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In-Stent Restenosis Lesion Morphology Related to Repeat Stenting Underexpansion as Evaluated by Optical Coherence Tomography

Running Title: Underexpansion of re-stenting in-stent restenosis

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ABSTRACT

Aims: To use optical coherence tomography (OCT) to predict newly implanted stent expansion for treatment of in-stent restenosis (ISR).

Methods and results: With OCT-guidance, 143 ISR lesions were treated with a new stent. Stent underexpansion was defined as minimum stent area (MSA) <4.5mm^2 and MSA/average of reference lumen area <70%. New stent underexpansion was found in 33 lesions (23%), had a smaller old stent MSA (4.13 [3.32-4.62] versus 5.18 [4.01-6.38] mm^2, p=0.001), and had a higher prevalence of multiple old stent layers (51.5% versus 10.9%, p<0.001) and neointimal or peri-stent calcium (69.7% versus 37.3%, p=0.001) compared to those without new stent underexpansion. Old stent underexpansion, multiple layers of old stent, maximum calcium angle >180°, and maximum calcium thickness >0.5mm were independently associated with new stent underexpansion. Patients with new stent underexpansion had a higher prevalence of major adverse cardiac events (35.5% vs 14.3%, p=0.009) mainly driven by a higher rate of myocardial infarction and target vessel revascularization at 2 years.

Conclusions: When re-stenting an ISR lesion, old stent underexpansion, the amount of neointimal or peri-stent calcium, and multiple old stent strut layers are important determinants of new stent underexpansion that is then associated with adverse long-term outcomes.

Classifications: Bare metal stent, drug-eluting stent, in-stent restenosis; optical coherence tomography

CONDENSED ABSTRACT

We used optical coherence tomography to investigate the morphological characteristics associated with underexpansion of a newly implanted stent used to treat in-stent restenosis. New stent underexpansion was found in 33 lesions (23%), had a smaller old stent MSA, and a higher prevalence of multiple old stent layers and neointimal or peri-stent calcium compared to those without new stent underexpansion. Old stent underexpansion, double layers of old stent, maximum calcium angle >180°, and maximum calcium thickness >0.5 mm were independently associated with new stent underexpansion that, in turn, was associated with more events at 2-year follow-up.

ABBREVIATIONS

CSA = cross-sectional area

DES = drug-eluting stents

ISR = in-stent restenosis

MACE = major adverse cardiac events

MI = myocardial infarction

MLA = minimum lumen area

MSA = minimum stent cross-sectional area

NIH = neointimal hyperplasia

OCT = optical coherence tomography

ROC = receiver operating characteristic

TVR = target vessel revascularization

INTRODUCTION

Although advances in drug-eluting stents (DES) have substantially reduced the risk of coronary in-stent restenosis (ISR) and the need for target lesion revascularization, ISR persists.[1,2] There are several treatment options for ISR (conventional balloon angioplasty, cutting or scoring balloons, drug-coated balloons, or bypass surgery); but repeat DES implantation has superior clinical and angiographic outcomes to other treatment strategies.[3] Nevertheless, there are few data that evaluate the morphological predictors of new stent underexpansion when treating an ISR lesion. We hypothesized that the morphological characteristics underlying the ISR lesion—i.e., neoatherosclerotic or peri-stent calcium—would impact expansion of a newly implanted stent and that these morphologic characteristics could be evaluated with optical coherence tomography (OCT).

METHODS

Patient population. This was a retrospective, observational study to assess morphological factors that contributed to new stent underexpansion when treating ISR lesions using OCT guidance at two hospitals (NewYork-Presbyterian Hospital, New York, NY, USA; St. Francis Hospital, Roslyn, NY, USA). The indication of treatment (symptoms and/or evidence of ischemia) and treatment strategy were at each operator's discretion. Patients with pre- and final (post-new stent implantation) OCT evaluation were enrolled. The research protocol was approved by the ethics committee of each hospital. Clinical follow-up was performed by hospital chart review, outpatient clinic visit, or telephone contact. Major adverse cardiac event (MACE)

was a composite of all-cause death, myocardial infarction (MI), or clinically driven target vessel revascularization (TVR).

Coronary angiograms were analyzed by an interventional cardiologist (D.Y.) at the Cardiovascular Research Foundation (New York, NY, USA) using QAngio XA version 7.2 (Medis Medical Imaging Systems, Leiden, the Netherlands) using conventional methods.[4] Angiographic restenosis was classified as: (i) focal ISR (<10mm in length); (ii) diffuse ISR (>10mm length, but within the stent); (iii) proliferative (>10mm in length, extending beyond the stent edges); and (iv) total occlusion.[5]

OCT imaging and analysis. Pre-intervention, an OCT catheter (C7 Dragonfly or Dragonfly Duo, Abbott Vascular, Santa Clara, CA, USA) was introduced distal to the lesion, and contrast media was injected via the guiding catheter at 3-4mL/s during pullback. Pre-OCT pre-dilation with a 1.5-2.0mm balloon was performed in severe ISR. OCT images were acquired using frequency-domain OCT (C7-XR, ILUMIEN, or ILUMIEN OPTIS, Abbott Vascular) with a frame interval of 0.1-0.2mm.[6] After successful restenting, OCT imaging was repeated. Off-line analysis was done by agreement of two independent cardiologists (D.Y. and A.M.) using proprietary software (Abbott Vascular).

All OCT slices were evaluated; and stent and intra-stent lumen cross-sectional areas (CSA) were measured at the minimum lumen CSA, minimum stent CSA (MSA), and maximum neointimal hyperplasia (NIH) CSA. Stent CSA was measured by joining strut blooming middle points. If the stent was covered by high signal attenuation tissue, stent CSA was interpolated using proximal and distal slices. Percentage of NIH was calculated as (1 – lumen/stent CSA) × 100. Proximal and distal reference lumen CSAs were at the slices with the largest lumen CSA

within 5mm proximal and distal to the stent edges, but before significant sidebranches (>1.5mm in diameter). Stent expansion was MSA divided by the average of the proximal and distal reference lumen CSA. Stent underexpansion was MSA <4.5mm^2 and stent expansion <70% based on the CLI-OPCI II study.[7]

Calcium was a region with a well-delineated border and subcategorized as either within the NIH or native plaque behind the stent (Figure 1A).[8] Maximum calcium angle (sum of angle in each slice) and maximum calcium thickness were measured, and lengths were calculated by the total slice number multiplied by the frame interval. Calcium fracture was defined as complete discontinuity of calcified plaque (Figure 1B). Double old stent layers were two layers of old stent struts within the same OCT frame (Figure 1C). (There was no lesion with more than two old stent layers.) Tissue protrusion, stent malapposition, and edge dissection were also assessed post–restenting.[9]

Statistical analysis. Normally distributed continuous variables were reported as mean and standard deviation and compared using Student's *t*-test. Non-normally distributed continuous variables were reported as median with interquartile range and compared using the Mann-Whitney *U*-test. Categorical variables were summarized as counts and percentages and compared using χ^2 statistics or Fisher's exact test. Receiver operating characteristic (ROC) curves were used to determine cut-off values (Youden index) for maximum calcium angle and thickness associated with new stent underexpansion. A multivariable logistic regression model was performed to identify factors associated with new stent underexpansion. Included variables were chosen based on their historical or mechanistic relationship to stent underexpansion.[10-12] Time-to-first event rates are shown as Kaplan-Meier estimates and compared with the log-lank test.

P<0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 22.0 software (IBM, Armonk, NY, USA).

RESULTS

Clinical characteristics. From February 2011 to March 2017, 655 lesions (633 patients) underwent OCT evaluation for ISR; 344 lesions did not have an intervention, 62 were treated by balloon angioplasty only, 13 were treated with atherectomy, 58 did not have final OCT, 35 lesions had poor OCT quality leaving 143 ISR lesions (143 patients) were enrolled. Duration from implantation was 5.8±4.8 years and was >5 years in 50.7%. Ninety-four had acute coronary symptoms, 30 had stable angina, and 16 had a positive stress test without symptoms. Based on final post–restenting OCT measurements, 33 lesions had an MSA <4.5mm^2 and stent expansion <70% and were considered to have new stent underexpansion; the rest were the comparison group (n=110) (Figure 2). There were no differences in clinical characteristics between groups (Table 1).

Procedural characteristics and angiographic findings. Restenotic stents included bare metal stents (12.6%), first-generation DES (30.8%), and second-generation DES (56.6%). Pre-dilation with a scoring balloon or a noncompliant balloon, maximum post-dilation pressure, and balloon/artery ratio were similar between the two groups. All but two ISR lesions were then treated using second-generation DES; and new stent diameter (2.75 [2.5-3.0] versus 3.0 [2.75-3.5] mm, p=0.001) and maximum post-dilation balloon diameter (3.0 [2.75-3.38] versus 3.25 [3.0-3.5] mm, p=0.009) were smaller in patients with versus without new stent underexpansion (Table 2). As shown in Table 3, angiographic pre- and final post-PCI in-stent dimensions and acute gain were not significantly different between the groups.

OCT findings. Based on pre-intervention OCT, old stent underexpansion (old stent MSA<4.5mm^2 and old stent expansion <70%) were identified in 12.6% (18/143), in-stent neoatherosclerosis was identified in 48.3% (69/143), and the rest of the ISR lesions were mainly due to NIH (ie, no old stent underexpansion, no neoatherosclerosis, 39.2%, 56/143). Lesions with new stent underexpansion had a smaller old stent MSA (4.13 [3.32-4.62] versus 5.18 [4.01-6.38] mm^2, p=0.001), and the mechanism of old stent failure was more often underexpansion (39.4% versus 4.5%, p<0.001) (Table 4). The prevalence of a double layer of old stents was higher in lesions with new stent underexpansion (51.5% versus 10.9%, p<0.001). There was no difference in new stent malapposition, stent tissue protrusion, or stent edge dissection between the two groups.

Calcium, including neointimal calcium or calcium in the plaque behind the old stent, was more common in new stent underexpansion (69.7% versus 37.3%, p=0.001) along with a larger angle and greater thickness, especially neointimal calcium (Table 4). Using ROC analysis, the cut-off value to predict new stent underexpansion was maximum calcium angle (either neointimal calcium or calcium behind stent) of 177° (area under the curve [AUC] 0.75, 95% confidence interval [CI] 0.62-0.88, p=0.001, sensitivity=68%, specificity=78%) and maximum calcium thickness (either neointimal calcium or calcium behind stent) of 0.49mm (AUC 0.71, 95% CI 0.56-0.86, p=0.007, sensitivity=81%, specificity=68%), especially when the two co-existed (Figure 3). Calcium fracture post-PCI was seen in only 8.7% (2/23 with calcium) in the new stent underexpansion group versus 14.6% (6/41 with calcium) that did not have new stent underexpansion. Among eight cases with calcium fracture post–re-stenting, five fractures were in neointimal calcium; and three fractures were in calcium in plaque behind the old stent.

Predictors of new stent underexpansion. In the multivariable analysis, old stent underexpansion (odd ratio [OR] 6.19, 95% CI 1.82-7.61, p=0.006), double layers of old stent (OR 8.62, 95% CI 2.15-13.3, p<0.001), calcium >180° (OR 5.80, 95% CI 1.76-7.84, p=0.005), and maximum calcium thickness >0.5mm (OR 4.83, 95% CI 1.58-6.81, p=0.009) were independently associated with new stent underexpansion when re-stenting an ISR lesion. When different definitions of stent underexpansion were used, predictive factors remained consistent (Supplemental Table).

Long-term outcomes. Patients with new stent underexpansion had a higher prevalence of MACE mainly driven by a higher rate of MI and TVR compared no new stent underexpansion (Table 5 and Figure 4).

DISCUSSION

The present OCT study demonstrated that ISR lesions that were associated with old stent underexpansion, significant neointimal or peri-stent calcium (based on thickness and angle), and multiple layers of old stent struts were associated with new stent underexpansion when re-stenting the ISR lesion and that new stent underexpansion was associated with a higher event rate at follow-up.

Stent underexpansion, a main mechanisms of ISR,[8] contributed to new stent underexpansion in the present study even when higher pressures or larger balloons were used.[13] An intravascular ultrasound study showed acute diameter gain decreased with increasing arc of calcification.[14] As expected, it was difficult to expand a new stent within an underexpanded old stent due to calcified plaque.

Severe calcification in *de novo* coronary arteries limits stent expansion.[9-13] Kobayashi[10] et al. assessed the relationship between stent expansion and coronary calcification using OCT and demonstrated that a larger arc and area of calcium were associated with significantly worse stent expansion. Fujino et al.[11] developed an OCT-based calcium scoring system to predict stent underexpansion; a maximum calcium angle >180°, maximum calcium thickness >0.5mm, and calcium length >5mm were risk factors, remarkably similar to current study cut-offs. Thus, the current study expanded our understanding of the effect of calcium on stent underexpansion from *de novo* coronary disease to ISR calcium (ie, neoatherosclerotic or peri-stent calcium).

In an OCT study by Song et al.[15], in-stent neointimal calcium was a dominant pattern of neoatherosclerosis, observed in 60% of ISR with neoatherosclerosis, consistent with our findings and previous autopsy studies.[16] A small OCT study evaluating the impact of neointimal calcification on stent-in-stent ISR treatment showed a trend for a smaller stent area and diameter at the site of neointimal calcification versus proximal to the neointimal calcification.[17] A recent study assessed prevalence, predictors, and implications of calcified neoatherosclerosis as the cause of ISR; ISR lesions with calcified neoatherosclerosis were associated with poorer angiographic and OCT.[18]

We observed calcium fracture post-restenting in 6 (14.6%) cases with good new stent expansion similar to *de novo* stenting.[19] Excimer laser coronary angioplasty or lithotripsy could disrupt calcium to facilitate full stent expansion especially when treating an ISR lesion with a new stent.[20, 21]

Repeat stenting a recurrent ISR lesion is associated with chronic stent underexpansion and a high rate of adverse events.[22] Stent-in-stent DES treatment of ISR is associated with

recurrent restenosis rates between 20%-40%.[12] In another OCT study,[20] one third of ISR cases had multiple old stent layers associated with new stent underexpansion. A small study reported 11 recurrent ISR with 2 or 3 layers of metal after treatment using a drug-coated balloon with 13% MACE over 38 months.[23] Thus, although 3 meta-analyses have demonstrated that re-stenting should be the preferred treatment,[3, 24, 25] a drug-coated balloon should be considered, when there are more than two layers of old stents unless calcium modification is used before re-stenting. However, a recent study showed drug-coated balloon was also less effective for ISR lesions with more than 3 stent layers.[26] Hence, multiple metallic layers should be avoided, if possible. Finally, when restenting an ISR lesion, it is important to optimize the ISR-treatment just as it is important to optimize *de novo* stent implantation because new stent underexpansion is associated with a higher rate of events just as is *de novo* stent underexpansion.

Limitations. This was a retrospective observational study in which we only included patients with pre- and post-restenting OCT. Second, >50% presented beyond 5 years of stent implantation, which may not be representative of daily practice. Third, there were no angiographic or OCT images of the original stent implantation. Fourth, only 50% of restenotic stents were newer generation DES.

CONCLUSION

When re-stenting an ISR lesion, old stent underexpansion, the amount of calcium, whether within the neointima or in peri-stent plaque, and multiple layers of old stent struts may be important determinants of new stent underexpansion that, in turn, may increase long-term events.

IMPACT ON DAILY PRACTICE

- When re-stenting an ISR lesion, old stent underexpansion, the amount of coronary calcium, whether within the neointima or in peri-stent plaque, and multiple layers of old stent struts are important determinants of new stent underexpansion.
- New stent underexpansion is associated with adverse long-term outcome and

optimization of ISR-treatment is as important as denovo stent implantation.

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There was no external funding source for this study.

APPENDIX

Collaborators:

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CONFLICTS OF INTEREST

Dong Yin: Dr. Yin reports grants from Boston Scientific during the conduct of the study. Gary Mintz: None. Lei Song: None. Zhaoyang Chen: Dr. Chen reports grants from Boston Scientific during the conduct of the study. Tetsumin Lee: None. Ajay Kirtane: Grants from Medtronic, Abbott Vascular, Boston Scientific, Abiomed, CathWorks, Siemens, Philips, ReCor Medical, and Spectranetics outside the submitted work. Manish Parikh: Dr. Parikh reports personal fees from Abbott Vascular, personal fees from Medtronic, Boston Scientific, CDI, and Corsica outside the submitted work. Jeffrey Moses: None. Khady Fall: None. Allen Jeremias: Grant and personal fees from Abbott outside the submitted work. Fernando Sosa: Employee of Abbott Vascular. Elizabeth Haag: None. Ziad Ali: Dr. Ali reports grants and personal fees from Abbott, Medtronic, and Cardiovascular Systems Inc, other from Shockwave, personal fees from Boston Scientific and Cardinal Health outside the submitted work. Richard Shlofmitz: None. Akiko Maehara: Institutional grant for Boston Scientific and Abbott Vascular.

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FIGURE LEGENDS

Figure 1. Angiography and Optical Coherence Tomography Examples of Re-Stenting In-Stent Restenosis Lesions

(A) Neointimal calcium and re-stent underexpansion. The angiogram shows in-stent restenosis (arrow) in the middle of the left anterior descending coronary artery (LAD), and pre-procedure optical coherence tomography (OCT) shows neointimal calcium (asterisks) within the old stent (arrows) with minimum lumen area (MLA) = 1.69mm^2 and minimum stent area (MSA) = 4.38mm^2. Post–re-stenting angiogram and OCT show new stent underexpansion (MSA=1.86mm^2, yellow circle). (B) Re-stenting with good expansion due to calcium fracture. The angiogram shows in-stent restenosis (arrow) in the proximal right coronary artery, and the pre-procedure OCT shows calcium (asterisks) behind the old stent (arrows) with MLA=2.33mm^2 and MSA=3.07mm^2. Post–re-stenting angiogram and OCT show calcium fracture (asterisks) with MSA=5.04mm^2. (C) New stent underexpansion due to 2 old stent layers. The angiogram shows in-stent restenosis (arrow) in the middle of the LAD, and pre-procedure OCT shows 2 old stent layers (arrows) with MLA=1.15mm^2 and MSA=3.25 mm^2 (inner layer). Post–re-stenting angiogram and OCT show new stent underexpansion with MSA=2.43mm^2.

Figure 2. Minimum Stent Area and Expansion of a New Stent

A new stent with both a minimum stent area (MSA) <4.5mm^2 and expansion <70% was defined as stent underexpansion.

Figure 3. Prevalence of New Stent Underexpansion in In-Stent Restenosis Lesions Stratified by Maximum Calcium Thickness and Maximum Calcium Angle

Calcium angle >180° and calcium thickness >0.5mm are additive in causing stent underexpansion.

Figure 4. MACE Rates Between Patients With Versus Without New Stent Underexpansion

Patients with new stent underexpansion had more than twice the event rate versus those without new stent underexpansion (35.5% versus 14.3%, p=0.009) at 2 years. MACE= major adverse cardiac event

Table 1. Clinical Characteristics

	New Stent Underexpansion		p Value
	Yes (n=33)	No (n=110)	
Time since implantation, years	6.3±5.0	5.6±4.7	0.49
>5 years	19 (57.6)	53 (48.6)	0.37
Age, years	67.5±10.2	66.5±11.9	0.67
Male	20 (60.6)	75 (68.2)	0.42
Diabetes mellitus	14 (42.4)	51 (46.4)	0.69
Insulin-treated	4 (12.1)	20 (18.2)	0.41
Hypertension	29 (87.9)	97 (88.2)	1.00
Hyperlipidemia	30 (90.9)	89 (80.9)	0.18
Current smoker	4 (12.1)	18 (16.4)	0.55
Renal insufficiency*	3 (9.1)	16 (14.5)	0.56
Hemodialysis	2 (6.1)	6 (5.5)	1.00
Prior myocardial infarction	15 (45.5)	52 (47.3)	0.85
Prior coronary artery bypass grafting	6 (18.2)	21 (19.1)	0.91
Clinical presentation			
STEMI/NSTEMI	5 (15.2)	12 (10.9)	0.54
Unstable angina	19 (57.6)	58 (52.7)	0.62
Stable coronary artery disease	9 (27.3)	40 (36.4)	0.34
LDL cholesterol, mg/dL	94±39	86±28	0.19
Medication at the time of in-stent restenosis			
Statin	28 (84.8)	100 (90.9)	0.33
Aspirin	30 (90.9)	99 (90.0)	1.00
ACE inhibitor/ARB	17 (51.5)	50 (45.5)	0.54

Values are mean±standard deviation or n (%). *Glomerular filtration rate <60mL/min/1.73 m^2 calculated using the Modification of Diet in Renal Disease formula. ACE=angiotensin-converting enzyme inhibitor; ARB=angiotensin receptor blocker; LDL=low-density lipoprotein; NSTEMI=non–ST-segment elevation myocardial infarction; STEMI=ST-segment elevation myocardial infarction.

Table 2. Procedural Characteristics

	New Stent Underexpansion		p Value
	Yes (n=33)	No (n=110)	
Restenotic stent type			0.88
Bare metal stent	5 (15.2)	13 (11.8)	
First-generation drug-eluting stent	10 (30.3)	34 (30.9)	
Second-generation drug-eluting stent	18 (54.5)	63 (57.3)	
Pre-dilatation	28 (84.8)	87 (79.1)	0.62
Non-compliant balloon	8 (24.2)	17 (15.5)	0.24
Scoring balloon	14 (42.4)	45 (40.9)	0.88
Maximum pre-dilatation pressure, atm	15 (12-19)	14 (12-18)	0.70
Mean new stent diameter, mm	2.75 (2.50-3.00)	3.00 (2.75-3.50)	0.001
Total new stent length, mm	23.0 (16.5-38.0)	22.0 (15.0-33.0)	0.64
Maximum post-dilation balloon diameter, mm	3.00 (2.75-3.38)	3.25 (3.00-3.50)	0.009
Maximum post-dilation pressure, atm	18 (14-20)	20 (16-20)	0.34
Balloon-to-artery ratio*	1.18 (1.04-1.42)	1.30 (1.09-1.44)	0.22

Values are n (%) or median (interquartile range). *Maximum balloon diameter divided by the reference vessel diameter obtained before the procedure.

Table 3. Angiographic Findings

	New Stent Underexpansion		p Value
	Yes (n=33)	No (n=110)	
Target vessel			0.10
Left anterior descending	15 (45.5)	60 (54.5)	
Left circumflex	11 (33.3)	18 (16.4)	
Right	7 (21.2)	32 (29.1)	
Lesion location			0.88
Ostial	1 (3.0)	5 (4.5)	
Proximal	8 (24.2)	33 (30.0)	
Middle	18 (54.5)	55 (50.0)	
Distal	6 (18.2)	17 (15.5)	
In-stent restenosis pattern			0.05
Focal	16 (48.5)	74 (67.3)	
Diffuse/proliferative/total occlusion	17 (51.5)	36 (32.7)	
Pre-percutaneous coronary intervention			
Restenosis lesion length, mm	12.3 (7.2-18.1)	10.2 (7.4-14.6)	0.26
Total old stent length, mm	26.5 (19.0-35.4)	27.0 (18.8-37.0)	0.84
Reference vessel diameter, mm	2.44 (2.06-2.85)	2.56 (2.12-2.93)	0.47
Minimum lumen diameter, mm	1.10 (0.84-1.43)	1.05 (0.62-1.42)	0.30
Diameter stenosis, %	53.3 (41.5-68.8)	56.7 (44.4-75.2)	0.18
Final			
Minimum lumen diameter, mm	2.35 (2.14-2.63)	2.40 (2.09-2.71)	0.48
Diameter stenosis, %	14.0 (9.9-21.9)	13.7 (10.0-17.3)	0.53
Acute gain, mm	1.26 (0.88-1.70)	1.35 (0.98-1.93)	0.09

Values are n (%) or median (interquartile range).

Table 4. Optical Coherence Tomography Findings

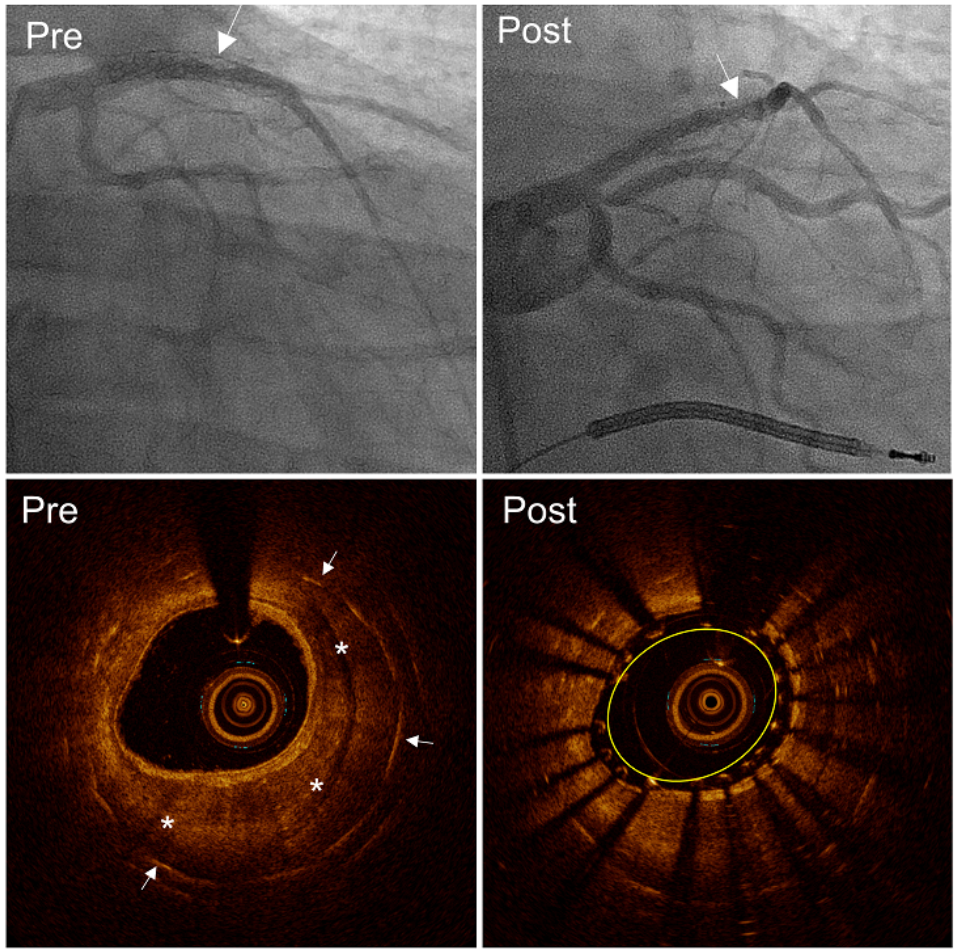
	New Stent Underexpansion		p Value
	Yes (n=33)	No (n=110)	
Pre-percutaneous coronary intervention			
Old stent MSA, mm^2	4.13 (3.32-4.62)	5.18 (4.01-6.38)	0.001
Mean reference lumen CSA, mm^2	5.26 (4.62-6.14)	5.08 (4.15-6.08)	0.50
Old stent expansion, %	74.0 (56.1-105.3)	101.0 (82.3-120.6)	0.001
Old stent underexpansion	13 (39.4)	5 (4.5)	<0.001
Minimum lumen CSA, mm^2	1.62 (1.27-2.13)	1.81 (1.35-2.26)	0.21
NIH area, mm^2	2.49 (1.40-3.56)	3.37 (2.34-4.72)	0.003
Max NIH, %	62.9 (41.9-74.0)	66.1 (56.2-75.3)	0.12
Double layers of old stent	17 (51.5)	12 (10.9)	<0.001
Presence of neoatherosclerosis	16 (48.5)	53 (48.2)	0.43
Presence of any calcium	23 (69.7)	41 (37.3)	0.001
Maximum calcium angle, °	262 (139-326)	129 (81-170)	0.001
Maximum calcium thickness, mm	0.62 (0.50-0.85)	0.44 (0.39-0.58)	0.007
Calcium length, mm	6.3 (2.4-9.8)	3.0 (1.9-4.7)	0.01
Calcium in NIH	11 (33.3)	21 (19.1)	0.09
Maximum calcium angle, °	311 (196-360)	129 (102-194)	0.009
Maximum calcium thickness, mm	0.72 (0.50-0.94)	0.47 (0.39-0.66)	0.01
Calcium length, mm	9.2 (6.6-10.0)	3.0 (1.8-4.7)	0.001
Calcium in native plaque	13 (39.4)	21 (19.1)	0.02
Maximum calcium angle, °	183 (108-277)	122 (77-170)	0.049
Maximum calcium thickness, mm	0.60 (0.35-0.70)	0.43 (0.37-0.47)	0.18
Calcium length, mm	2.6 (1.9-6.3)	2.9 (1.6-5.0)	0.86
Final			
New stent MSA, mm^2	3.07 (2.41-3.55)	4.86 (4.10-6.04)	<0.001
New stent expansion, %	59.0 (52.4-64.9)	89.6 (80.0-100.1)	<0.001
Calcium fracture	2 (8.7)	6 (14.6)	0.70
Edge dissection	12 (36.4)	31 (29.0)	0.42
Malapposition	7 (21.2)	29 (26.4)	0.55
Tissue protrusion	14 (42.4)	59 (53.6)	0.26

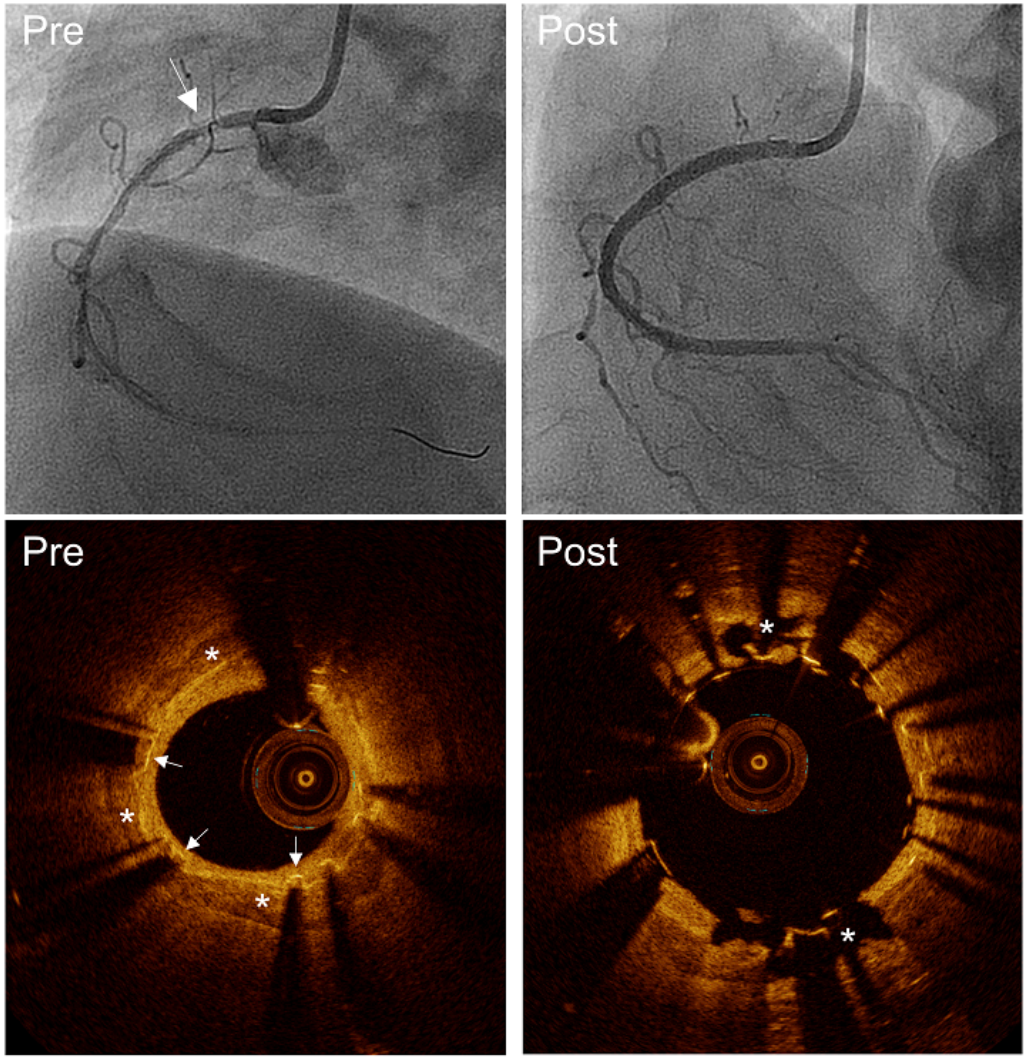
Values are n (%) or median (interquartile range). CSA=cross-sectional area; MSA=minimum stent area; NIH=neointimal hyperplasia.

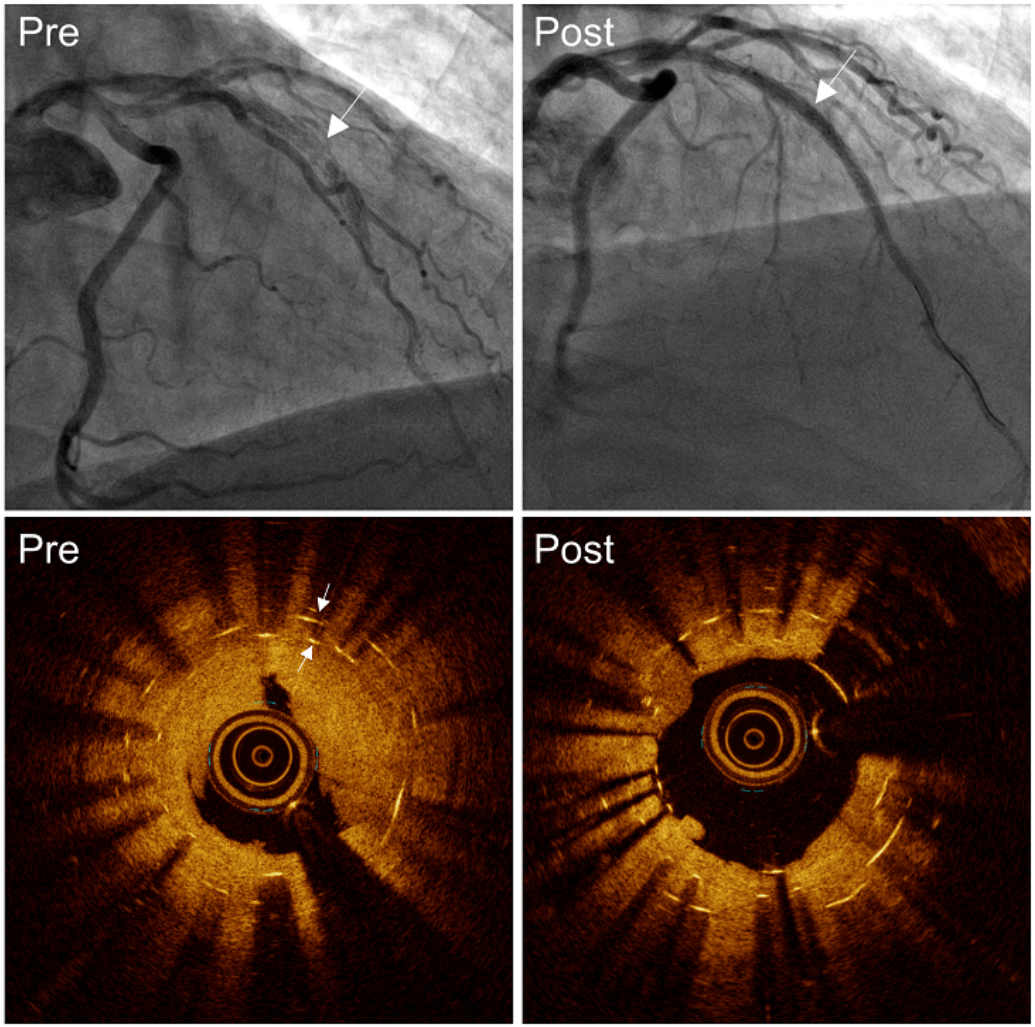
Table 5. Clinical outcomes at 2 years

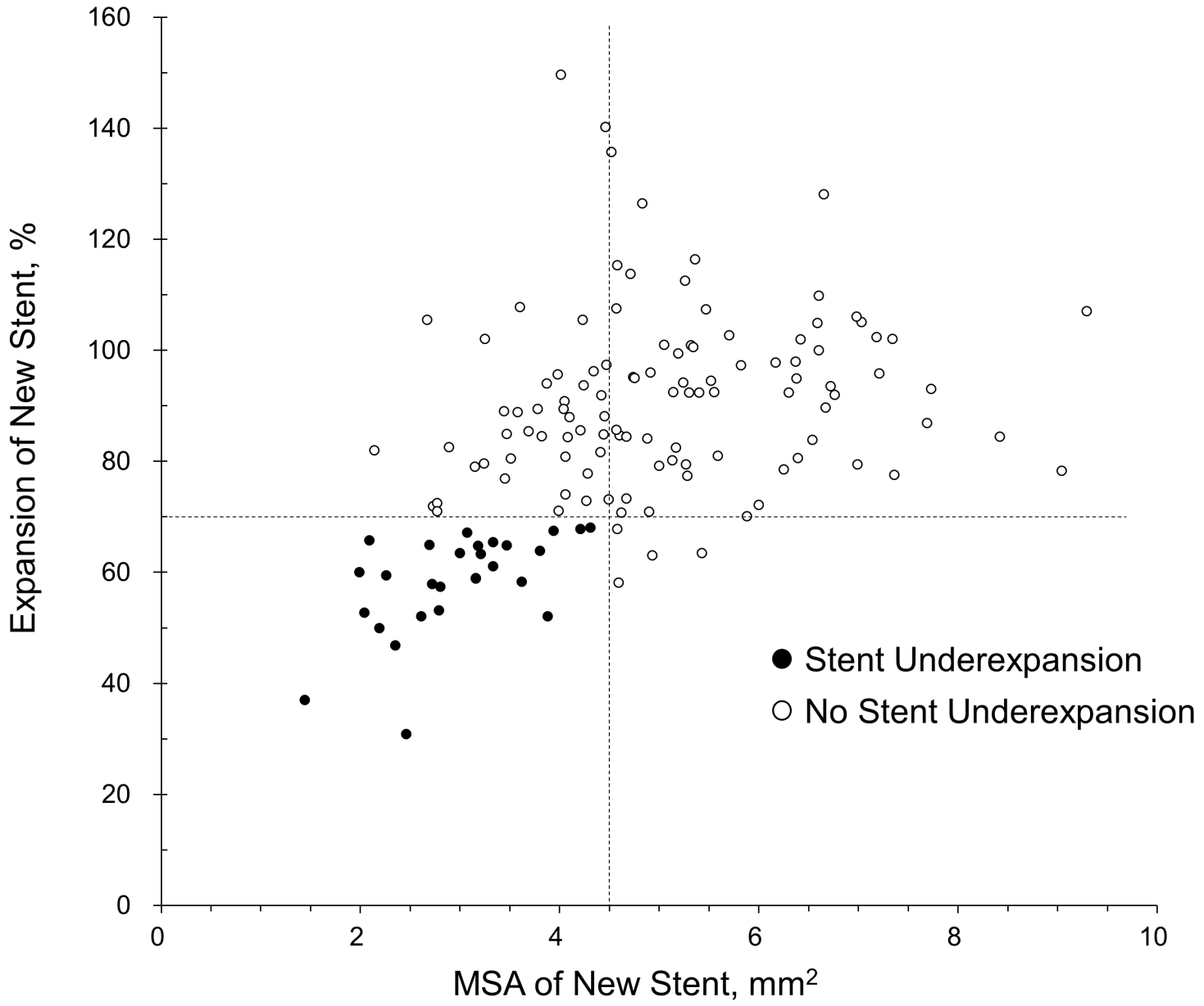
	New Stent Underexpansion		p Value
	Yes (n=33)	No (n=110)	
Major adverse cardiac event*	35.5% (11)	14.3% (14)	0.009
Death	3.3% (1)	1.0% (1)	0.36
Myocardial infarction	9.7% (3)	1.9% (2)	0.046
Target vessel revascularization	32.4% (10)	13.3% (14)	0.01

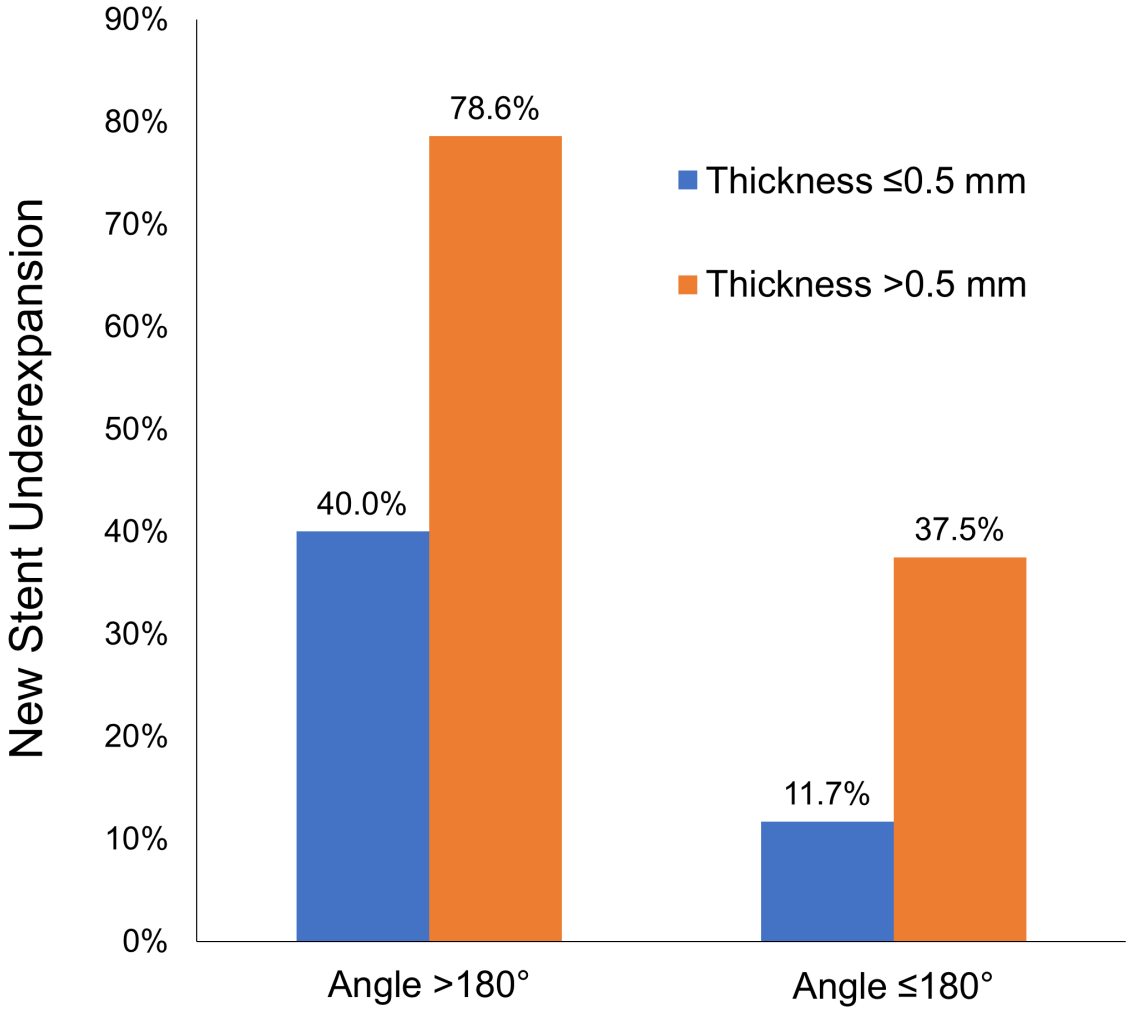
Data is shown as Kaplan Meier estimate (n). *Major adverse cardiac event includes death, myocardial infarction, or target vessel revascularization.

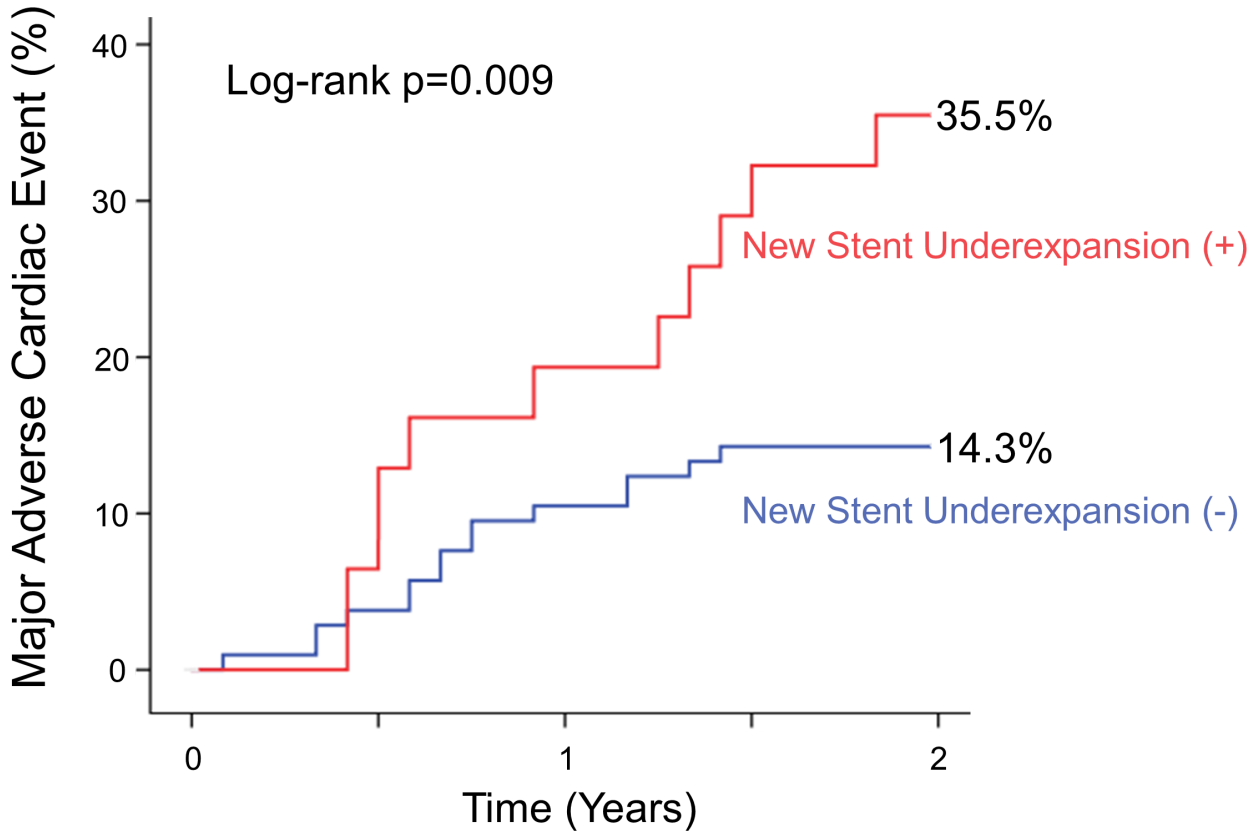












Number at risk

New Stent Underexpansion (+)	110	98	89
New Stent Underexpansion (-)	33	21	19

Supplemental Table. Predictors of New Stent Underexpansion Using Different Definitions of Stent Underexpansion

Definition: MSA <4.5mm^2 and stent expansion <70%

Predictive variables	**Odds ratio (95% CI)**	**p-value**
Old stent underexpansion	6.16 (1.82 - 7.61)	0.006
Double layers of old stent	8.62 (2.15 - 13.30)	<0.001
Maximum calcium arc >180º	5.80 (1.76 - 7.84)	0.005
Maximum calcium thickness >0.5mm	4.83 (1.58 – 6.81)	0.009

Definition: MSA <5.0mm^2 and stent expansion <70%

Predictive variables	**Odds ratio (95% CI)**	**p-value**
Old stent underexpansion	5.45 (1.70-6.76)	0.009
Double layers of old stent	6.03 (1.80-10.61)	0.001
Maximum calcium arc >180º	6.48 (1.87-9.71)	0.002
Maximum calcium thickness >0.5mm	3.27 (1.19-4.30)	0.04

Definition: MSA <4.0mm^2 and stent expansion <70%

Predictive variables	**Odds ratio (95% CI)**	**p-value**
Old stent underexpansion	5.52 (1.71-6.65)	0.01

Double layers of old stent	13.07 (2.57-14.47)	<0.001
Maximum calcium arc >180º	5.56 (1.72-6.55)	0.01
Maximum calcium thickness >0.5mm	9.43 (2.24-11.04)	0.001

CI-confidence interval; MSA=minimum stent area