic risk stratification tool used for objective evaluation of lesions to determine patient suitability for PCI vs coronary artery bypass grafting[25,26]; however, there is lack of consensus with regard to its applicability as a bedside risk prediction tool.[27,28] In contrast to the SYNTAX Score, the five complex PCI components described in this study serve as a simple and standardized long-term risk stratification tool that is useful in real-world clinical practice.

Following are the limitations of this study: (a) The single-center design and relatively small sample size, particularly the small number of patients in the complex PCI group are drawbacks of this study. Large-scale studies are necessary to validate findings in the complex PCI group. (b) Detailed information regarding medications, including the duration of antiplatelet therapy, statins, beta-blockers, and renin-angiotensin system inhibitors was unavailable during follow-up. Notably, the duration of dual antiplatelet therapy may affect long-term outcomes. Long-term dual antiplatelet therapy is associated with a reduced risk of ischemic events, although it increases the risk of bleeding events. First-generation DES and complex PCI are known to predict stent thrombosis; therefore, prolonged dual antiplatelet therapy might have benefitted some patients in this study. Japanese patients show a lower rate of ischemic and a higher rate of bleeding events during antiplatelet therapy, which may affect morbidity and mortality rates. Whether patients who undergo SES implantation should receive prolonged dual antiplatelet therapy remains controversial, and further research is required to clarify this issue. (c) Compared with patients in

the noncomplex PCI group, those in the complex PCI group were more commonly treated with small stents (minimum diameter <3 mm); we cannot exclude the possible effects, if any, on our results owing to this fact. (d) Important anatomical and procedural complexity indicators, such as the SYNTAX score, calcified lesions, and use of debulking devices were not assessed in this study. Therefore, future research should consider the aforementioned limitations.

In conclusion, our long-term observational study in this Japanese population who underwent SES implantation revealed that the cumulative incidence of adverse cardiac events over 10 years was significantly higher in the complex PCI than in the noncomplex PCI group (classified based on 5 complex PCI components described in this study). These data underscore the need for close long-term follow-up of patients who undergo SES implantation, particularly those with complex lesions.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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Supplemental Tables

Supplemental Table 1 Cause of death beyond 4-year after PCI

	Complex PCI n=84	**Non-complex PCI n=299**	**P value**
All-cause death	20 (23.8%)	51 (17.1%)	0.159
Cardiac death	10 (11.9%)	18 (6.0%)	0.067
Sudden death	8 (9.5%)	7 (2.3%)	0.007
Congestive heart failure	2 (2.4%)	9 (3.0%)	0.553
Acute myocardial infarction	0 (0%)	2 (0.7%)	0.609
Non-cardiac death	10 (11.9%)	33 (11.0%)	0.824
Cancer	4 (4.8%)	9 (3.0%)	0.312
Infectious disease	3 (3.6%)	7 (2.3%)	0.381
Stroke	0 (0%)	5 (1.7%)	0.288
Peripheral artery disease	0 (0%)	1 (0.3%)	0.781
Pulmonary disease	0 (0%)	4 (1.3%)	0.370
Gastrointestinal disease	0 (0%)	1 (0.3%)	0.781
Renal disease	1 (1.2%)	0 (0%)	0.219
Haematologic disease	0 (0%)	1 (0.3%)	0.781
Subarachnoid haemorrhage	1 (1.2%)	0 (0%)	0.219
Suffocation	0 (0%)	1 (0.3%)	0.781
Suicide	0 (0%)	1 (0.3%)	0.781
Undetermined death	1 (1.2%)	3 (1.0%)	0.630

Data are expressed as number (percentages).

Supplemental Table 2 Univariate and multivariate analysis for prediction of TVR through 10 years

	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Men	1.16	0.67–2.01	0.605			
Age	0.99	0.96–1.01	0.147			
Body mass index	1.01	0.95–1.10	0.686			
Hypertension	0.60	0.37–0.96	0.033	0.572	0.36–0.92	0.022
Diabetes	1.04	0.66–1.66	0.856			
Dyslipidemia	0.78	0.49–1.23	0.781			
Current smoking	1.08	0.65–1.78	0.763			
Hemodialysis	3.85	1.55–9.58	0.004	3.400	1.36–8.48	0.009
ACS	1.02	0.64–1.64	0.935			
Complex PCI	2.03	1.25–2.03	0.004	1.889	1.15–3.12	0.013

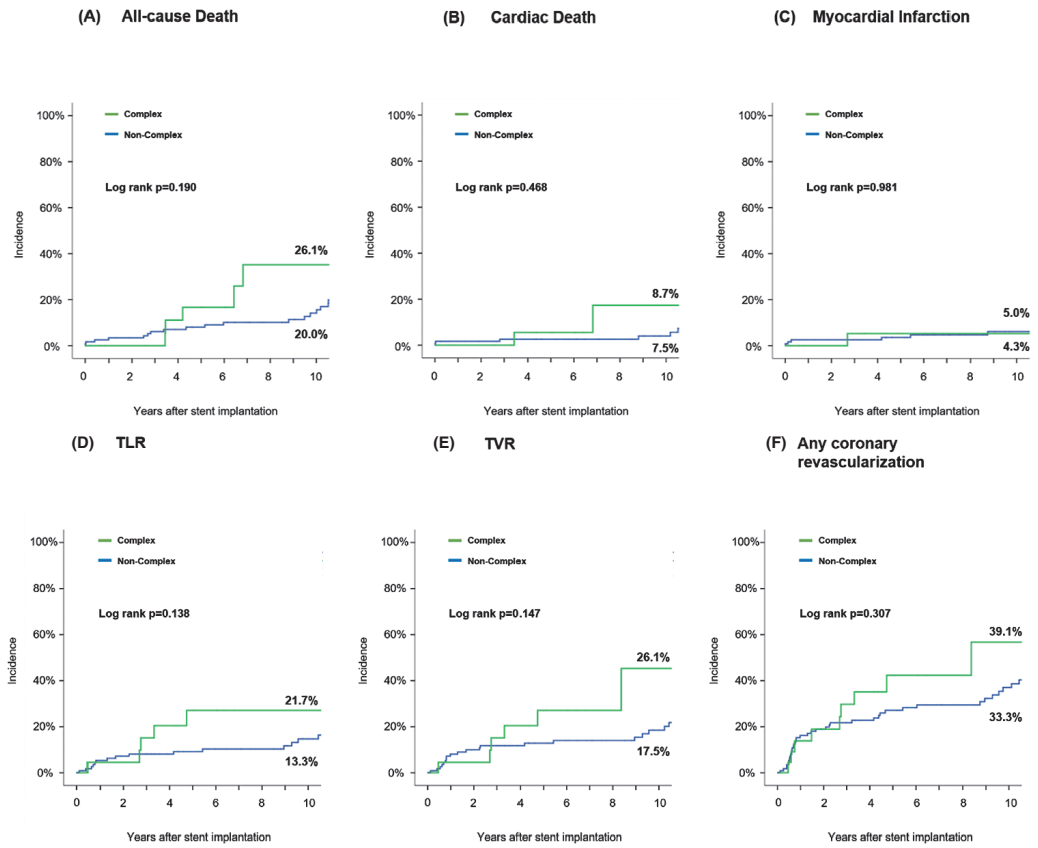
Multivariate model includes all variables at baseline with $p < 0.10$ by univariate analysis.

Univariate and multivariate analysis for prediction of TVR beyond 1 year

	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
Men	2.42	1.03–5.68	0.042	2.41	1.03–5.66	0.043
Age	0.98	0.96–1.01	0.185			
Body mass index	0.99	0.92–1.08	0.850			
Hypertension	0.50	0.29–0.86	0.012	0.47	0.27–0.83	0.009
Diabetes	0.74	0.43–1.30	0.744			
Dyslipidemia	0.75	0.43–1.31	0.313			
Current smoking	1.11	0.62–2.01	0.727			
Hemodialysis	4.98	1.79–13.9	0.002	4.02	1.43–11.3	0.008
ACS	0.89	0.50–1.60	0.704			
Complex PCI	2.07	1.15–3.70	0.015	2.14	1.18–3.87	0.012

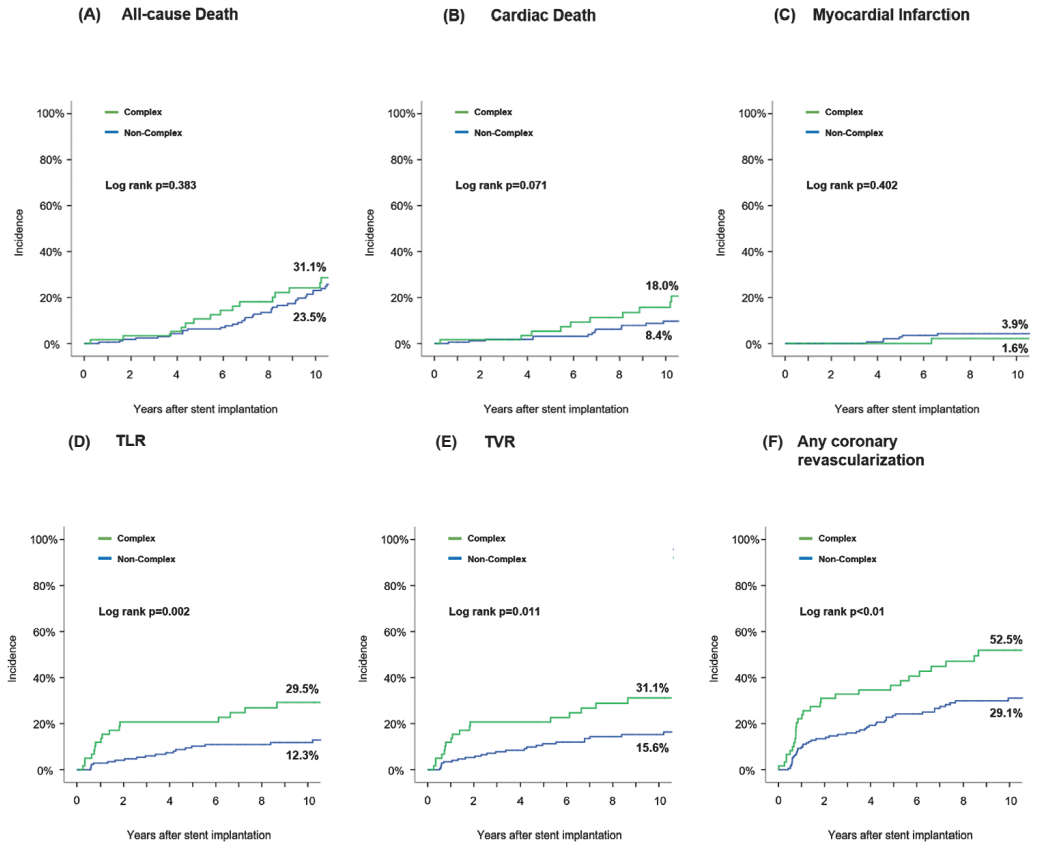
Multivariate model includes all variables at baseline with $p < 0.10$ by univariate analysis.
CI: confidence interval
TVR: target vessel revascularization
ACS: acute coronary syndrome
PCI: percutaneous coronary intervention

Supplemental Figures



Suppl Fig. 1 Cumulative incidences of all-cause death, cardiac death, myocardial infarction, TLR, TVR and any coronary revascularization in patients with ACS

Suppl Fig. 1A: All-cause death
Suppl Fig. 1B: Cardiac death
Suppl Fig. 1C: Myocardial infarction
Suppl Fig. 1D: TLR
Suppl Fig. 1E: TVR
Suppl Fig. 1F: Any coronary revascularization
ACS: acute coronary syndrome



Suppl Fig. 2 Cumulative incidences of all-cause death, cardiac death, myocardial infarction, TLR, TVR, and any coronary revascularization in patients with non-ACS

Suppl Fig. 2A: All-cause death
Suppl Fig. 2B: Cardiac death
Suppl Fig. 2C: Myocardial infarction
Suppl Fig. 2D: TLR
Suppl Fig. 2D: TVR
Suppl Fig. 2F: Any coronary revascularization
non-ACS: non-acute coronary syndrome
TLR: target lesion revascularization
TVR: target vessel revascularization