

Original Article



Effectiveness of a Zotarolimus-Eluting Stent (Resolute Onyx™) in Patients With Diffuse Long Coronary Artery Disease: Intravascular Ultrasound-guided vs. Angiography-guided Percutaneous Coronary Intervention

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ABSTRACT

Background: Only a few studies have evaluated the efficacy of the Resolute Onyx™ zotarolimus-eluting stent (R-Onyx). Therefore, we aimed to assess the effectiveness of the R-Onyx stent in diffuse long coronary artery disease (CAD) and compare clinical outcomes between intravascular ultrasonography (IVUS)-guided and angiography-guided percutaneous coronary intervention (PCI).

Methods: In total, 1,978 patients who underwent PCI with R-Onyx for diffuse long CAD were enrolled in this study. The primary endpoint was the cumulative incidence of major adverse cardiovascular events (MACE), including cardiac death, non-fatal myocardial infarction, and target vessel revascularization. Clinical events were evaluated over a follow-up period of up to 12 months in the IVUS-guided PCI group (n = 1,064) and the angiography-guided PCI group (n = 914).

Results: The mean age of study participants was 65.1 ± 11.9 years; 77.8% were men, and complex target lesions were present in 43.7% of the study population. The overall incidence of 12-month MACE was 2.7%. IVUS-guided PCI significantly reduced both the incidence and the risk of MACE compared to angiography-guided PCI among patients with anatomically complex target lesions (1.5% vs. 4.7%; adjusted hazard ratio, 0.34; 95% confidence interval, 0.14–0.86; *P* = 0.022).

Conclusions: The R-Onyx stent demonstrated favorable 12-month clinical outcomes in patients with diffuse long CAD. Furthermore, IVUS-guided PCI provided superior clinical outcomes compared with angiography-guided PCI, particularly in patients with anatomically complex lesions.

Trial Registration: ClinicalTrials.gov Identifier: [NCT04825886](https://clinicaltrials.gov/ct2/show/study/NCT04825886)

Keywords: Drug-eluting stent; Coronary artery disease

INTRODUCTION

Clinical outcomes in patients with coronary artery disease (CAD) have improved significantly over the past 2 decades, primarily due to advancements in drug-eluting stents (DES) and technical improvements in percutaneous coronary intervention (PCI).^{1,2} Generally, next-generation DES feature thinner stent struts, more biocompatible polymers, and enhanced antiproliferative drug-release kinetics with lower tissue toxicity compared to earlier-generation DES.^{3,4} Among next-generation DES, the Resolute Onyx™ zotarolimus-eluting stent (R-Onyx; Medtronic, Santa Rosa, CA, USA) is representative of the zotarolimus-eluting stent (ZES) family.^{5,6} Ideally, the improved profile of the R-Onyx stent is expected to yield superior clinical outcomes, particularly in complex coronary artery lesions.^{7,8}

Both American and European coronary revascularization guidelines strongly recommend intravascular ultrasonography (IVUS)-guided PCI for left main CAD and for identifying stent-related mechanical issues during stent failure.^{9,10} Additionally, recent major clinical trials have demonstrated the superiority of IVUS-guided PCI over angiography-guided PCI across a broad spectrum of complex coronary artery lesions.^{11,12} Previously, our research group evaluated the efficacy of the Resolute™ Integrity ZES in diffuse long CAD (≥ 25 mm).¹³ Consequently, in the current study, we aimed to assess the clinical efficacy of the R-Onyx stent in diffuse long CAD (≥ 25 mm). Additionally, we compared the clinical outcomes of IVUS-guided PCI vs. angiography-guided PCI using real-world clinical data.

study process, including data collection, and analysis of the results.

Conflict of Interest

All authors have completed the ICMJE uniform disclosure form. Min Chul Kim, Seung Hun Lee, Ung Kim and Hyun Kuk Kim have served as editors of the *Journal of Cardiovascular Intervention* since 2022. Young Joon Hong has been the Editor-in-Chief of the journal since 2022. They were not involved in the review process. The other authors declare no conflicts of interest.

Author Contributions

Conceptualization: Kim DI, Ahn Y; Data curation: Ahn JH, Kim MC, Moon K; Formal analysis: Ahn JH, Kim MC; Funding acquisition: Kim DI, Ahn Y; Investigation: Kim MC, Oh S, Lim Y, Hyun DY, Lee SH, Cho KH, Sim DS, Hong YJ, Kim JH, Kim DK, Yang TH, Cha KS, Chun KJ, Shin ES, Park K, Kim U, Nam CW, Ryu JK, Chae JK, Cho JH, Rhew JY, Lee SU, Oh SK, Kim HK, Park SH, Kang TS, Park SH, Park MW, Kang MG, Park HS, Choi WG; Methodology: Kim MC, Oh S, Lim Y, Hyun DY, Lee SH, Cho KH, Sim DS, Hong YJ, Kim JH, Kim DK, Yang TH, Cha KS, Chun KJ, Shin ES, Park K, Kim U, Nam CW, Ryu JK, Chae JK, Cho JH, Rhew JY, Lee SU, Oh SK, Kim HK, Park SH, Kang TS, Park SH, Park MW, Kang MG, Park HS, Choi WG, Ahn Y; Project administration: Kim MC, Moon K, Oh S, Lim Y, Hyun DY, Lee SH, Cho KH, Sim DS, Hong YJ, Kim JH, Kim DK, Yang TH, Cha KS, Chun KJ, Shin ES, Park K, Kim U, Nam CW, Ryu JK, Chae JK, Cho JH, Rhew JY, Lee SU, Oh SK, Kim HK, Park SH, Kang TS, Park SH, Park MW, Kang MG, Park HS, Choi WG; Resources: Kim DI, Ahn Y; Software: Kim DI, Ahn Y; Supervision: Kim DI, Ahn Y; Validation: Ahn JH, Kim MC; Visualization: Ahn JH, Kim MC; Writing - original draft: Ahn JH, Kim MC; Writing - review & editing: Kim DI, Ahn Y.

METHODS

Study participants and design

We designed a prospective, multicenter, observational study to evaluate the clinical outcomes of patients with diffuse long CAD (≥ 25 mm) who underwent successful PCI using R-Onyx at 29 large-volume PCI centers in Korea, from June 2020 to March 2022. The enrollment of the last patient was completed in March 2021. The inclusion criteria for this study were as follows: patients older than 18 years with CAD who were suitable candidates for PCI with lesions treatable by R-Onyx stent implantation; target lesions characterized by diameter stenosis $\geq 70\%$ by visual estimation with evidence of myocardial ischemia; lesion length ≥ 25 mm; and reference vessel diameter between 2.5 and 4.5 mm. Exclusion criteria were cardiogenic shock, hypersensitivity or contraindications to antiplatelet agents, an active bleeding state, life expectancy less than 12 months, and end-stage kidney disease requiring dialysis. Among 2,000 total patients, 17 were excluded due to insufficient initial baseline clinical data, and 5 were excluded due to loss to follow-up. Finally, 1,978 patients were included and categorized into IVUS-guided PCI ($n = 1,064$) and angiography-guided PCI ($n = 914$) groups (Supplementary Fig. 1).

Definition of complex target lesion

To define the anatomical complexity of target lesions, we adopted the inclusion criteria from the Randomized Controlled Trial of Intravascular Imaging Guidance versus Angiography-Guidance on Clinical Outcomes after Complex PCI (RENOVATE-COMPLEX-PCI) trial and from those recommended by the Society for Cardiovascular Angiography and Interventions.^{12,14} Briefly, for the current study, a complex target lesion was defined as a diffuse long lesion requiring an expected stent length ≥ 38 mm, severe calcification, a bifurcation lesion, in-stent restenosis (ISR), chronic total occlusion (CTO), or left main disease.

Patient management and procedures

Coronary angiography and PCI using the R-Onyx stent were performed according to standard methods. The diameter and length of the R-Onyx stent were selected based on visual estimation. The use of IVUS was determined by operator discretion. All patients received dual antiplatelet therapy consisting of aspirin combined with clopidogrel or another potent P2Y₁₂ receptor inhibitor, such as prasugrel or ticagrelor. Additional medical therapies, including β -blockers, renin-angiotensin system (RAS) blockers, and statins, were also recommended. Periprocedural transthoracic echocardiography was conducted, and left ventricular ejection fraction (LVEF) was evaluated in all patients.

Data collection and outcome measurements

Baseline clinical characteristics—including demographics and cardiovascular risk factors such as hypertension, diabetes, and dyslipidemia—were collected through patient history-taking or review of medical records. During hospitalization, angiographic and procedural characteristics of PCI and discharge medication information were documented. The primary endpoint was the cumulative incidence of major adverse cardiovascular events (MACE), defined as cardiac death, non-fatal myocardial infarction (MI), and target vessel revascularization (TVR), evaluated over a 12-month clinical follow-up period. Secondary endpoints included all-cause death, any repeat revascularization, and stroke. Definitions of all clinical endpoints followed the Academic Research Consortium criteria.¹⁵ All deaths were classified as cardiac deaths unless a definitive non-cardiovascular cause was identified. Non-fatal MI was defined as new-onset chest pain accompanied by electrocardiographic changes

or imaging evidence of new regional wall-motion abnormalities, combined with an elevation of cardiac biomarkers. TVR was defined as any repeat PCI or bypass surgery involving any segment of the target vessel. Any repeat revascularization was defined as recurrent PCI or bypass surgery involving either target or non-target vessels. Stroke was defined as a neurological deficit requiring hospitalization, accompanied by clinically documented brain lesions identified via magnetic resonance imaging or computed tomography. Patients underwent routine follow-up visits at 1, 6, and 12 months after the index procedure through outpatient visits or telephone contact.

Statistical analysis

Categorical variables were presented as numbers (percentages) and compared using the χ^2 test. Continuous variables were presented as means $\pm$ standard deviations and compared using the Student's t-test or the Mann-Whitney U test.

Cumulative event rates were estimated by the Kaplan-Meier method and compared using the log-rank test. The risk associated with each clinical endpoint was compared using a Cox proportional hazards regression model adjusted for covariables that demonstrated statistical significance ($P < 0.1$) in the univariate analysis or were considered clinically important in the multivariate model. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated.

All statistical analyses were performed using SPSS software, version 25 for Windows (SPSS-PC, Armonk, NY, USA). All tests were 2-tailed, and P values < 0.05 were considered statistically significant.

Ethical statement

The study protocol was conducted in accordance with the Good Clinical Practice Guidelines and the Declaration of Helsinki (2013). The protocol was approved by the local Institutional Review Board (Approval Number: 2017-319) of Chonnam National University Hospital. All patients provided written informed consent for participation either before or after PCI. This study was registered at ClinicalTrials.gov (NCT04825886). The current study was performed according to the recommendations of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement reporting guidelines.

RESULTS

Baseline clinical and procedural characteristics and medications

The mean age of participants was 65.1 ± 11.9 years, and 77.8% were men. A total of 45.8% of patients initially presented with acute MI, while 55.2% and 31.9% had medical histories of hypertension and diabetes mellitus, respectively. The study population was further analyzed according to IVUS-guided vs. angiography-guided PCI. Patients in the IVUS-guided PCI group were younger and predominantly men. Clinical presentations of stable or unstable angina were more frequent in the IVUS-guided PCI group. Conversely, acute MI (particularly ST-segment elevation MI) was more common among patients in the angiography-guided PCI group. Additionally, the IVUS-guided PCI group had higher proportions of patients with prior MI, prior PCI, and prior coronary artery bypass grafting. In contrast, dyslipidemia was more prevalent among patients in the angiography-guided PCI group (**Table 1**).

Table 1. Baseline clinical characteristics

IVUS vs. Angiography	Total population (n = 1,978)	IVUS-guided PCI (n = 1,064)	Angiography-guided PCI (n = 914)	P value
Age (years)	65.1 ± 11.9	63.9 ± 11.4	65.2 ± 11.3	0.018
Men	1,539 (77.8)	846 (79.5)	693 (34.9)	0.048
Body mass index (kg/m ²)	25.2 ± 8.2	25.1 ± 6.7	25.2 ± 9.5	0.833
Clinical presentation				
Stable angina	432 (21.8)	272 (25.6)	160 (17.5)	< 0.001
Unstable angina	641 (32.4)	367 (34.5)	274 (30.0)	0.032
Acute myocardial infarction	905 (45.8)	425 (39.9)	480 (52.5)	< 0.001
NSTEMI	488 (24.7)	244 (22.9)	244 (26.7)	0.053
STEMI	417 (21.1)	181 (17.0)	236 (25.8)	< 0.001
Risk factors				
Hypertension	1,092 (55.2)	577 (54.2)	515 (56.3)	0.345
Diabetes mellitus	631 (31.9)	334 (31.4)	297 (32.5)	0.600
Dyslipidemia	631 (31.9)	458 (43.0)	478 (52.3)	< 0.001
Previous MI	57 (2.9)	44 (4.1)	13 (1.4)	< 0.001
Previous PCI	106 (5.4)	69 (6.5)	37 (4.0)	0.016
Previous CABG	11 (0.6)	10 (0.9)	1 (0.1)	0.013
Previous HF	58 (2.9)	31 (2.9)	27 (3.0)	0.958
Previous CVA	136 (6.9)	70 (6.6)	66 (7.2)	0.574
Chronic kidney disease	51 (2.6)	30 (2.8)	21 (2.3)	0.465
Smoking	627 (31.7)	335 (31.5)	292 (31.9)	0.826
LV ejection fraction (%)	56.3 ± 11.4	56.3 ± 10.7	56.2 ± 12.4	0.845
Laboratory findings				
Hemoglobin (g/dL)	13.9 ± 3.7	13.8 ± 3.5	13.9 ± 3.9	0.531
Creatinine (mg/dL)	1.19 ± 0.48	1.18 ± 0.45	1.19 ± 0.50	0.687
Total cholesterol (mg/dL)	175.8 ± 48.5	175.2 ± 48.4	176.5 ± 48.6	0.597
LDL cholesterol (mg/dL)	100.1 ± 43.3	98.4 ± 42.6	101.9 ± 44.1	0.110
HDL cholesterol (mg/dL)	45.1 ± 11.8	45.6 ± 11.4	44.5 ± 12.2	0.057
Triglyceride (mg/dL)	156.2 ± 91.5	160.8 ± 92.1	151.0 ± 92.4	0.068

Values are expressed as mean ± standard deviation or number (%).

IVUS = intravascular ultrasonography; PCI = percutaneous coronary intervention; NSTEMI = non-ST-segment elevation myocardial infarction; STEMI = ST-segment elevation myocardial infarction; CABG = coronary artery bypass grafting; HF = heart failure; CVA = cerebrovascular accident; LV = left ventricular; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

Regarding procedural characteristics, 74.3% of interventions were performed using the trans-radial approach, 57.0% of patients had multivessel disease, and 49.2% had target lesions located in the left anterior descending artery. Complex target lesions were observed in 43.7% of patients. The IVUS-guided PCI group had higher proportions of multivessel disease and left anterior descending artery target lesions. Conversely, a trans-radial approach was more frequently selected in the angiography-guided PCI group, along with a higher proportion of patients having target lesions in the right coronary artery. Additionally, the IVUS-guided PCI group had significantly higher proportions of complex lesions, including diffuse long lesions, severely calcified lesions, and bifurcation lesions. The total stent length was longer, and the stent diameter was larger in the IVUS-guided PCI group compared to the angiography-guided PCI group. Furthermore, the number of stents implanted was greater in the IVUS-guided PCI group. Regarding discharge medications, prescriptions of β -blockers and RAS blockers were significantly higher in the angiography-guided PCI group (**Table 2**).

Clinical outcomes

In the current study, the total incidence of the primary endpoint, 12-month MACE, was 2.7%. Overall, the incidence and risk of 12-month MACE were similar between the IVUS-guided and angiography-guided PCI groups (1.9% vs. 3.6%; adjusted HR, 0.57; 95% CI, 0.32–1.02; $P = 0.056$), as were other secondary endpoints (**Table 3**, **Fig. 1**). We further analyzed the prognostic implications of IVUS-guided PCI for each clinical outcome according to the complexity of the target lesion. In patients with complex target lesions, IVUS-guided PCI significantly reduced

Table 2. Procedural characteristics and medications

IVUS vs. Angiography	Total population (n = 1,978)	IVUS-guided PCI (n = 1,064)	Angiography-guided PCI (n = 914)	P value
Procedural characteristics				
Trans-radial approach	1,469 (74.3)	742 (69.7)	727 (79.5)	< 0.001
Multivessel disease	1,127 (57.0)	673 (63.1)	454 (49.7)	< 0.001
Target lesion				
Left main coronary artery	100 (5.0)	78 (7.3)	21 (2.3)	< 0.001
Left anterior descending artery	974 (49.2)	537 (50.5)	437 (47.8)	0.238
Left circumflex artery	280 (14.2)	141 (13.3)	139 (15.2)	0.213
Right coronary artery	624 (31.5)	307 (28.9)	317 (34.7)	0.005
Complex lesion				
Lesion length $\geq$ 38 mm	864 (43.7)	548 (51.5)	316 (34.6)	< 0.001
Severe calcified lesion	507 (25.6)	321 (30.2)	186 (20.4)	< 0.001
Bifurcation lesion	346 (17.5)	229 (21.5)	117 (12.8)	< 0.001
ISR lesion	51 (2.6)	41 (3.9)	10 (1.1)	< 0.001
CTO lesion	8 (0.4)	6 (0.6)	2 (0.2)	0.228
	92 (4.7)	44 (4.1)	48 (5.3)	0.240
Number of stents	1.4 $\pm$ 0.5	1.5 $\pm$ 0.7	1.3 $\pm$ 0.4	< 0.001
Total stent length (mm)	36.5 $\pm$ 14.9	38.8 $\pm$ 15.4	34.1 $\pm$ 13.9	0.002
Stent diameter (mm)	3.1 $\pm$ 0.5	3.2 $\pm$ 0.5	3.0 $\pm$ 0.4	< 0.001
Medications				
Aspirin	1,945 (98.3)	1,047 (98.4)	898 (98.2)	0.791
Clopidogrel	1,261 (63.8)	685 (64.4)	576 (63.0)	0.530
Potent P2Y ₁₂ inhibitor	717 (36.2)	379 (35.6)	338 (37.0)	0.530
Beta-blocker	1,245 (62.9)	630 (59.2)	615 (67.3)	< 0.001
RAS blocker	1,320 (66.7)	672 (63.2)	648 (70.9)	< 0.001
Statin	1,903 (96.2)	1,026 (96.4)	877 (96.0)	0.580

Values are expressed as mean $\pm$ standard deviation or number (%).

IVUS = intravascular ultrasonography; PCI = percutaneous coronary intervention; ISR = in-stent restenosis; CTO = chronic total occlusion; RAS = renin angiotensin system.

the incidence and risk of 12-month MACE (1.5% vs. 4.7%; adjusted HR, 0.34; 95% CI, 0.14–0.86; $P = 0.022$). This reduction was primarily driven by significant decreases in non-fatal MI (0.5% vs. 2.5%; adjusted HR, 0.22; 95% CI, 0.05–0.94; $P = 0.041$) and TVR (0.4% vs. 2.5%; adjusted HR, 0.12; 95% CI, 0.02–0.66; $P = 0.014$). However, among patients with non-complex target lesions, the incidence and risk of 12-month MACE were similar between groups (2.3% vs. 3.0%; adjusted HR, 0.78; 95% CI, 0.36–1.69; $P = 0.531$) (**Table 4, Fig. 1**). In multivariate Cox regression analysis, LVEF < 50% was independently associated with an increased risk of 12-month MACE in the total study population (adjusted HR, 2.07; 95% CI, 1.09–3.94; $P = 0.026$) (**Table 5**). Among patients with complex target lesions, IVUS-guided PCI (adjusted HR, 0.34; 95% CI, 0.14–0.86; $P = 0.022$) and the presence of multivessel disease (adjusted HR, 2.39; 95% CI, 1.01–5.68; $P = 0.047$) were independently associated with 12-month MACE. In patients with non-complex target lesions, only LVEF < 50% was independently associated with 12-month MACE (adjusted HR, 3.06; 95% CI, 1.34–6.98; $P = 0.008$).

DISCUSSION

This was a large-scale, multicenter, prospective observational study based on real-world clinical registry data from Korea, evaluating clinical outcomes of patients with diffuse long CAD who received the R-Onyx stent. Additionally, we compared clinical outcomes between IVUS-guided and angiography-guided PCI groups. Our data demonstrated a relatively low incidence of 12-month MACE, indicating that R-Onyx stent implantation yielded excellent clinical outcomes in patients with diffuse long CAD. Importantly, based on these real-world data, we established that IVUS-guided PCI significantly reduced the risk of 12-month MACE compared to angiography-guided PCI in patients with anatomically complex target lesions.

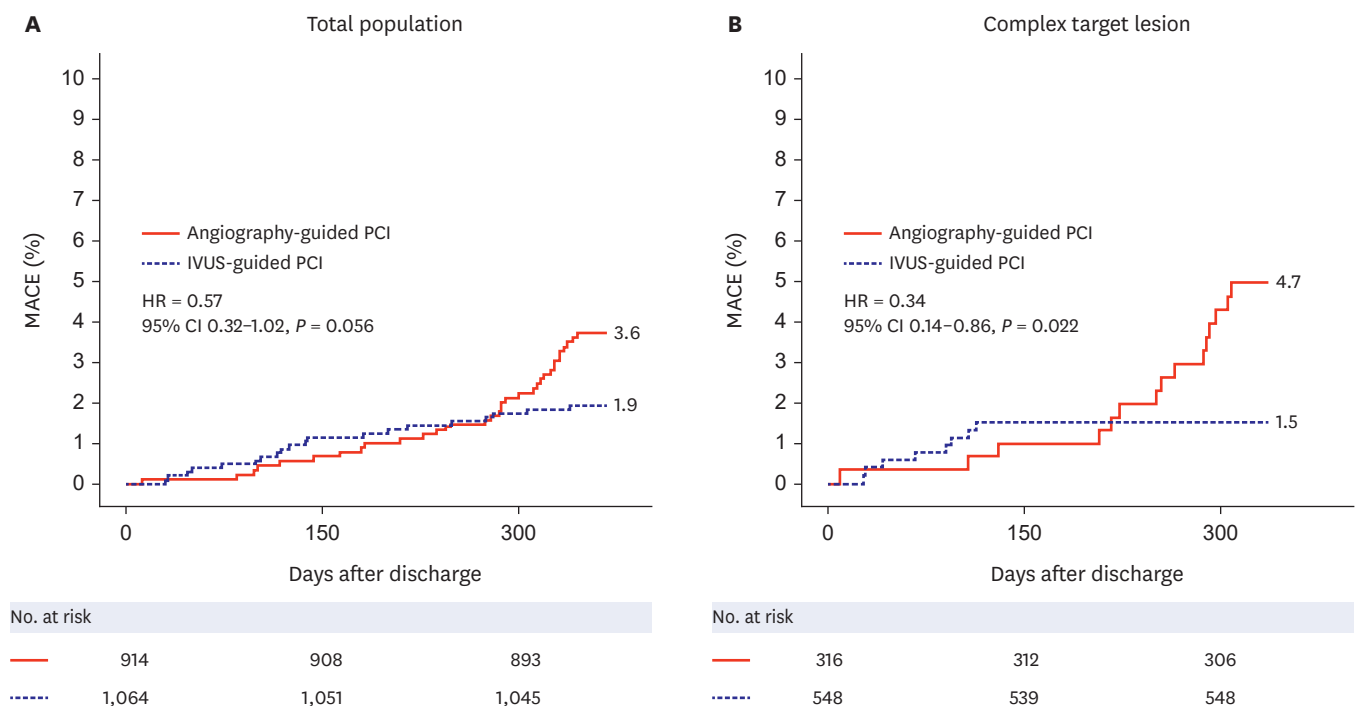
Table 3. Clinical outcomes

IVUS vs. Angiography	Total population (n = 1,978)	IVUS-guided PCI (n = 1,064)	Angiography-guided PCI (n = 914)	Adjusted HR (95% CI)	P value
MACE ^a	53 (2.7)	20 (1.9)	33 (3.6)	0.57 (0.32–1.02)	0.056
Cardiac death	8 (0.4)	3 (0.3)	5 (0.5)	0.69 (0.16–3.05)	0.625
Non-fatal MI	22 (1.1)	8 (0.8)	14 (1.5)	0.56 (0.23–1.39)	0.209
TVR	27 (1.4)	10 (0.9)	17 (1.9)	0.55 (0.24–1.24)	0.148
All cause death	19 (1.0)	9 (0.8)	10 (1.1)	0.68 (0.27–1.75)	0.429
Any repeated revascularization	60 (3.0)	26 (2.4)	34 (3.7)	0.70 (0.41–1.19)	0.185
Stroke	14 (0.7)	6 (0.6)	8 (0.4)	0.70 (0.23–2.08)	0.511

Values are presented as the number (%) of patients.

IVUS = intravascular ultrasonography; PCI = percutaneous coronary intervention; HR = hazard ratio; CI = confidence interval; MACE = major adverse cardiac events; MI = myocardial infarction; TVR = target vessel revascularization.

^aComposite of cardiac death, non-fatal MI, and TVR.

**Fig. 1.** Kaplan-Meier curves for MACE in the total population (A) and the complex target lesion group (B).

MACE = major adverse cardiac events; HR = hazard ratio; CI = confidence interval; PCI = percutaneous coronary intervention; IVUS = intravascular ultrasonography.

Table 4. Clinical outcomes according to target lesion complexity

IVUS vs. Angiography	Complex target lesion				Non-complex target lesion			
	IVUS-guided PCI (n = 548)	Angiography-guided PCI (n = 316)	Adjusted HR (95% CI)	P value	IVUS-guided PCI (n = 499)	Angiography-guided PCI (n = 615)	Adjusted HR (95% CI)	P value
MACE ^a	8 (1.5)	15 (4.7)	0.34 (0.14–0.86)	0.022	12 (2.3)	18 (3.0)	0.78 (0.36–1.69)	0.531
Cardiac death	2 (0.4)	3 (0.9)	0.49 (0.08–3.22)	0.461	1 (0.2)	2 (0.3)	0.90 (0.07–9.27)	0.939
Non-fatal MI	3 (0.5)	8 (2.5)	0.22 (0.05–0.94)	0.041	5 (1.0)	6 (1.0)	0.91 (0.26–3.21)	0.886
TVR	2 (0.4)	8 (2.5)	0.12 (0.02–0.66)	0.014	8 (1.6)	9 (1.5)	1.09 (0.40–2.98)	0.861
All cause death	4 (0.7)	4 (1.3)	0.66 (0.15–2.86)	0.580	5 (1.0)	6 (1.0)	0.76 (0.22–2.69)	0.670
Any repeated revascularization	10 (1.8)	13 (4.1)	0.48 (0.20–1.15)	0.101	16 (3.1)	21 (3.5)	0.89 (0.45–1.77)	0.739
Stroke	4 (0.7)	4 (1.3)	0.61 (0.14–2.57)	0.499	2 (0.4)	4 (0.7)	0.64 (0.10–3.96)	0.631

Values are presented as the number (%) of patients.

IVUS = intravascular ultrasonography; PCI = percutaneous coronary intervention; HR = hazard ratio; CI = confidence interval; MACE = major adverse cardiac events; MI = myocardial infarction; TVR = target vessel revascularization.

^aComposite of cardiac death, non-fatal MI, and TVR.

Table 5. Clinical predictors of major adverse cardiac events

Clinical predictors	Univariate analysis		Multivariate analysis ^a	
	HR (95% CI)	P value	HR (95% CI)	P value
Total population				
LVEF < 50%	2.04 (1.16–3.59)	0.014	2.07 (1.09–3.94)	0.026
IVUS-guided PCI	0.51 (0.29–0.89)	0.019	0.57 (0.32–1.01)	0.055
Age (per 1-year increase)	1.02 (0.99–1.05)	0.074	1.02 (0.98–1.07)	0.109
Hypertension	1.63 (0.94–2.83)	0.081	1.75 (0.97–3.15)	0.064
Multivessel disease	1.62 (0.94–2.81)	0.083	1.58 (0.90–2.77)	0.113
Presented as myocardial infarction	1.45 (0.85–2.50)	0.097	1.21 (0.64–2.29)	0.560
Men	0.79 (0.43–1.47)	0.454		
Diabetes mellitus	1.47 (0.77–2.74)	0.246		
Chronic kidney disease	1.39 (0.19–8.23)	0.749		
Smoking	1.60 (0.84–3.17)	0.154		
Use of beta-blocker	0.83 (0.47–1.44)	0.497		
Use of RAS blocker	0.95 (0.53–1.69)	0.852		
Complex target lesion group				
IVUS-guided PCI	0.31 (0.13–0.74)	0.009	0.34 (0.14–0.86)	0.022
Multivessel disease	2.65 (1.13–6.20)	0.024	2.39 (1.01–5.68)	0.047
Presented as myocardial infarction	1.97 (0.84–4.61)	0.117	1.98 (0.78–5.05)	0.159
LVEF < 50%	1.46 (0.61–3.49)	0.295	1.24 (0.49–3.18)	0.651
HTN	1.73 (0.75–3.98)	0.199	1.63 (0.68–3.89)	0.274
Age (per 1-year increase)	1.01 (0.98–1.05)	0.480	1.08 (0.97–1.05)	0.714
Smoking	1.95 (0.66–5.79)	0.228		
Men	0.72 (0.29–1.77)	0.471		
Chronic kidney disease	1.55 (0.20–9.95)	0.676		
Diabetes mellitus	1.22 (0.50–3.01)	0.662		
Use of beta-blocker	0.81 (0.33–1.99)	0.646		
Use of RAS blocker	0.97 (0.40–2.39)	0.951		
Non-complex target lesion group				
LVEF < 50%	2.68 (1.27–5.65)	0.010	3.06 (1.34–6.98)	0.008
IVUS-guided PCI	0.82 (0.39–1.71)	0.593	0.78 (0.36–1.69)	0.531
Age (per 1-year increase)	1.03 (0.99–1.06)	0.138	1.03 (0.98–1.07)	0.150
Hypertension	1.56 (0.75–3.24)	0.236	1.71 (0.79–3.71)	0.174
Diabetes mellitus	1.71 (0.69–4.23)	0.243	1.55 (0.62–3.90)	0.349
Smoking	1.43 (0.63–3.23)	0.395	1.42 (0.59–3.41)	0.434
Use of beta-blocker	0.62 (0.30–1.29)	0.201		
Chronic kidney disease	1.76 (0.61–6.09)	0.397		
Multivessel disease	1.12 (0.54–2.32)	0.753		
Presented as myocardial infarction	1.15 (0.56–2.37)	0.712		
Men	0.86 (0.36–2.02)	0.722		
Use of RAS blocker	0.89 (0.41–1.92)	0.766		

HR = hazard ratio; CI = confidence interval; LVEF = left ventricular ejection fraction; IVUS = intravascular ultrasonography; PCI = percutaneous coronary intervention; RAS = renin angiotensin system; HTN = hypertension.

^aMultivariate Cox model was constructed using variables with $P < 0.1$ in univariable analyses and the final model was selected using backward stepwise method.

In 2009, the ZES was introduced; since then, it has been undergoing ongoing development. The R-Onyx stent is one of the representative products in the ZES family.^{5,6} Compared to other next-generation DES, the R-onyx stent has distinctive features.¹⁶⁻¹⁸ First, zotarolimus is a sirolimus-derived antiproliferative agent that is more lipophilic than sirolimus.¹⁶ Second, the BioLinx polymer is a 3-component durable polymer that facilitates rapid drug release and greater biocompatibility.¹⁷ Third, the R-onyx stent platform consists of a single continuous wire that is helically wrapped, sinusoidal-shaped, and locally laser-fused.¹⁸

Several randomized clinical trials have validated the theoretical benefits of the R-Onyx stent.^{19,20} In the Bioresorbable Polymer Orsiro Versus Durable Polymer Resolute Onyx Stents (BIONYX) trial, the R-Onyx stent was compared with an ultrathin cobalt-chromium strut in the bioresorbable polymer-coated Orsiro (Biotronik, Bülach, Switzerland) stent in

an all-comer CAD patient cohort. The primary endpoint of 12-month target vessel failure occurred in 55 patients (4.5%) in the R-Onyx group and 58 patients (4.7%) in the Orsiro group, demonstrating the non-inferiority of the R-Onyx stent for the combined efficacy endpoint at 12-month follow-up (4.5% vs. 4.7%, difference 0.2%, upper limit of CI 1.1%; P for non-inferiority = 0.0005). The BIONYX trial was the first major randomized clinical trial demonstrating the efficacy of the R-Onyx stent in an all-comer CAD population.¹⁹ In comparison, our present data showed a lower 12-month MACE incidence of 2.7%, relatively lower than the results observed in the BIONYX trial and similar to the previous study using Resolute™ Integrity ZES (3.0%) in diffuse long CAD. In the randomized controlled Resolute Onyx in One-month Dual Antiplatelet Therapy for High-Bleeding-Risk Patients (Onyx ONE) trial, safety and efficacy outcomes (cardiac death, MI, definite or probable ST) for the R-Onyx stent were compared with polymer-free umirolimus-coated stents in high bleeding-risk patients undergoing 1-month dual antiplatelet therapy. Results demonstrated non-inferior clinical outcomes for the R-Onyx stent compared to the polymer-free umirolimus-coated stent (17.1% vs. 16.9%, respectively; difference 0.2%; upper limit of CI 3.0%; P for non-inferiority = 0.011) at 12 months.²⁰

We further compared patient outcomes based on IVUS-guided vs. angiography-guided PCI in this real-world clinical registry data. Our results indicated that IVUS-guided PCI significantly reduced the risk of 12-month MACE compared to angiography-guided PCI in patients with anatomically complex target lesions, defined as expected stent length ≥ 38 mm, severely calcified lesions, bifurcation lesions, ISR lesions, CTO lesions, and left main disease. Landmark randomized clinical trials have previously established the clinical significance of IVUS-guided PCI.^{11,12} The Impact of Intravascular Ultrasound Guidance on Outcomes of Xience Prime Stents in Long Lesions (IVUS-XPL) trial randomized 1,400 CAD patients with long coronary lesions (implanted stent length ≥ 28 mm) to IVUS-guided or angiography-guided PCI. IVUS guidance was associated with a significantly lower composite MACE rate.¹¹ In the extended 5-year follow-up data, IVUS use was associated with a significant 50% relative reduction in MACE risk compared to angiographic guidance, primarily driven by a lower rate of target lesion revascularization.²¹ Furthermore, recent results from the RENOVATE-COMPLEX-PCI trial provided even more encouraging outcomes, demonstrating that imaging-guided PCI significantly reduced the risk of hard clinical endpoints, such as target vessel-related MI or cardiac death, over a 2-year follow-up period compared to angiography-guided PCI in complex coronary lesions.¹² Our data showed a lower incidence of 12-month MACE compared to patients enrolled in the R-Onyx group of the BIONYX trial (2.7% vs. 4.5%). Such differences in clinical outcomes may reflect the significantly lower use of intracoronary imaging in the BIONYX trial compared with our study (1.2% vs. 53.8%), despite the BIONYX trial having a higher proportion of complex coronary artery lesions (75.3% vs. 43.7%).¹⁹

This study has some limitations. First, it was a prospective, observational study based on clinical registry data. Although nearly 2,000 patients were enrolled and most potential confounders were adjusted and evaluated, the possibility of selection bias or other systematic confounders cannot be entirely excluded. Second, detailed IVUS data—including pre-PCI lesion characteristics and post-PCI IVUS measurements such as minimal stent diameter, minimal stent area, edge dissections, or acute malapposition—were not recorded. The discretionary use of IVUS by physicians and absence of explicit PCI guidance and stent optimization criteria may underestimate the beneficial effects of IVUS use. Third, concomitant medical therapies, including duration of dual antiplatelet therapy and patient

compliance, may have influenced clinical outcomes, but this was not fully evaluated. Fourth, our study lacks long-term follow-up clinical data beyond 12 months. Future studies with longer-term clinical outcomes should be considered.

In patients with diffuse long CAD, implantation of the R-Onyx stent was effective, with an incidence of 12-month MACE at 2.7% according to real-world clinical data. Additionally, IVUS-guided PCI significantly reduced the incidence and risk of 12-month MACE compared to angiography-guided PCI in patients with anatomically complex target lesions, primarily driven by reductions in non-fatal MI and TVR.

SUPPLEMENTARY MATERIAL

Supplementary Fig. 1

Study flow chart.

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