Ostial right coronary artery lesion morphology and outcomes after treatment with drug-eluting stents

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This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-23-00406

ABSTRACT

BACKGROUND: Outcomes after percutaneous coronary intervention (PCI) for *de novo* ostial right coronary artery (RCA) lesions are poor.

AIMS: We used intravascular ultrasound (IVUS) to clarify the morphological patterns of *de novo* ostial RCA lesions and their associated clinical outcome.

METHODS: Among 5,102 RCA IVUS studies, 170 *de novo* ostial RCA stenoses (within 3 mm from the aorto-ostium) were identified. These were classified as 1) isolated ostial lesions (no disease extending beyond 10 mm from the ostium and without a calcified nodule [CN]); 2) ostial CN, typically with diffuse disease (disease extending beyond 10 mm); and 3) ostial lesions with diffuse disease but without a CN. The primary outcome was target lesion failure (TLF: cardiac death, target vessel myocardial infarction, definite stent thrombosis, and ischaemia-driven target lesion revascularisation).

RESULTS: The prevalence of an isolated ostial lesion was 11.8% (n=20), 47.6% (n=81) were ostial CN, and 40.6% (n=69) were ostial lesions with diffuse disease. Compared to ostial lesions with diffuse disease, isolated lesions were more common in women (75.0% vs 42.0%; p=0.01), and CN were associated with older age (median [first, third quartile] 76 [70, 83] vs 69 [63, 81] years old; p=0.002). The Kaplan-Meier rate of TLF at 2 years was significantly higher in patients with CN (21.6%) compared to diffuse lesions (8.2%) (p=0.04), and patients with isolated lesions had no events. A multivariable Cox proportional hazard model revealed that CN were significantly associated with TLF (hazard ratio 6.63, 95% confidence interval: 1.28-34.3; p=0.02).

CONCLUSIONS: Ostial RCA lesions have specific morphologies – detectable by IVUS – that may be associated with long-term clinical outcomes.

ABSTRACT

Although the rate of in-stent restenosis (ISR) has decreased in the current drug-eluting stent (DES) era[1], percutaneous coronary intervention (PCI) of lesions located at the ostium of the right coronary artery (RCA) still remains challenging and is strongly associated with subsequent target lesion revascularisation[2]. On the one hand, *de novo* ostial RCA lesions have severe calcium, poor distensibility, and excessive hinge motion which may cause stent deformation and fracture, resulting in poor long-term outcomes[2-4]. On the other hand, prior literature has reported that isolated lesions have less atherosclerosis and are more frequently found in younger patients and in women[5-7]. Nevertheless, the morphology of ostial RCA lesions has not been systematically evaluated with intravascular imaging. We hypothesised that there are distinct types of ostial RCA lesions, each with different characteristics that can be detected by intravascular ultrasound (IVUS) and that are related to subsequent specific outcomes.

Methods

STUDY DESIGN AND PATIENT POPULATION

This was a retrospective, observational, single-centre study conducted at New York-Presbyterian Hospital/Columbia University Medical Center (New York, NY, USA). An ostial RCA lesion is defined as a lesion within 3 mm of the aorto-ostial junction[8]. Inclusion criteria were 1) patients who underwent PCI for ostial RCA lesions with clinical symptoms and 2) patients with analysable IVUS images to evaluate ostial RCA morphology. Exclusion criteria were 1) in-stent restenosis, 2) prior coronary artery bypass graft to the RCA, and 3) implantation of a bare metal stent.

Patient demographics were obtained from electronic medical records. This study was approved by the institutional review board of Columbia University Medical Center; they waived informed consent for the retrospective review of records because of the minimal risk. For patients with no outcomes recorded in the electronic database, a waiver of documentation of consent was approved by the institutional review board. These subjects were then called to confirm subsequent outcomes after informed consent was obtained.

ANGIOGRAPHIC ANALYSIS AND ASSESSMENT

Quantitative and qualitative angiographic analyses were performed by experienced analysts blinded to clinical and IVUS findings (T. Sato and Y. Chen) using QAngioXA (Medis Medical Imaging) according to standardised methodology[8]. Only the distal reference was used to calculate angiographic diameter stenosis. Multivessel disease was defined as the presence of ≥50% luminal diameter stenosis in two or more major epicardial arteries. Procedural success was defined as stent implantation with a residual stenosis <30%[9].

Impact on daily practice

There were three distinct IVUS ostial RCA lesion morphologies: isolated ostial RCA disease, CN, and diffuse distal disease. Because the morphology may impact outcomes after DES implantation, it makes sense to evaluate ostial RCA lesion morphology with IVUS after disengagement of the guiding catheter.

IVUS ANALYSIS AND ASSESSMENT

IVUS was performed using rotational imaging catheters (40 or 60 MHz Atlantis/OptiCross [Boston Scientific]; 45 MHz Revolution [Philips]; or 60 MHz Kodama HD [ACIST Medical Systems]) and motorised pullback at 0.5-1.0 mm/s. In order to obtain analysable IVUS images of sufficient quality to evaluate ostial RCA morphology, the guiding catheter was disengaged to visualise the transition from the RCA into the aorta.

IVUS analysis was performed by consensus of two experienced readers (K. Yamamoto and A. Maehara) using planimetry software (echoPlaque 4.0, INDEC Medical Systems).

Reference sites were defined as the least diseased cross-sections that were within 10 mm from the ostium. The remodelling index (RI) was calculated as the vessel area at the minimum lumen area (MLA) site divided by the distal reference vessel area[10]. The ostial RCA lesions were classified as one of three types: 1) isolated – isolated ostial lesions without significant distal disease, 2) calcified nodule (CN) – ostial CN with or without diffuse distal disease, and 3) diffuse – ostial lesions with diffuse distal disease without CN. An isolated ostial RCA lesion was limited to the 10 mm proximal to the aorto-ostium without a CN **(Figure 1A)**[7]. A CN was defined as irregular, convex-shaped calcium on the calcified plate **(Figure 1B)**, with or without diffuse disease[11]. Diffuse lesions were ostial lesions with distal disease that did not contain a CN **(Figure 1C)**. Post-PCI aorto-ostial stent coverage was further categorised as full (360° of visible struts at the ostium), partial (<360° of visible stent struts at the ostium), or no coverage (no visible stent struts at the ostium). Stent expansion was calculated as the minimum stent area (MSA) divided by the distal reference lumen or stent area within 10 mm distal to the ostium[12]. Minimum stent eccentricity was defined as the smallest minimum/maximum stent diameter ratio at a single slice within the stent.

CLINICAL ENDPOINTS

The primary endpoint was target lesion failure (TLF) at 2 years. TLF was defined as a composite of cardiac death, target vessel myocardial infarction (MI), definite stent thrombosis, or ischaemia-driven target lesion revascularisation (TLR). Clinical events were confirmed by investigators reviewing electronic medical records and/or telephone contacts.

Abbreviations

CN	calcified nodule	**MSA**	minimum stent area	**RCA**	right coronary artery
DES	drug-eluting stent	**NSTEMI**	non-ST-elevation myocardial infarction	**STEMI**	ST-elevation myocardial infarction
IVUS	intravascular ultrasound			**TLF**	target lesion failure
MLA	minimum lumen area	**PCI**	percutaneous coronary intervention		
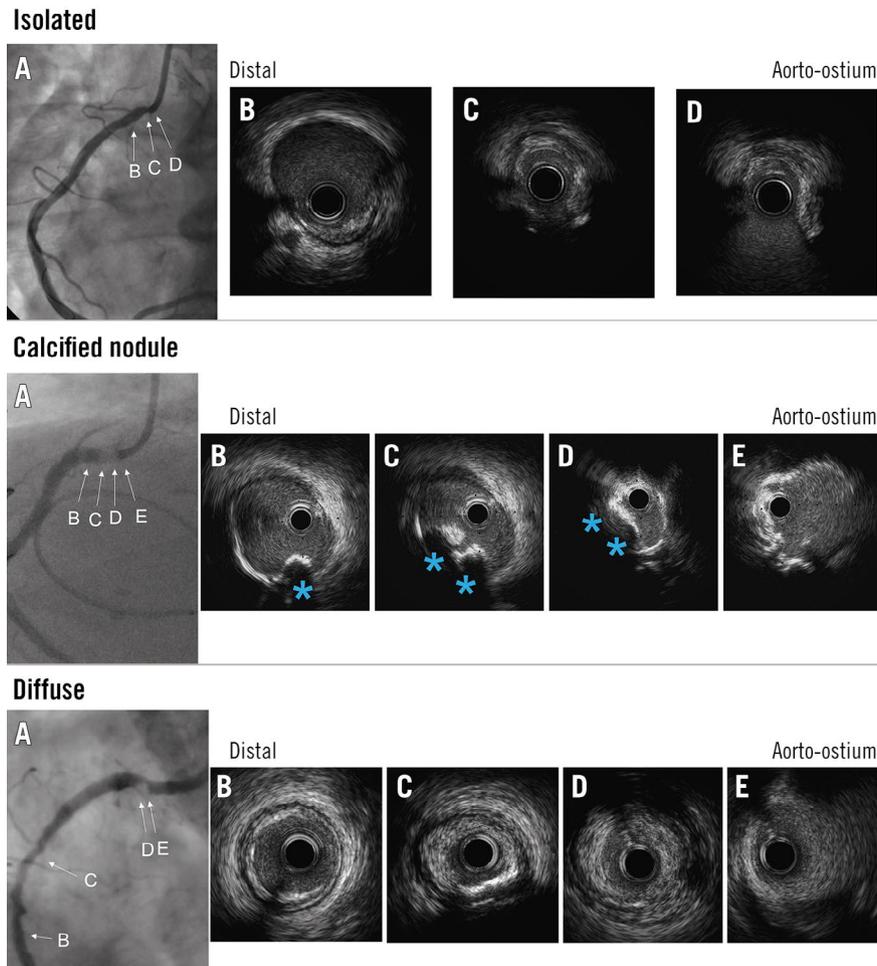
Figure 1. *Representative cases of each group. In each example, the preprocedural coronary angiogram is shown (A) with the angiograms corresponding to the IVUS images (B,C,D,E). The top row shows an isolated lesion: the lesion was limited to the ostium (C,D) and showed negative remodelling (remodelling index 0.61). The middle row shows a calcified nodule: a calcified nodule (CN; blue asterisk) was seen at the ostium of the right coronary artery (B,C,D). The bottom row shows an ostial lesion with diffuse disease (diffuse lesions): non-CN plaque was seen at the ostium (D,E) as well as in the mid-segment (C). IVUS: intravascular ultrasound*

STATISTICAL ANALYSIS

Categorical variables are presented as count and percentage and were compared with the χ^2 or Fisher's exact test, as appropriate. Normally distributed continuous variables were compared with the Student's t-test, and non-normally distributed continuous variables were compared with the non-parametric Mann-Whitney U test. Multivariable logistic regression models were used to identify clinical factors associated with IVUS lesion morphology. The cumulative rate of TLF was estimated from Kaplan-Meier curves and compared using the log-rank test. Cox proportional hazard models were used to identify factors associated with TLF. A two-sided p<0.05 was considered statistically significant. Statistical analysis was performed with R statistics, version 4.0.3 (R Foundation for Statistical Computing).

Results

Between January 2005 and September 2020, IVUS was performed in 5,102 RCA lesions including 368 ostial RCA *de novo* lesions, from which we identified 170 lesions meeting the inclusion criteria **(Supplementary Figure 1)**. Compared to the 106 excluded lesions with missing IVUS images, the 170 included lesions had similar clinical backgrounds except for age (median [first quartile, third quartile] 73 [64, 81] years in patients with included lesions vs 69 [60, 76] years in patients with excluded lesions; p=0.009) **(Supplementary Table 1)**. Out of the 170 included lesions, 20 lesions (11.8%) were isolated, 81 lesions (47.6%) had a CN, and 69 lesions (40.6%) had diffuse distal disease. Among 81 CN lesions, there were only three lesions with disease not extending more than 10 mm from the ostium, while the other 78 CN had diffuse distal disease.

CLINICAL CHARACTERISTICS

Clinical characteristics have been summarised in **Table 1**. Compared to diffuse lesions, isolated lesions were more common in women (75.0% vs 42.0%; p=0.01); and the CN group was older (76 [70, 83] vs 69 [63, 81] years old;

Table 1. Clinical characteristics.

	1. Isolated (n=20)	2. CN (n=81)	3. Diffuse (n=69)	p-value 1. vs 3.	p-value 2. vs 3.
Age, years	66 (63, 78)	76 (70, 83)	69 (63, 81)	0.78	0.002
Women	15 (75.0)	37 (45.7)	29 (42.0)	0.01	0.74
Hypertension	17 (85.0)	71/80 (88.8)	58/67 (86.6)	0.99	0.80
Dyslipidaemia	20 (100)	80/80 (100)	66/67 (98.5)	0.99	0.46
Diabetes mellitus	6 (30.0)	39/80 (48.8)	28/67 (41.9)	0.43	0.41
Insulin-treated	2 (10.0)	14/80(17.5)	10/67 (14.9)	0.73	0.82
Chronic kidney disease*	10 (50.0)	36/80 (45.0)	29/67 (43.3)	0.62	0.87
Dialysis	1 (5.0)	5/80 (6.3)	2/67 (3.0)	0.55	0.46
Peripheral artery disease	2 (10.0)	21/80 (26.3)	19/67 (28.4)	0.14	0.85
Prior PCI	5 (25.0)	27/80 (33.8)	26/67 (38.8)	0.30	0.61
Prior MI	4 (20.0)	15/80 (18.8)	9/67 (13.4)	0.49	0.50
Prior or current moderate or severe AS	4 (20.0)	16/80 (20.0)	8/67 (11.9)	0.46	0.26
Clinical presentation at the time of PCI				0.69	0.22
STEMI	0 (0)	2/80 (2.5)	0 (0)		
NSTEMI	2 (10.0)	9/80 (11.3)	12/67 (17.9)		
Unstable angina	9 (45.0)	25/80 (31.3)	26/67 (38.8)		
Stable coronary artery disease	9 (45.0)	44/80 (55.0)	29/67 (43.3)		
Medication at discharge					
Dual antiplatelet therapy	20 (100)	78/78 (100)	67/67 (100)	-	-
Statin	20 (100)	78/78 (100)	67/67 (100)	-	-
ACE-I/ARB	7 (35.0)	31/78 (39.7)	32/67 (47.8)	0.44	0.40
Beta blocker	9 (45.0)	43/78 (55.1)	38/67 (56.7)	0.45	0.86

Values are n (%), n/N (%) or median (first, third quartile). *Defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2, calculated using the Modification of Diet in Renal Disease equation. ACE-I: angiotensin-converting enzyme inhibitor; ARB: angiotensin II receptor blockers; AS: aortic stenosis; CN: calcified nodule; MI: myocardial infarction; NSTEMI: non-ST-elevation myocardial infarction; PCI: percutaneous coronary intervention; STEMI: ST-elevation myocardial infarction

Table 2. Associated clinical variables for lesion morphology in the multivariable logistic regression model.

	Isolated		CN	
	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value
Age, per 10 years	0.73 (0.44-1.19)	0.25	1.63 (1.16-2.29)	0.002
Women	5.86 (1.60-21.5)	0.004	0.87 (0.43-1.79)	0.71
Diabetes mellitus	0.61 (0.17-2.17)	0.44	1.66 (0.79-3.53)	0.18
Chronic kidney disease*	2.49 (0.70-8.89)	0.16	0.82 (0.39-1.75)	0.60
Peripheral artery disease	0.26 (0.05-1.47)	0.10	0.62 (0.27-1.41)	0.25
Prior or current moderate or severe AS	2.57 (0.45-14.6)	0.29	1.66 (0.59-4.68)	0.33
Prior MI	1.35 (0.28-6.31)	0.71	1.51 (0.58-3.93)	0.40
MI presentation	0.53 (0.10-2.81)	0.44	0.66 (0.26-1.72)	0.40

Each morphology was compared with diffuse lesions. *Defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2, calculated using the Modification of Diet in Renal Disease equation. AS: aortic stenosis; CI: confidence interval; CN: calcified nodule; MI: myocardial infarction

p=0.002) **(Supplementary Figure 2)**. The multivariable logistic model revealed that women were significantly associated with isolated lesions (odds ratio [OR] 5.86, 95% confidence interval [CI]: 1.60-21.5; p=0.004), whereas older age was significantly associated with CN (OR 1.63, 95% CI: 1.16-2.29 per 10-year increase; p=0.002) **(Table 2)**.

ANGIOGRAPHICAL AND PROCEDURAL FINDINGS

Angiographic and procedural findings have been summarised in **Table 3**. Compared to diffuse lesions, isolated lesions had less multivessel disease (15.0% vs 62.3%; p=0.0002) and a shorter RCA lesion length (3.5 [2.7, 4.9] mm vs 5.8 [4.0, 20.3] mm; p=0.0002). CN had worse

Table 3. Angiographic and procedural findings.

	1. Isolated (n=20)	2. CN (n=81)	3. Diffuse (n=69)	*p*-value 1. vs 3.	*p*-value 2. vs 3.
Angiographic findings					
Multivessel disease	3 (15.0)	59 (72.8)	43 (62.3)	0.0002	0.22
Calcification of ascending aorta	2 (10.0)	30 (37.0)	18 (26.1)	0.22	0.16
Calcification of target lesion	4 (20.0)	61 (75.3)	31 (44.9)	0.07	0.0001
Moderate	3 (15.0)	38 (46.9)	18 (26.1)	0.38	0.01
Severe	1 (5.0)	23 (28.4)	13 (18.8)	0.18	0.19
Radiolucent mass	0 (0)	24 (29.6)	0 (0)	-	<0.0001
Lesion length, mm	3.5 (2.7, 4.9)	5.2 (3.6, 9.1)	5.8 (4.0, 20.3)	0.0002	0.07
Reference vessel diameter, mm	2.60 (2.45, 2.95)	2.89 (2.62, 3.28)	2.94 (2.53, 3.20)	0.20	0.49
Minimum lumen diameter, mm					
Pre-PCI	1.30 (1.02, 1.49)	1.03 (0.63, 1.40)	1.17 (0.93, 1.51)	0.60	0.04
Post-PCI	2.92 (2.60, 3.16)	2.90 (2.59, 3.22)	2.85 (2.53, 3.14)	0.77	0.21
Diameter stenosis, %					
Pre-PCI	50.2 (42.5, 63.0)	66.3 (55.4, 76.9)	57.9 (49.1, 66.4)	0.27	0.003
Post-PCI	9.1 (5.5, 13.5)	11.1 (7.8, 16.7)	10.5 (6.8, 14.7)	0.28	0.59
Procedural findings					
Max device diameter, mm	3.5 (3.0, 4.0)	3.5 (3.5, 4.0)	3.5 (3.5, 4.0)	0.39	0.08
Balloon/artery ratio	1.35 (1.16, 1.51)	1.30 (1.16, 1.42)	1.29 (1.16, 1.39)	0.55	0.82
Total stent length, mm	15 (14, 17)	22 (15, 48)	38 (18, 61)	<0.0001	0.04
Max inflation pressure, atm	17 (15, 20)	18 (16, 20)	20 (16, 20)	0.09	0.20
Predilation before IVUS	5 (25.0)	25 (30.9)	21 (30.4)	0.78	0.99
Predilation before stent implantation	19 (95.0)	81 (100)	65 (94.2)	0.99	0.04
Stent type				0.69	0.19
1st-generation DES	3 (15.0)	3 (3.7)	7 (10.1)		
2nd-generation DES	17 (85.0)	78 (96.3)	62 (89.9)		
Adjunctive device					
Cutting/scoring balloon	1 (5.0)	10/79 (12.7)	3/65 (4.6)	0.99	0.14
Rotational atherectomy	3 (15.0)	9/80 (11.3)	6/67 (9.0)	0.42	0.79
Orbital atherectomy	0 (0)	1/80 (1.3)	2/67 (3.0)	0.99	0.59
Intravascular lithotripsy	0 (0)	1/80 (1.3)	0 (0)	-	0.99
Ostial flash	5 (25.0)	10/80 (12.5)	7/67 (10.5)	0.14	0.80
Procedural complication*	0 (0)	2/80 (2.5)	0 (0)	-	0.50

Values are n (%), n/N (%) or median (first, third quartile). *Coronary perforation that required covered stents.
CN: calcified nodule; DES: drug-eluting stent; PCI: percutaneous coronary intervention; IVUS: intravascular ultrasound

diameter stenosis (66.3 [55.4, 76.9]% vs 57.9 [49.1, 66.4]%; p=0.003).

Predilation before IVUS was required in 51 lesions (30.0%). Second-generation DES were used in most cases. All lesions were treated successfully.

IVUS ANALYSIS

IVUS findings have been summarised in **Table 4**. Compared to diffuse lesions, isolated lesions had more negative remodelling (remodelling index 0.82 [0.67, 0.94] vs 0.93 [0.82, 1.04]; p=0.009), less plaque burden at the MLA site (65.9 [56.5, 72.5]% vs 77.1 [70.5, 80.9]%; p<0.0001), and less reference plaque burden (35.7 [35.1, 37.3]% vs 53.0 [43.7,

63.5]%; p<0.0001). Compared with diffuse lesions, CN had more plaque burden at the MLA site (81.0 [74.3, 84.9]% vs 77.1 [70.5, 80.9]%; p=0.002), greater maximum calcium arc (283 [167, 360]° vs 130 [11, 240]°; p<0.0001), and worse stent expansion (68.0 [61.1, 79.4]% vs 79.6 [70.4, 86.7]%; p<0.0001).

CLINICAL OUTCOMES

Clinical outcomes have been summarised in **Table 5** and **Figure 2**. The median follow-up duration after treatment was 2.0 (0.4, 4.4) years (2.5 [1.8, 4.8] years in the isolated group, 1.8 [0.4, 4.3] years in the CN group, and 1.7 [0.3, 4.4] years in the diffuse disease group). The Kaplan-Meier

Table 4. Intravascular ultrasound findings.

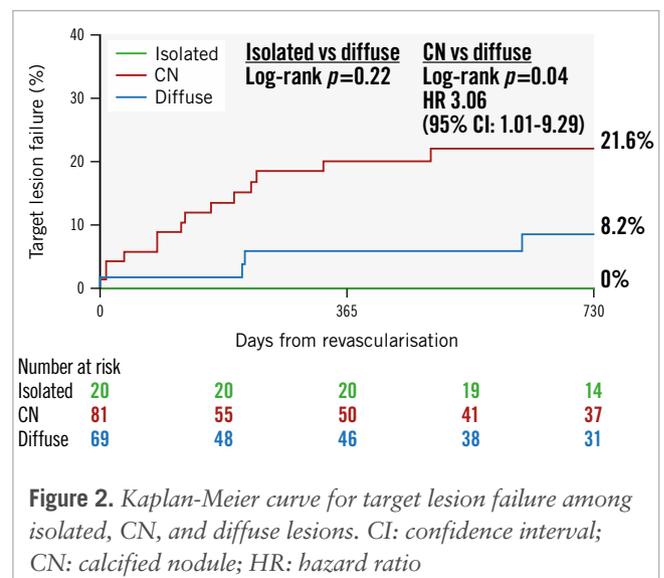|	1) Isolated (n=20)	2) CN (n=81)	3) Diffuse (n=69)	p-value 1 vs 3	p-value 2 vs 3
Presence of calcium	9 (45.0)	81 (100)	32 (46.4)	0.99	<0.0001
Calcium in ascending aorta	6 (30.0)	65/79 (82.3)	14/64 (21.9)	0.55	<0.0001
Preprocedure	n=20	n=62	n=52		
Minimum lumen area, mm^2	3.5 (2.1, 3.7)	3.1 (2.5, 3.9)	3.3 (2.7, 3.8)	0.37	0.33
Vessel area, mm^2	10.1 (8.0, 11.5)	15.1 (13.3, 20.7)	14.2 (10.7, 16.3)	0.0002	0.02
Plaque burden, %	65.9 (56.5, 72.5)	81.0 (74.3, 84.9)	77.1 (70.5, 80.9)	<0.0001	0.002
Reference lumen area within 10 mm, mm^2	7.6 (6.4, 9.4)	8.0 (5.8, 10.5)	6.8 (5.0, 8.4)	0.06	0.03
Reference vessel area within 10 mm, mm^2	12.2 (10.2, 14.6)	16.6 (13.9, 20.5)	13.9 (12.0, 18.1)	0.01	0.02
Reference plaque burden, %	35.7 (35.1, 37.3)	51.6 (45.9, 59.5)	53.0 (43.7, 63.5)	<0.0001	0.81
Remodelling index	0.82 (0.67, 0.94)	0.97 (0.87, 1.04)	0.94 (0.83, 1.06)	0.007	0.52
Remodelling index <1.0	18 (90.0)	38/62 (61.3)	34/52 (65.8)	0.04	0.70
Lesion length, mm	4.9 (3.7, 6.0)	21.7 (13.9, 41.7)	31.3 (21.0, 45.2)	<0.0001	0.03
Maximum calcium arc, °	90 (0,170)	283 (167, 360)	130 (11, 240)	0.20	<0.0001
Post-procedure	n=17	n=74	n=57		
Minimum stent area, mm^2	8.2 (5.9, 9.3)	7.3 (5.7, 7.3)	7.5 (6.4, 9.7)	0.98	0.07
Stent expansion, %	82.5 (76.0, 90.8)	68.0 (61.1, 79.4)	79.6 (70.4, 86.7)	0.22	<0.0001
Minimum stent eccentricity index	0.84 (0.77, 0.86)	0.65 (0.59, 0.73)	0.75 (0.68, 0.82)	0.006	<0.0001
Stent coverage of ostium				0.03	0.25
Full coverage	16/17 (94.1)	54/68 (79.4)	36/54 (66.7)		
Partial	1/17 (5.9)	9/68 (13.2)	13/54 (24.1)		
No coverage	0/17 (0)	5/68 (7.4)	5/54 (9.3)		

Values are n (%), n/N (%) or median (first, third quartile). CN: calcified nodule

Table 5. Clinical and morphological factors associated with target lesion failure in the multivariable Cox proportional hazard model.

	Hazard ratio (95% CI)	p-value
Calcified nodule (vs isolated or diffuse)	9.97 (2.31-43.0)	0.002
Age, per 10 years	0.57 (0.35-0.94)	0.02
Chronic kidney disease	10.3 (2.61-40.4)	0.0008
Post-PCI minimum stent area, per 1 mm^2	1.09 (0.82-1.41)	0.53

CI: confidence interval; DES: drug-eluting stent; PCI: percutaneous coronary intervention

Figure 2. Kaplan-Meier curve for target lesion failure among isolated, CN, and diffuse lesions. CI: confidence interval; CN: calcified nodule; HR: hazard ratio

rate of TLF at 2 years was higher in the CN group compared to the diffuse disease group (21.6% vs 8.2%, hazard ratio [HR] 3.06, 95% CI: 1.02-9.29; p=0.04), whereas there were no events in patients with an isolated ostial RCA lesion (p=0.22) **(Supplementary Table 2)**. Univariate and multivariable Cox proportional hazard modelling were performed to include CN, age, chronic kidney disease, and post-PCI MSA. CN (HR 9.97 [95% CI: 2.31-43.0]; p=0.002), younger age (HR 0.57 [95% CI: 0.35-0.94]; p=0.02), and chronic kidney disease (HR 10.3 [95% CI: 2.61-40.4]; p=0.0008) were all associated with TLF **(Supplementary Table 3, Table 5)**.

Discussion

Historically, ostial RCA lesions have been associated with worse outcomes regardless of whether they were treated with balloon angioplasty[4], directional or rotational atherectomy or laser angioplasty[13], bare metal stenting[14], or drug-eluting stent implantation[2]. Therefore, it is surprising that there have been few, if any, morphological studies of ostial RCA lesions using

IVUS; imaging of aorto-ostial lesions with optical coherence tomography is difficult because the guiding catheter must be engaged in order to clear the blood-filled lumen. The key findings of the present study are as follows. There were three distinct IVUS morphologies: infrequent isolated ostial RCA lesions without significant diffuse distal disease; ostial RCA lesions with significant diffuse distal disease, but without a CN; and CNs almost always accompanied by diffuse distal disease. In terms of post-PCI outcomes, patients treated for ostial RCA lesions with CN morphology had the worst outcomes, while those with isolated disease had the best outcomes (Central illustration).

The aetiology of an ostial RCA lesion can include atherosclerosis, autoimmune aortitis (Takayasu disease or syphilis), aortic valve calcification, iatrogenic complication, and tumours[5,6,15,16]. Histologically, an ostial RCA has a muscle bundle which independently arises from the elastin-muscle fibre of the aorta, frequently containing a circumferential sphincter-like muscle[17] and a higher prevalence of fibrotic and sclerotic plaque, including smooth muscle collagen tissue and calcification and less lipid[13]. Previous IVUS reports revealed that negative remodelling was frequently seen in 86% of ostial RCA lesions[10], consistent with our data. The present study revealed that the overall TLF rate was 13.4%, corresponding to previous reports[2,9]. Tsunoda et al reported on an IVUS analysis of 18 ostial RCA lesions comparing patients with and without subsequent restenosis. The restenosis group had more visible calcium (58% vs 5%) and a smaller stent area (8.1 mm^2 vs 10.4 mm^2)[18].

ISOLATED LESIONS

Previous reports revealed that the prevalence of an isolated lesion varied from 8-24%, and they were more common in women[5,6]. Barner et al included 41 patients with aorto-ostial RCA and found 10 (24%) isolated lesions, with 70% of these in women[6]. Darabian et al included 256 left main lesions and 36 (14.1%) aorto-ostial lesions, with 47.2% of these in women[5]. The present data were consistent with these previous reports.

In the current study, the 20 patients with isolated ostial lesions had no events. Isolated lesions had less calcium and larger stent expansion, which may explain the optimal outcomes[19]. In addition, isolated lesions were fully covered with the stents, which might contribute to less stent edge restenosis due to an uncovered stent.
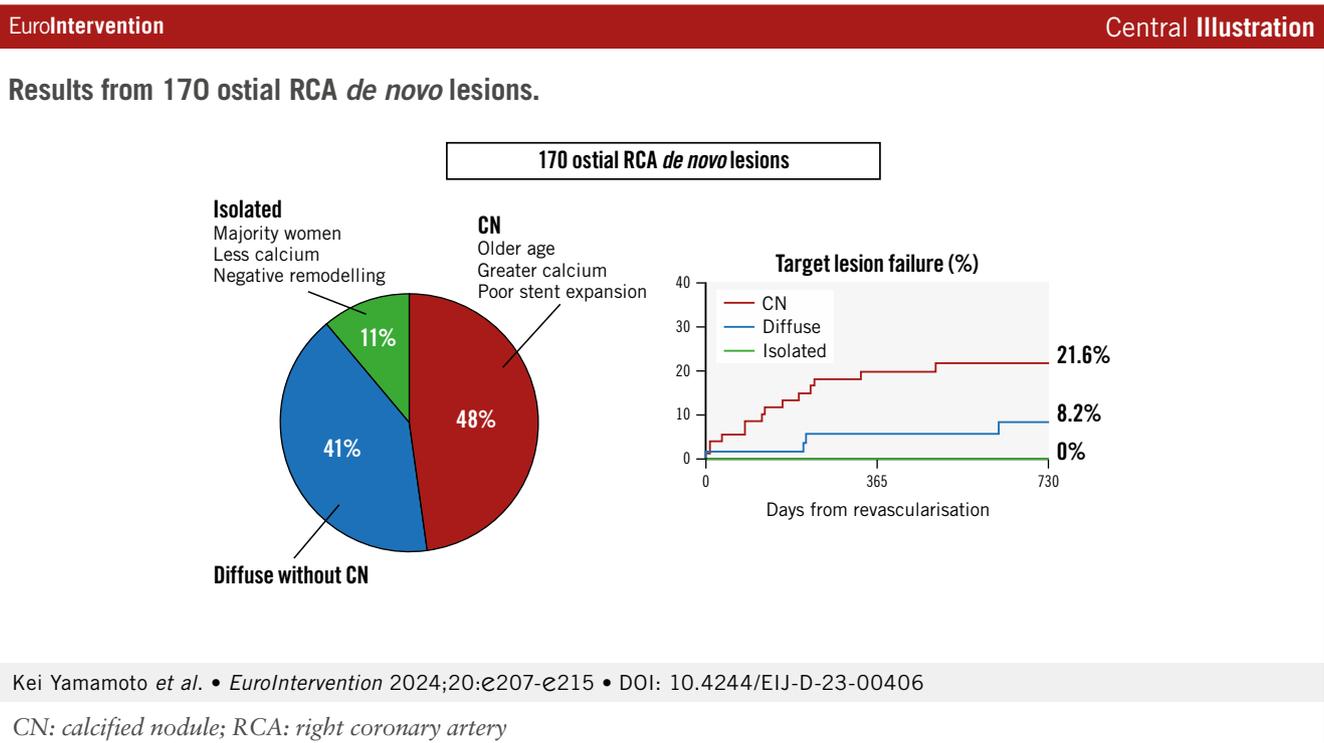
CALCIFIED NODULES

CNs were found in half of the aorto-ostial RCA lesions in the present study, a higher prevalence compared to previous studies including any coronary artery segments: 5.3-17.0% by IVUS[20,21], 4.2-12.5% by optical coherence tomography[22,23], and 3.6% by pathology[24]. The presence of CN has been associated with an atherosclerotic background, such as older age, more plaque burden, and calcium[21], which corresponds with the findings in the present study.

In the present study, CN was strongly associated with TLF. Morofuji et al reported that the presence of CN was associated with poor outcomes among patients with calcified lesions requiring atherectomy[25]. Nakamura et al suggested that protruding CN within a stent are an important factor in stent failure[26].

DIFFUSE LESIONS WITHOUT A CALCIFIED NODULE

While isolated lesions and CN were specific categories, diffuse lesions were considered to be close to general atherosclerosis morphology. The present study revealed IVUS characteristics such as plaque burden (median 77%) and calcium arc (median 130°) were similar to previous IVUS reports[27,28].

EuroIntervention — Central **Illustration**

Results from 170 ostial RCA de novo lesions.

CN: calcified nodule; RCA: right coronary artery

In the present study, the TLF rate of diffuse lesions was 8.2%. The current second-generation DES registry reported that the 2-year TLF rate of overall vessels was 3-10%[29,30], which corresponds to the present study. Ostial lesions with diffuse disease without a CN had numerically worse, but statistically similar, outcomes compared to isolated lesions.

TECHNICAL ISSUES ASSOCIATED WITH IMAGING OSTIAL RCA LESIONS

To assess lesion morphology or postprocedural results by IVUS, the guide catheter needs to be disengaged[10]. However, there are technical difficulties with disengaging the catheter in some cases, such as a deeply inserted guiding catheter or when disengaging the catheter risks injury to the patient. The present study had 21 cases that could not be analysed because the guiding catheter was not disengaged.

Limitations

There are several limitations in the present study. First, this was a retrospective, observational study of only patients with analysable preinterventional IVUS. There was selection bias, so caution is needed during interpretation. Second, the procedure depended on each operator's decision-making, which might have affected the outcomes. Third, as we included patients over a period of 15 years, interventional devices and techniques and medical treatment changed during the study period. However, 92% of cases were treated with second-generation DES, and clinical outcomes including only patients treated with second-generation DES were consistent with the entire cohort **(Supplementary Table 2)**. Unfortunately, data on medication during follow-up could not be obtained. Fourth, the number of patients was small, especially in the "isolated" subgroup. Similarly, because of the small number of events, multiple outcome variables were analysed, which could have led to a type I error. Therefore, this study should be considered as hypothesis-generating, and further large-scale studies are required. Finally, even though the present study revealed the predictor of TLF after PCI for ostial RCA, optimal treatment remains unclear.

Conclusions

Ostial RCA lesions have specific morphologies detectable by IVUS: about half were CNs, a few were isolated lesions, and the rest had diffuse disease. Long-term clinical outcomes may depend on the lesion type. In particular, our data, obtained on a relatively small patient population, suggest that DES implantation in ostial RCA lesions with CNs might result in worse clinical outcomes compared to other morphologies.

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Conflict of interest statement

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Supplementary data

Supplementary Table 1. Comparison between included lesions and lesions that were excluded because of missing IVUS images.

Supplementary Table 2. Clinical outcomes at 2 years.

Supplementary Table 3. Clinical and morphological factors associated with target lesion failure in the univariate Cox proportional hazards model.

Supplementary Figure 1. Study flowchart.

Supplementary Figure 2. Prevalence of age and gender among each group.

The supplementary data are published online at:
https://eurointervention.pcronline.com/
doi/10.4244/EIJ-D-23-00406

Supplementary data

Supplementary Table 1. Comparison between included lesions and lesions that were excluded because of missing IVUS images.

Variable	Included lesions (n=170)	Excluded lesions (n=106)	P value
Age (years)	73 (64, 81)	69 (60, 76)	0.009
Women	81 (47.7)	44 (41.5)	0.38
Hypertension	146/167 (87.4)	92/105 (87.6)	1.00
Dyslipidemia	166/167 (99.4)	102/105 (97.1)	0.30
Diabetes mellitus	73/167 (43.7)	38/105 (36.2)	0.25
Chronic kidney disease*	75/167 (44.9)	35/105 (33.3)	0.08
Peripheral artery disease	42/167 (25.2)	24/105 (22.9)	0.77
Prior PCI	58/167 (34.7)	46/105 (43.8)	0.16
Prior MI	28/167 (16.8)	26/105 (24.8)	0.12
Prior or current moderate or severe aortic stenosis	28/167 (16.8)	12/105 (11.3)	0.29
STEMI/NSTEMI presentation	25/167 (14.7)	12/105 (11.3)	0.33

Values are n/N (%) or median (first, third quartile). *Defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2 calculated using the Modification of Diet in Renal Disease equation. IVUS denotes intravascular ultrasound; PCI denotes percutaneous coronary intervention; MI denotes myocardial infarction; STEMI denotes ST elevated MI; NSTEMI denotes non-ST elevated MI.

Supplementary Table 2. Clinical outcomes at 2 years.

	1) Isolated	2) CN	3) Diffuse	P value 1 vs 3	P value 2 vs 3
Total cohort (n=170)	n=20	n=81	n=69		
Target lesion failure	0 (0)	21.6 (14)	8.2 (4)	0.22	0.04
Cardiac death	0 (0)	4.3 (3)	0 (0)	-	0.12
Target vessel myocardial infraction	0 (0)	1.3 (1)	1.5 (1)	0.92	0.59
Peri-procedural	0 (0)	1.3 (1)	1.5 (1)	0.92	0.59
Non-procedural	0 (0)	0 (0)	0 (0)	-	-
Definite stent thrombosis	0 (0)	0 (0)	0 (0)	-	-
Ischaemic-driven target lesion revascularisation	0 (0)	17.2 (10)	7.2 (3)	0.25	0.09
Patients treated with 2nd generation DES (n=157)	n=17	n=78	n=62		
Target lesion failure	0 (0)	20.8 (13)	6.0 (3)	0.31	0.03
Cardiac death	0 (0)	4.4 (3)	0 (0)	-	0.13
Target vessel myocardial infraction	0 (0)	1.3 (1)	1.6 (1)	0.92	0.88
Peri-procedural	0 (0)	1.3 (1)	1.6 (1)	0.92	0.88
Non-procedural	0 (0)	0 (0)	0 (0)	-	-
Definite stent thrombosis	0 (0)	0 (0)	0 (0)	-	-
Ischaemic-driven target lesion revascularisation	0 (0)	16.1 (9)	4.7 (2)	0.25	0.07

Values are n (%). Kaplan-Meier estimate (number of event). Target lesion failure; cardiac death, target vessel myocardial infarction, definite stent thrombosis, or ischaemic-driven target lesion revascularisation

Supplementary Table 3. Clinical and morphological factors associated with target lesion failure in the univariate Cox proportional hazards model.

	Hazard ratio (95% CI)	P-value
Clinical characteristics		
Age, per 10 years	0.99 (0.68-1.51)	0.97
Male sex	0.88 (0.34-2.22)	0.78
Diabetes mellitus	1.95 (0.76-5.03)	0.17
Chronic kidney disease	4.63 (1.52-14.1)	0.007
Prior or current moderate or severe aortic stenosis	1.49 (0.42-4.17)	0.49
STEMI/NSTEMI presentation	1.55 (0.51-4.71)	0.44
2nd generation DES use	0.49 (0.11-2.17)	0.39
Angiographical findings		
Multi vessel disease	1.86 (0.66-5.20)	0.24
Calcification at target lesion	1.54 (0.60-4.42)	0.39
Post-PCI minimum lumen diameter, per 1mm	1.15 (0.41-2.93)	0.78
Intravascular findings		
Calcified nodule (versus isolated or diffuse)	4.21 (1.39-12.8)	0.005
Lesion length, per 10mm	1.04 (0.73-1.37)	0.82
Remodelling index, per 0.1	1.15 (0.80-1.62)	0.45
Post MSA, per 1mm^2	0.98 (0.76-1.23)	0.85
Minimum stent eccentricity index, per 0.1	0.42 (0.25-0.69)	0.0009

CI denotes confidence interval. IVUS denotes intravascular ultrasound; PCI denotes percutaneous coronary intervention; MI denotes myocardial infarction; STEMI denotes ST elevated MI; NSTEMI denotes non-ST elevated MI.MSA denotes minimum stent area.

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│ 5102 procedures that underwent IVUS-guided PCI for RCA lesions│
│ between 2005 January and 2020 September                       │
└─────────────────────────────────────────────────────────────┘
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                           ▼
┌─────────────────────────────────────────────────────────────┐
│ 584 procedures that underwent IVUS-guided PCI for ostial RCA lesions │
└─────────────────────────────────────────────────────────────┘
                           │        ┌──────────────────────────────────┐
                           │───────▶│ 216 procedures for in-stent ostial RCA lesions │
                           │        └──────────────────────────────────┘
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┌─────────────────────────────────────────────────────────────────────┐
│ 368 procedures that underwent IVUS-guided PCI for de novo ostial RCA lesions │
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                           │        ┌────────────────────────────────────────────────────────────────────┐
                           │───────▶│ 183 lesions excluded                                                   │
                           │        │    106 missing IVUS images for review                                  │
                           │        │    24 prior CABG to RCA                                                 │
                           │        │    23 deferred by IVUS                                                  │
                           │        │    21 unable to access because the guiding catheter was not disengaged  │
                           │        │    15 treated with BMS                                                  │
                           │        │    8 insufficient imaging quality                                       │
                           │        │    1 spontaneous coronary artery dissection                             │
                           ▼        └────────────────────────────────────────────────────────────────────┘
┌────────────────────────────────────────────────────────────────────┐
│ 170 de novo ostial RCA lesions that underwent IVUS-guided PCI in 170 patients │
└────────────────────────────────────────────────────────────────────┘
          │                    │                        │
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┌─────────────────────┐ ┌──────────────────┐ ┌──────────────────────────┐
│ 20 lesions with     │ │ 81 lesions with CN│ │ 69 lesions with diffuse  │
│ isolated lesions    │ │                   │ │ lesions                  │
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Supplementary Figure 1. Study flowchart.

Among 5102 procedures that underwent IVUS-guided PCI for RCA lesions, 170 de novo RCA ostial lesions represented the current cohort that was divided into 20 isolated lesions, 81 CN lesions, and 69 diffuse lesions. PCI denotes percutaneous coronary intervention; IVUS denotes intravascular ultrasound; RCA denotes right coronary artery; CABG denotes coronary artery bypass grafting; BMS denotes bare-metal stent; CN denotes calcified nodule.
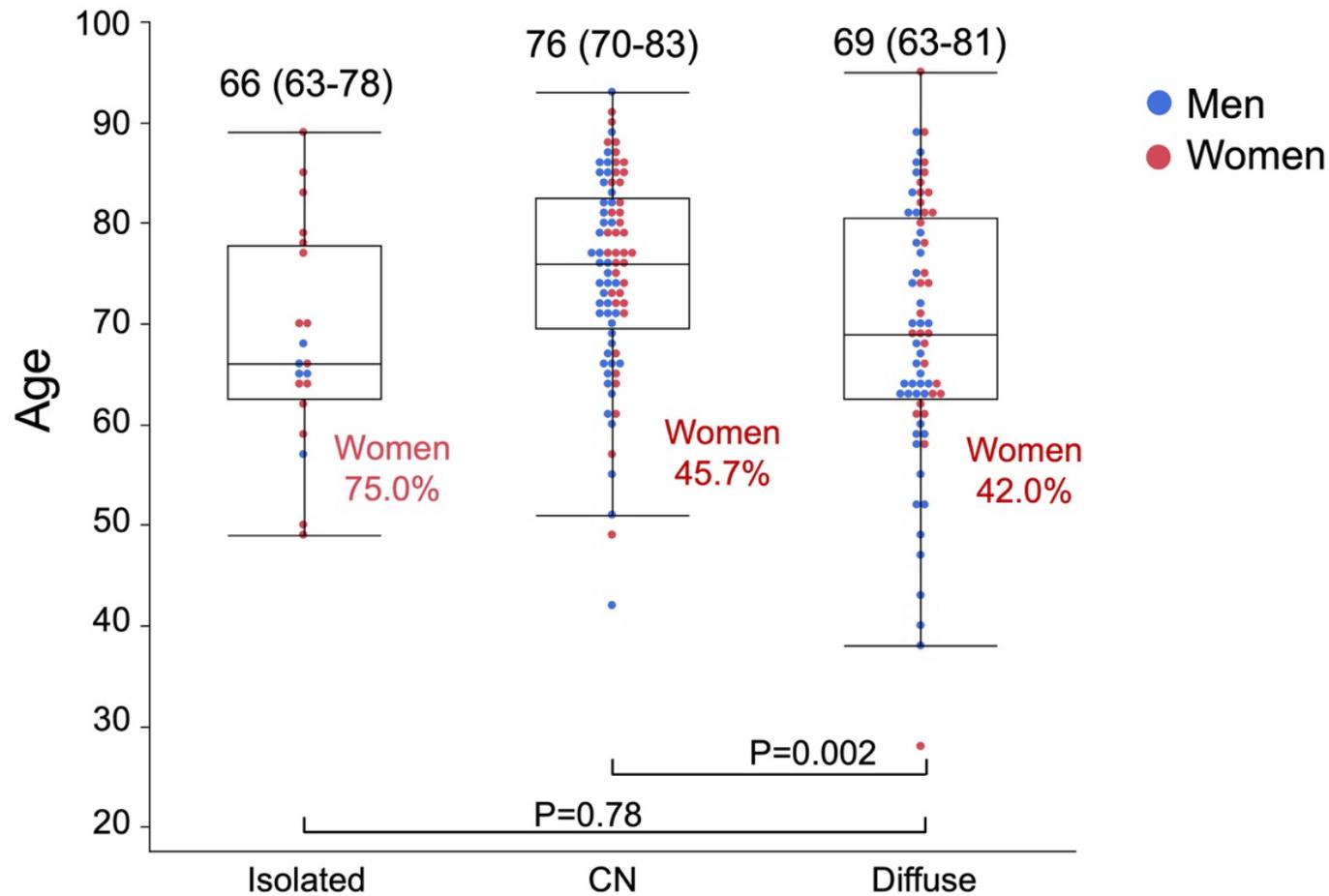
Supplementary Figure 2. Prevalence of age and gender among each group.

Compared to diffuse lesions, the frequency of women was higher in isolated lesions. On the other hand, CN was more common in older patients. CN denotes calcified nodule.