Differential Prognostic Effect of Intravascular Ultrasound Use According to Implanted Stent Length

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It is unknown whether the use of intravascular ultrasound (IVUS) guidance during percutaneous coronary intervention can attenuate the stent length effect on clinical outcomes. The aim of the present study was to determine the differential prognostic effect of IVUS according to the implanted stent length. We enrolled 3,244 consecutive patients from the Interventional Cardiology Research In-cooperation Society-Drug-Eluting Stents (IRIS-DES) registry who had undergone single or overlapping stent implantation. The primary end point was major adverse cardiac events (MACE; a composite of death, myocardial infarction, and target vessel revascularization). The study population was divided by the tertiles of implanted stent length and IVUS usage. IVUS use was at the discretion of the operator. After adjusting for significant covariates, the stent length was significantly associated with the risk of MACE in the no-IVUS group (hazard ratio 1.13, 95% confidence interval 1.01 to 1.28, p = 0.042) but not in the IVUS group (hazard ratio 1.08, 95% confidence interval 0.97 to 1.20, p = 0.16). In addition, in patients with an implanted stent length of ≤22 mm (n = 998), the risk of MACE was not significantly different between the IVUS group and the no-IVUS group (hazard ratio 1.06, 95% confidence interval 0.50 to 2.28, p = 0.88). In contrast, in patients with a longer implanted stent length, the risk of MACE was significantly lower in the IVUS group than in the no-IVUS group (hazard ratio 0.47, 95% confidence interval 0.24 to 0.92, p = 0.027 for 23 to 32 mm, n = 1,109; hazard ratio 0.57, 95% confidence interval 0.33 to 0.98, p = 0.042 for ≥33 mm, n = 1,137). In conclusion, IVUS usage can attenuate the detrimental effect of the increase in the implanted stent length, supporting IVUS usage, particularly during percutaneous coronary intervention with long stent implantation. **© 2013 Elsevier Inc. All rights reserved.** **(Am J Cardiol 2013;111:829–835)**

Recently, the clinical benefits of intravascular ultrasound (IVUS) guidance in the drug-eluting stent (DES) era have been investigated. Studies have shown a significant reduction in the rate of ischemic complications in patients who have undergone percutaneous coronary intervention (PCI) with IVUS guidance.[1–5] IVUS use during PCI allows for more accurate information about the coronary artery and implanted stents and earlier detection of procedure-related complications and suboptimal stent deployment. Therefore, we hypothesized that IVUS use during PCI could modify the effect of the stent length and thus improve clinical outcomes, particularly in patients who are undergoing long stent implantation. Therefore, the aim of the present study was to determine the differential prognostic effect of IVUS use on the implanted stent length in an unrestricted, multicenter, prospective cohort of patients undergoing PCI in everyday clinical practice, as recorded in the Interventional Cardiology Research In-cooperation Society–Drug-Eluting Stents (IRIS-DES) registry.[6]

Methods

The IRIS-DES registry involves the prospective, multicenter recruitment of 6,066 consecutive patients who underwent PCI with DESs from 46 academic and community hospitals in Korea from April 1, 2008 to June 30, 2010 and for whom complete follow-up data were available for ≥1 year and ≤3 years after PCI. During the enrollment period, sirolimus-eluting or everolimus-eluting stents were used as the default device for PCI. The exclusion criteria were minimal. Patients with cardiogenic shock, malignant disease, or other co-morbid conditions with a life expectancy of <12 months; a known intolerance to the study drugs, antiplatelet drugs, metal alloys, or contrast media;

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See page 834 for disclosure information.

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Table 1
Baseline patient characteristics according to stent length

Variable	Stent Length (mm)			p Value
	≤22 (n = 998)	23−32 (n = 1,109)	≥33 (n = 1,137)	
Age (yrs)	62.6 ± 10.9	62.7 ± 11.1	63.5 ± 10.8	0.12
Men	641 (64%)	731 (66%)	777 (68%)	0.13
Diabetes mellitus	288 (29%)	321 (29%)	407 (36%)	<0.001
Hypertension	586 (59%)	652 (59%)	697 (61%)	0.37
Hyperlipidemia	336 (34%)	375 (34%)	482 (42%)	<0.001
Current smoker	283 (28%)	344 (31%)	343 (30%)	0.40
Previous myocardial infarction	13 (1%)	12 (1%)	22 (2%)	0.22
Previous heart failure	18 (2%)	27 (2%)	15 (1%)	0.15
Renal failure	27 (3%)	30 (3%)	48 (4%)	0.066
Cerebrovascular disease	71 (7%)	74 (7%)	70 (6%)	0.67
Peripheral vascular disease	7 (1%)	6 (1%)	14 (1%)	0.17
Chronic lung disease	28 (2.8)	39 (3.5)	21 (1.8)	0.05
Left ventricular ejection fraction (%)	60.6 ± 10.2	59.4 ± 10.2	58.9 ± 9.4	<0.001
Clinical indication				<0.001
Stable angina pectoris	376 (38%)	415 (37%)	522 (46%)	
Unstable angina pectoris	376 (38%)	358 (32%)	356 (31%)	
Non−ST-segment elevation myocardial infarction	123 (12%)	130 (12%)	124 (11%)	
ST-segment elevation myocardial infarction	123 (12%)	206 (19%)	135 (12%)	
Drug-eluting stents				<0.001
Everolimus-eluting	660 (66%)	703 (63%)	350 (31%)	
Sirolimus-eluting	338 (34%)	406 (37%)	787 (69%)	
Left main narrowing	49 (5%)	25 (2%)	100 (9%)	<0.001
Left anterior descending artery disease	567 (57%)	693 (63%)	717 (63%)	0.006
Bifurcation disease	139 (14%)	195 (18%)	496 (44%)	<0.001
Total obstruction	99 (10%)	164 (15%)	157 (14%)	0.002
Stents (n)	1.00 ± 0.03	1.02 ± 0.13	1.83 ± 0.77	<0.001
Stent length (mm)	16.8 ± 2.0	25.3 ± 2.5	49.5 ± 18.4	<0.001
Stent diameter (mm)	3.24 ± 0.45	3.21 ± 0.43	3.13 ± 0.31	<0.001
Intravascular ultrasound use	395 (40%)	487 (44%)	734 (65%)	<0.001

Data are presented as mean ± SD or absolute n (%).

Hypertension defined as systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, antihypertensive drug use; hypercholesterolemia defined as total cholesterol >200 mg/dl or receiving lipid-lowering treatment; renal failure defined as serum creatinine >2.0 mg/dl.

those treated with a mixture of different DES types; and those with planned surgery necessitating interruption of antiplatelet drugs within 6 months after the procedure were excluded from the present study.

In addition, we also included study-specific exclusion criteria to avoid potential confounding effects on the relation between stent length and clinical outcomes. Patients who underwent stent implantation for multiple lesions and/or in multiple vessels (n = 2,074), patients who had previously undergone PCI (n = 760) or bypass surgery (n = 58), and patients who developed in-stent restenosis treated by stent implantation (n = 30) were excluded. Thus, the remaining 3,244 patients who underwent single or overlapping stent implantation in de novo coronary artery stenosis constituted the current study population.

The study cohort was divided by tertiles of implanted stent length (≤22, 23 to 32, and ≥33 mm) and by IVUS use. IVUS use was considered present when the IVUS examination was performed before the procedure (n = 100) or after the procedure (n = 192), or both (n = 1,324).

The ethics committee at each participating center approved the study protocol, and all patients provided written informed consent to participate.

All interventions were done according to the current practice guidelines for PCI. The operator was responsible for the decision to choose a specific treatment strategy, including the IVUS examination. In addition, the response to the IVUS findings was at the discretion of the treating physician.

Before or during the procedure, all patients received ≥200 mg of aspirin and a 300 to 600-mg loading dose of clopidogrel. Heparin was administered throughout the procedure to maintain an activated clotting time of ≥250 seconds. The administration of glycoprotein IIb/IIIa inhibitors was at the discretion of the operator. After the intervention, all patients were prescribed 100 to 200 mg/day aspirin indefinitely, clopidogrel 75 mg/day for ≥12 months, and other cardiac drugs, according to the judgment of the patient's physician.[7]

The baseline demographics, clinical and angiographic features, and procedural and outcome events were assessed. Clinical follow-up examinations were conducted during hospitalization and at 30 days, 6 months, and 12 months after surgery and every 6 months thereafter. At these visits, data pertaining to the patient's clinical status, all interventions, and outcome events were recorded. The follow-up period extended to July 31, 2011 to ensure that all patients had an opportunity for ≥12 months of follow-up.

The primary end point of the study was major adverse cardiac events (MACE; composite of death, nonfatal

Table 2
Baseline patient characteristics stratified by intravascular ultrasound (IVUS) use

Variables	IVUS Use		p Value
	Yes (n = 1,616)	No (n = 1,628)	
Age (yrs)	61.6 ± 10.6	64.3 ± 11.1	<0.001
Men	1,115 (69%)	1,034 (64%)	0.001
Diabetes mellitus	500 (31%)	516 (32%)	0.64
Hypertension	916 (57%)	1019 (63%)	0.001
Hyperlipidemia	645 (40%)	548 (34%)	<0.001
Current smoker	492 (30%)	478 (29%)	0.50
Previous myocardial infarction	22 (1%)	25 (2%)	0.68
Previous heart failure	26 (2%)	34 (2%)	0.31
Renal failure	48 (3%)	57 (4%)	0.39
Cerebrovascular disease	107 (7%)	108 (7%)	0.99
Peripheral vascular disease	14 (1%)	13 (1%)	0.83
Chronic lung disease	44 (3%)	44 (3%)	0.97
Left ventricular ejection fraction (%)	59.9 ± 8.9	59.3 ± 10.9	0.07
Clinical indication			<0.001
Stable angina pectoris	791 (49%)	522 (32%)	
Unstable angina pectoris	480 (30%)	610 (38%)	
Non−ST-segment elevation myocardial infarction	141 (8%)	236 (15%)	
ST-segment elevation myocardial infarction	204 (13%)	260 (16%)	
Drug-eluting stents			<0.001
Everolimus-eluting	791 (49%)	922 (57%)	
Sirolimus-eluting	825 (51%)	706 (43%)	
Left main narrowing	148 (9%)	26 (2%)	<0.001
Left anterior descending	1019 (63%)	958 (59%)	0.014
Bifurcation disease	568 (35%)	262 (16%)	<0.001
Total obstruction	154 (10%)	266 (16%)	<0.001
Stents (n)	1.44 ± 0.71	1.16 ± 0.43	<0.001
Stent length (mm)	35.5 ± 20.4	26.9 ± 13.3	<0.001
Stent diameter (mm)	3.28 ± 0.38	3.10 ± 0.39	<0.001

Data are presented as mean ± SD or absolute n (%).

Hypertension defined as systolic blood pressure >140 mm Hg, diastolic blood pressure >90 mm Hg, or antihypertensive drug; hypercholesterolemia defined as total cholesterol >200 mg/dl or receiving lipid-lowering treatment; and renal failure as serum creatinine >2.0 mg/dl.

myocardial infarction [MI], and target vessel revascularization). The secondary clinical end points were the individual component of the primary end point: a composite of death and MI, MI, target vessel revascularization, and stent thrombosis.

Death was defined as death from any cause. MI was defined as follows: (1) within the first 48 hours after the procedure: new Q waves and either an elevation in the creatinine kinase-MB fraction or troponin I concentration >3 times the upper limit, and (2) 48 hours after the procedure: any creatinine kinase-MB or troponin increase greater than the upper range limit with or without the development of Q waves on the electrocardiogram. Target vessel revascularization was defined as any percutaneous or surgical revascularization procedure associated with the target vessel. Stent thrombosis was defined according to the Academic Research Consortium definitions,[8] and the definite and definite/probable occurrence of a thrombotic event were regarded as the secondary end points.

Table 3
Two-year clinical outcomes according to implanted stent length and intravascular ultrasound (IVUS) use

Stent Length (mm)	All Patients (n = 3,244)	IVUS (n = 1,616)	No IVUS (n = 1,628)	p Value
Death, myocardial infarction, or target vessel revascularization				
≤22 (n = 998)	3.9*	3.4	4.2	0.57
23−32 (n = 1,109)	5.1	2.9	7.0	0.009
≥33 (n = 1,137)	6.0	4.7	8.2	0.006
p Value	0.13	0.46	0.025	
Death or myocardial infarction				
≤22 (n = 998)	2.0	1.3	2.5	0.26
23−32 (n = 1,109)	3.0	1.4	4.4	0.018
≥33 (n = 1,137)	3.5	2.2	5.7	<0.001
p Value	0.081	0.56	0.010	
Target vessel revascularization				
≤22 (n = 998)	2.1	2.1	2.1	0.98
23−32 (n = 1,109)	2.4	1.6	3.1	0.12
≥33 (n = 1,137)	3.2	2.8	4.3	0.33
p Value	0.50	0.48	0.42	
Stent thrombosis, definite or probable				
≤22 (n = 998)	0.4	0	0.7	0.22
23−32 (n = 1,109)	0.3	0	0.5	0.12
≥33 (n = 1,137)	0.4	0.1	1.0	0.036
p Value	0.59	0.55	0.35	

* Two-year event rate (%) was estimated using Kaplan-Meier survival curve and compared using log-rank test.

Differences between groups were evaluated using Student's *t* test or 1-way analysis of variance for continuous variables and the chi-square test or Fisher's exact test for categorical variables. Cumulative event curves were constructed using Kaplan-Meier estimates and compared with the log-rank test. To have the stent length effect adjusted for statistically or clinically meaningful factors, we used the multivariate Cox proportional regression model as follows. To select statistically significant variables, we used a backward variable selection approach, with the possible adjustment factors presented in Table 1. In the multivariate regression analysis, we also considered the stent length as a continuous type variable and a 3-level categorical variable for analysis completeness. This adjusted stent length effect was re-evaluated according to the IVUS usage group. In contrast, the effectiveness of IVUS usage was tested using the log-rank test within the 3 stent length groups. Furthermore, to reduce the possible effect of potential confounding in the present observational study, we considered an inverse probability of treatment weighting method using a propensity score method.[9] The weighted Cox models for testing the IVUS effects were fitted on the overall patient group and selected patient subgroups according to the implanted stent length. The proportional hazards assumption was confirmed by examination of log [−log(survival)] curves and the partial Schoenfeld residuals tests. We could not detect any significant violations. To

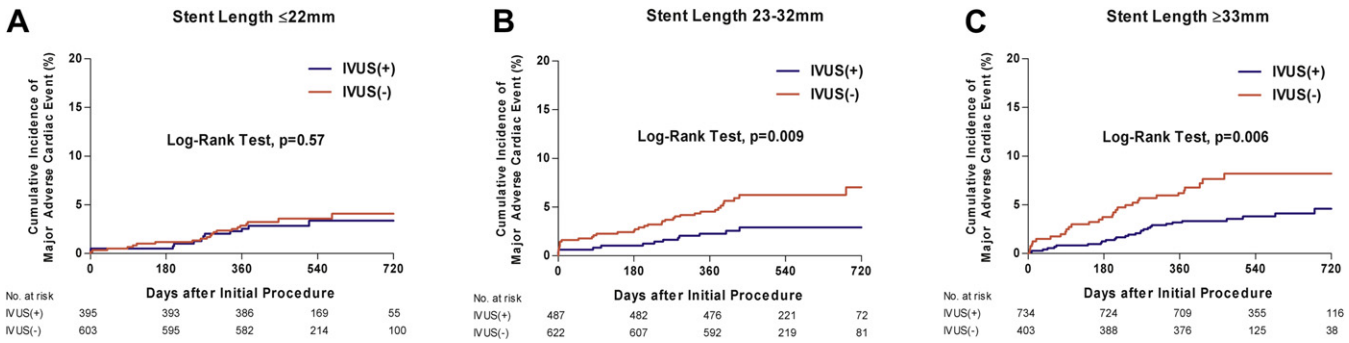

Figure 1. Kaplan-Meier curves of incidence of MACE according to categories of implanted stent length.

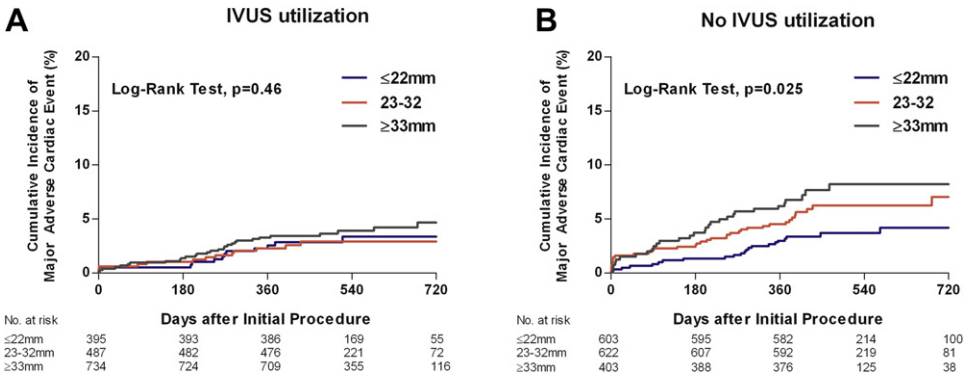

Figure 2. Kaplan-Meier curves of incidence of MACE according to IVUS use.

obtain propensity scores for inverse probability weighting, we adopted an automated procedure using the twang package using generalized boosted regression in the R program (R Foundation, Vienna, Austria). Generalized boosted regression analysis included nonlinear effects and interactions in covariates so we could obtain statistically and numerically stable propensity scores. All reported p values are 2-sided, and $p < 0.05$ was considered statistically significant. SAS software, version 9.1 (SAS Institute, Cary, North Carolina), and the R programming language (R Foundation) were used for the statistical analyses.

Results

From April 2008 to June 2010, 3,244 patients underwent single or overlapping stent implantation in a de novo coronary artery stenosis, and these patients were enrolled in the present study. The average number and length of the implanted stents was 1.30 ± 0.61 and 31.1 ± 17.8 mm, respectively. We used IVUS guidance in 1,616 patients (49.8%) during the PCI procedure.

The patient characteristics according to the tertiles of implanted stent length (≤22, 23 to 32, and ≥33 mm) are listed in Table 1. A longer implanted stent length was associated with a greater incidence of diabetes, hyperlipidemia, stable angina at presentation, a greater risk angiographic profile, and a lower left ventricular ejection fraction. IVUS guidance was used more often in those with a longer implanted stent length than in patients with shorter stents (395 [39.5%], 487 [43.9%], and 734 [64.6%] for the first, second, and third tertiles, respectively, $p < 0.001$).

The patient characteristics stratified by IVUS use are listed in Table 2. IVUS use was associated with younger age, male gender, hyperlipidemia, stable angina at presentation, a greater risk angiographic profile, and a lower incidence of hypertension. In addition, IVUS use was associated with an increased number of implanted stents (1.44 ± 0.71 vs 1.16 ± 0.43, $p < 0.001$), longer stenting (35.5 ± 20.4 mm vs 26.9 ± 13.3 mm, $p < 0.001$), and larger stents (3.28 ± 0.38 vs 3.10 ± 0.39 mm, $p < 0.001$).

Complete follow-up data for major clinical events were obtained for all patients. During the 1 to 3 years of follow-up (mean 1.4 ± 0.4 years), 145 events (4.5%) of the primary end point occurred, including 69 deaths (2.1%), 16 MIs (0.5%), and 76 target vessel revascularizations (2.3%). Ten patients (0.3%) had definite or probable stent thrombosis.

The observed 2-year clinical outcomes according to implanted stent length in the IVUS and no-IVUS groups are listed in Table 3 and Figures 1 and 2. Among the patients in the IVUS group, no significant differences were found according to the tertile of implanted stent length in the risk of MACE. However, among the patients in the no-IVUS group, the incidence of MACE and the composite of death and MI increased significantly with increasing implanted stent length. In the subgroup analysis stratified by implanted stent length, in the short stent length group, no statistically significant difference in the rate of MACE was found. However, in the longer stent length group, the IVUS group had a lower rate of MACE than did the no-IVUS group.

After adjusting for baseline covariates using the weighted Cox model with inverse probability of treatment weighting, the findings noted in the previous paragraph were found to

Table 4
Adjusted hazard ratios of implanted stent length on clinical outcomes

Stent Length (mm)	All Patients (n = 3,244)		IVUS (n = 1,616)		No IVUS (n = 1,628)	
	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Death, myocardial infarction, or target vessel revascularization						
Continuous variable (10-mm increase)	1.10 (1.02−1.20)	0.014	1.08 (0.97−1.20)	0.16	1.13 (1.01−1.28)	0.042
Tertile						
≤22 (n = 998)	Reference		Reference		Reference	
23−32 (n = 1,109)	1.39 (0.90−2.14)	0.14	0.89 (0.41−1.93)	0.77	1.62 (0.95−2.75)	0.075
≥33 (n = 1,137)	1.60 (1.03−2.47)	0.036	1.05 (0.53−2.08)	0.89	1.98 (1.13−3.45)	0.017
Death or myocardial infarction						
Continuous variable (by 10-mm increase)	1.11 (0.99−1.24)	0.08	1.11 (0.94−1.32)	0.22	1.18 (1.01−1.39)	0.035
Tertile						
≤22 (n = 998)	Reference		Reference		Reference	
23−32 (n = 1,109)	1.85 (0.98−3.46)	0.06	1.03 (0.29−3.67)	0.96	2.08 (1.00−4.32)	0.051
≥33 (n = 1,137)	2.39 (1.26−4.52)	0.007	1.52 (0.49−4.72)	0.47	2.96 (1.38−6.34)	0.005
Target vessel revascularization						
Continuous variable (10-mm increase)	1.11 (1.00−1.23)	0.041	1.10 (0.97−1.26)	0.15	1.13 (0.96−1.34)	0.14
Tertile						
≤22 (n = 998)	Reference		Reference		Reference	
23−32 (n = 1,109)	1.11 (0.62−1.99)	0.74	0.81 (0.31−2.18)	0.69	1.33 (0.63−2.78)	0.46
≥33 (n = 1,137)	1.14 (0.65−2.02)	0.65	0.88 (0.38−2.06)	0.77	1.50 (0.68−3.29)	0.32
Stent thrombosis, definite or probable						
Continuous variable (10-mm increase)	1.24 (0.96−1.61)	0.11	1.29 (0.66−2.52)	0.46	1.26 (0.94−1.68)	0.13
Tertile						
≤22 (n = 998)	Reference		Reference		Reference	
23−32 (n = 1,109)	1.78 (0.29−11.05)	0.54	NA	NA	1.89 (0.30−11.97)	0.50
≥33 (n = 1,137)	3.86 (0.72−20.74)	0.12	NA	NA	3.62 (0.63−20.69)	0.15

*Multivariate Cox models were fitted and possible adjustment factors are presented in Table 1. Statistically or clinically significant adjustment factors were remained in the final models.

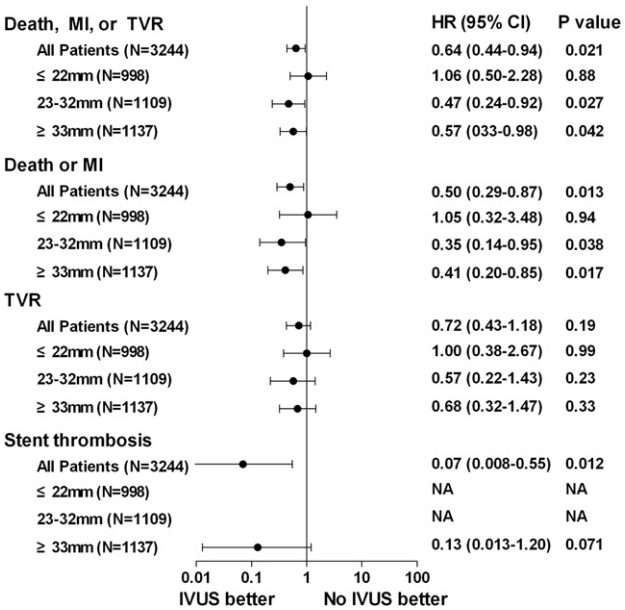

Figure 3. Adjusted hazard ratio for clinical outcomes according to IVUS use in subgroup of implanted stent length. *Inverse probability of treatment weighting methods used for each analysis. NA indicates a separation problem occurred because of 0 event counts for some category levels.

be consistent (Table 4 and Figure 3). Among the patients in the IVUS group, no significant differences were found according to the tertile of implanted stent length in the adjusted hazard ratio of MACE. However, in the no-IVUS group, the risk of MACE significantly increased with increasing implanted stent length. In the subgroup analysis according to the implanted stent length, no statistically different rate of MACE was found in the short stent length group. However, in the longer stent length group, the IVUS group had a lower risk of MACE. In addition, after adjusting the center effect, the overall results were constant.

Discussion

We have demonstrated that IVUS use can modify the stent length effects on clinical outcomes. A previous study has shown that the stent length effects on clinical outcomes were attenuated after the introduction of DES.[10] Hence, more aggressive stent implantations have frequently been performed to provide full stent coverage of the atherosclerotic lesion.[11] However, an increased stent length has still been associated with poorer clinical outcomes, because it can increase the risk of suboptimal stent implantation, which is associated with stent-related thrombotic events that offset the benefits of stent-based treatments. Previous studies have demonstrated that stent underexpansion and stent malapposition were associated with implanted stent length.[12,13] IVUS examinations can, however, detect such mechanical factors earlier and more frequently prompt additional interventions for optimal stent implantation, thereby minimizing the stent-related adverse clinical outcomes associated with increased implanted stent length.

Our findings do not support routine IVUS use, consistent with current PCI guidelines. Conventional IVUS use in relatively low-risk populations does not provide any clinical benefit.[14] In addition, several observational studies in MI populations have shown that IVUS-guided PCI does not appear to reduce adverse clinical outcomes.[15] In contrast, in left main coronary artery disease and bifurcation disease, IVUS-guided PCI has been associated with a lower rate of adverse clinical outcomes.[3–5] In such complex diseases, for which coronary angiography itself has limitations in the evaluation, IVUS allows accurate anatomic characterization, which could optimize stent placement. Taken together, it can be suggested from our findings that IVUS use could have clinical benefit, particularly in patients with hemodynamically stable, but anatomically complex, coronary artery disease. In addition, we extended the clinical indication of IVUS into long stent implantation, another complex coronary artery disease subset.

The main benefit of IVUS usage in the DES era is the reduction of thrombotic complications, rather than a reduction in the restenosis rate. In the bare metal stent era, several randomized trials demonstrated that IVUS use during PCI was associated with larger post-stent minimal lumen and subsequently reduce restenosis and target vessel revascularization.[16] However, owing to the pronounced antirestenotic efficacy of DES, treatment superiority in reducing restenosis is not easily assessed. Instead, DES has been associated with delayed arterial healing and potential inflammation, generating a propensity for stent-related thrombotic events, especially under suboptimal stent implantation conditions within high-risk lesions such as long coronary segments.[17] Therefore, IVUS use was closely associated with the reduction of thrombotic complications. Our present findings also revealed that stent thrombosis occurs less frequently in an IVUS PCI group. In addition, the composite of death and MI showed similar trends. However, every study regarding these issues, including our present report, was observational and, thus, considered hypothesis generating. Therefore, future randomized studies of sufficient sample sizes and prespecified protocols to assess the use of IVUS in DES placement for long lesion treatment are needed.

A major limitation of the present study was its nonrandomized, observational nature. IVUS use during the PCI procedure was at the treating operator's discretion. Therefore, although we adopted vigorous statistical adjustments, a hidden selection bias could be present in our analysis. Second, no specific protocol regarding the IVUS examination was available, although we believe large differences would not have been present between the methods used by different physicians. Third, we assessed the stent lengths according to the manufacturer's specifications and not from the physical measurements made on site. Thus, the real length of the implanted stent might have been overestimated. Fourth, quantitative IVUS assessments were not performed; therefore, we could not assess the relation between quantitative imaging parameters and clinical outcomes. Fifth, the present study reflects IVUS use in routine practice in a geographic region with a high IVUS penetration rate (about 50%) in the current DES era. Finally, we did not report the IVUS findings that could have affected the late outcomes, such as the detection of edge dissections or under expanded stents requiring additional therapy. In addition, we did not find specific lesion characteristics for which IVUS use was particularly useful. Regarding this issue, additional study might be required.

Our findings have extrapolated the benefit of IVUS use during PCI to cases of long stent implantation. To reduce adverse clinical outcomes and obtain more optimal stent results, physicians should consider IVUS examinations, particularly when they attempt to perform long stent implantation.

Disclosures

The authors have no conflicts of interest to disclose.

1. Hur SH, Kang SJ, Kim YH, Ahn JM, Park DW, Lee SW, Yun SC, Lee CW, Park SW, Park SJ. Impact of intravascular ultrasound-guided percutaneous coronary intervention on long-term clinical outcomes in a real world population. *Catheter Cardiovasc Interv* Epub 2011 Jul 29.
2. Roy P, Steinberg DH, Sushinsky SJ, Okabe T, Pinto Slottow TL, Kaneshige K, Xue Z, Satler LF, Kent KM, Suddath WO, Pichard AD, Weissman NJ, Lindsay J, Waksman R. The potential clinical utility of intravascular ultrasound guidance in patients undergoing percutaneous coronary intervention with drug-eluting stents. *Eur Heart J* 2008;29:1851–1857.
3. Patel Y, Depta JP, Novak E, Yeung M, Lavine K, Banerjee S, Lin CH, Zajarias A, Kurz HI, Lasala JM, Bach RG, Singh J. Long-term outcomes with use of intravascular ultrasound for the treatment of coronary bifurcation lesions. *Am J Cardiol* 2012;109:960–965.
4. Park SJ, Kim YH, Park DW, Lee SW, Kim WJ, Suh J, Yun SC, Lee CW, Hong MK, Lee JH, Park SW. Impact of intravascular ultrasound guidance on long-term mortality in stenting for unprotected left main coronary artery stenosis. *Circ Cardiovasc Interv* 2009;2:167–177.
5. Kim SH, Kim YH, Kang SJ, Park DW, Lee SW, Lee CW, Hong MK, Cheong SS, Kim JJ, Park SW, Park SJ. Long-term outcomes of intravascular ultrasound-guided stenting in coronary bifurcation lesions. *Am J Cardiol* 2010;106:612–618.
6. Park DW, Kim YH, Song HG, Ahn JM, Kim WJ, Lee JY, Kang SJ, Lee SW, Lee CW, Park SW, Yun SC, Her SH, Hur SH, Park JS, Kim MK, Choi YS, Kim HS, Cho JH, Lee SG, Park YW, Jeong MH, Lee BK, Lee NH, Lim DS, Yoon J, Seung KB, Shin WY, Rha SW, Kim KS, Tahk SJ, Park BE, Ahn T, Yang JY, Jeong YS, Rhew JH, Park SJ; IRIS-DES Investigators. Outcomes after unrestricted use of everolimus-eluting and sirolimus-eluting stents in routine clinical practice: a multicenter, prospective cohort study. *Circ Cardiovasc Interv* 2012;5:365–371.
7. Park SJ, Park DW, Kim YH, Kang SJ, Lee SW, Lee CW, Han KH, Park SW, Yun SC, Lee SG, Rha SW, Seong IW, Jeong MH, Hur SH, Lee NH, Yoon J, Yang JY, Lee BK, Choi YJ, Chung WS, Lim DS, Cheong SS, Kim KS, Chae JK, Nah DY, Jeon DS, Seung KB, Jang JS, Park HS, Lee K. Duration of dual antiplatelet therapy after implantation of drug-eluting stents. *N Engl J Med* 2010;362:1374–1382.
8. Laskey WK, Yancy CW, Maisel WH. Thrombosis in coronary drug-eluting stents: report from the meeting of the Circulatory System Medical Devices Advisory Panel of the Food and Drug Administration Center for Devices and Radiologic Health, December 7–8, 2006. *Circulation* 2007;115:2352–2357.
9. Robins JM, Hernan MA, Brumback B. Marginal structural models and causal inference in epidemiology. *Epidemiology* 2000;11:550–560.
10. Caputo RP, Goel A, Pencina M, Cohen DJ, Kleiman NS, Yen CH, Waksman R, Tolerico P, Dhar G, Gordon P, Bach RG, Lopez JJ. Impact of drug eluting stent length on outcomes of percutaneous coronary intervention (from the EVENT Registry). *Am J Cardiol* 2012;110:350–355.
11. Lee CW, Park KH, Kim YH, Hong MK, Kim JJ, Park SW, Park SJ. Clinical and angiographic outcomes after placement of multiple overlapping drug-eluting stents in diffuse coronary lesions. *Am J Cardiol* 2006;98:918–922.
12. Kang SJ, Mintz GS, Park DW, Lee SW, Kim YH, Whan Lee C, Han KH, Kim JJ, Park SW, Park SJ. Mechanisms of in-stent restenosis after

drug-eluting stent implantation: intravascular ultrasound analysis. *Circ Cardiovasc Interv* 2011;4:9−14.
13. Hong MK, Mintz GS, Lee CW, Park DW, Park KM, Lee BK, Kim YH, Song JM, Han KH, Kang DH, Cheong SS, Song JK, Kim JJ, Park SW, Park SJ. Late stent malapposition after drug-eluting stent implantation: an intravascular ultrasound analysis with long-term follow-up. *Circulation* 2006;113:414−419.
14. Park KW, Kang SH, Yang HM, Lee HY, Kang HJ, Cho YS, Youn TJ, Koo BK, Chae IH, Kim HS. Impact of intravascular ultrasound guidance in routine percutaneous coronary intervention for conventional lesions: data from the EXCELLENT trial. *Int J Cardiol* Epub 2012 Apr 3.
15. Ahmed K, Jeong MH, Chakraborty R, Ahn Y, Sim DS, Park K, Hong YJ, Kim JH, Cho KH, Kim MC, Hachinohe D, Hwang SH, Lee MG, Cho MC, Kim CJ, Kim YJ, Park JC, Kang JC. Role of intravascular ultrasound in patients with acute myocardial infarction undergoing percutaneous coronary intervention. *Am J Cardiol* 2011;108:8−14.
16. Parise H, Maehara A, Stone GW, Leon MB, Mintz GS. Meta-analysis of randomized studies comparing intravascular ultrasound versus angiographic guidance of percutaneous coronary intervention in pre-drug-eluting stent era. *Am J Cardiol* 2011;107:374−382.
17. Suh J, Park DW, Lee JY, Jung IH, Lee SW, Kim YH, Lee CW, Cheong SS, Kim JJ, Park SW, Park SJ. The relationship and threshold of stent length with regard to risk of stent thrombosis after drug-eluting stent implantation. *JACC Cardiovasc Interv* 2010;3: 383−389.