

Ramus Intermedius Anatomy and Left Main Coronary Geometry on Coronary Computed Tomography Angiography: A Retrospective Single-Center Study

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Abstract

Background

Ramus intermedius (RI) changes the left main (LM) coronary division from bifurcation to trifurcation, but its associations with LM geometry, CT-derived fractional flow reserve (CT-FFR), and adjacent-vessel atherosclerotic features remain incompletely characterized.

Methods

In this retrospective single-center study, consecutive adults who underwent clinically indicated coronary computed tomography angiography between December 2024 and April 2025 were screened. The final age-matched cohort included 300 patients (150 with RI and 150 without RI). LAD-LCX angle, vessel diameter and cross-sectional area (CSA), plaque features, stenosis severity, and CT-FFR were evaluated. RI-specific analyses by ostial location, diameter, and functional status were exploratory. Benjamini-Hochberg false-discovery-rate correction was applied within prespecified outcome families. Because sex distribution differed between groups, the primary LAD-LCX angle comparison was supplemented by an aggregate tipping-point sensitivity analysis.

Results

Patients with RI had a wider LAD-LCX angle than patients without RI ($99.35^\circ \pm 25.61^\circ$ vs. $69.22^\circ \pm 17.83^\circ$; $P < 0.001$), with a mean difference of 30.13° (95% CI, 25.11° - 35.15°), and had larger LM diameter and CSA. Diseased-segment analyses showed no significant between-group differences in plaque composition or stenosis severity. Within the RI group, proximal-LAD RI origin remained associated after multiplicity correction with smaller LAD CSA ($q < 0.008$) and more frequent LAD CT-FFR positivity ($q = 0.009$), whereas nominal anatomic stenosis signals were attenuated ($q = 0.051$). Only 10 patients had RI CT-FFR ≤ 0.80 ; findings stratified by RI CT-FFR status were therefore presented descriptively. In the aggregate sensitivity analysis, a male-female LAD-LCX angle difference of approximately 105.1° would be required for the observed sex imbalance alone to reduce the primary group contrast to zero, but this calculation does not replace patient-level adjustment.

Conclusions

RI presence was associated with a wider LM bifurcation angle and larger LM dimensions on CCTA. Selected RI ostial-location associations persisted after multiplicity correction. These observational findings do not establish causality, and residual confounding and the sparse RI CT-FFR-positive subgroup warrant cautious interpretation and external validation.

1. Introduction

Coronary artery disease (CAD) remains a leading cause of morbidity and mortality worldwide [1, 2]. Beyond systemic risk factors, local vascular geometry has been associated with the development and progression of coronary atherosclerosis [3]. Coronary branch points are common sites of plaque formation [3]. A shift from bifurcation to trifurcation anatomy may alter local coronary geometry, but the clinical relevance of this common anatomic variant has not been fully defined [4–15].

The left main coronary artery (LM) bifurcation is a major anatomic site because it supplies most of the left ventricular myocardium [4–8]. In standard anatomy, the LM divides into the left anterior descending (LAD) and left circumflex (LCX) arteries [4–8]. In a proportion of individuals, a ramus intermedius (RI) arises between the LAD and LCX and forms a true trifurcation [5–12]. This variant is associated with a different local geometry, most visibly by widening the LAD-LCX take-off angle [10–17]. Previous studies have linked bifurcation geometry with plaque distribution and lesion burden [10, 13–26]. Coronary computed tomography angiography (CCTA) is widely used for noninvasive anatomic assessment of CAD, and CT-FFR adds functional assessment of lesion-specific ischemia from the same imaging dataset [27–33].

Several questions remain unresolved despite the recognized prevalence of the RI [5–15]. First, whether RI presence alone corresponds to measurable differences in LM bifurcation geometry is uncertain [10–15]. Second, RI ostial location within the trifurcation, including a take-off closer to the LAD or to the LCX, has not been adequately characterized [9–15]. Third, the relationship of RI-specific anatomic features with CT-FFR abnormalities and with plaque or stenosis in adjacent vessels remains unclear [10–15, 26, 31–36]. We therefore conducted a retrospective single-center CCTA study to compare LM bifurcation geometry between patients with and without an RI. Within the RI subgroup, we also assessed the associations of RI ostial location, RI diameter, and RI CT-FFR with vessel dimensions, CT-FFR findings, and local atherosclerotic features. We hypothesized that RI-related anatomy would be associated with geometric and functional differences, while treating RI-specific subgroup analyses as exploratory.

2. Methods

2.1 Study design and setting

This retrospective observational CCTA study was performed at the Department of Diagnostic CT, Cangzhou Central Hospital, China. Consecutive adults who underwent clinically indicated CCTA between December 2024 and April 2025 were screened to define the source population. The final analytic cohort was assembled after eligibility assessment and selection of the non-RI comparison group by 1:1 age matching. Thus, “consecutive” refers to screening of the source population rather than to a simple consecutive sample of the final 300 participants. The study compared patients with an RI with patients without an RI and included prespecified RI subgroup analyses based on RI-specific anatomic and functional features.

2.2 Participants

2.2.1 Eligibility criteria

Patients were assigned to the RI group if they were 18 years of age or older and had an RI with a diameter of ≥ 2 mm on CCTA [5–12]. The comparison group was drawn from eligible patients without an RI who underwent CCTA during the same study period and was selected by 1:1 age matching. Exclusion criteria were: (1) nondiagnostic or poor-quality CCTA images that prevented reliable measurement; (2) previous coronary stenting, coronary artery bypass grafting, or other cardiac surgery; (3) congenital coronary anomalies [5–8]; and (4) severe coronary calcification or other imaging features that prevented reliable lumen assessment or CT-FFR processing [30, 37–41]. Baseline clinical variables included age, sex, body mass index, smoking status, alcohol consumption, hypertension, hyperlipidemia, and diabetes mellitus [1, 2, 28, 29].

2.2.2 Handling of incomplete data

Primary group assignment was based on evaluable CCTA examinations [30, 37–39]. The final matched cohort contained 150 patients with an RI and 150 age-matched patients without an RI. For analyses requiring RI-specific variables, only patients with available measurements for the relevant variable were included. RI ostial location analyses were therefore restricted to the 150 patients in the RI group, RI CT-FFR analyses were restricted to the RI group, and RI diameter subgroup analyses were performed in the subset with complete RI diameter and plaque data ($n = 111$). Missing data were handled by complete-case analysis for each prespecified comparison [42–44].

2.2.3 Sample size

The sample size was estimated for the primary comparison of LAD-LCX angle between the RI and non-RI groups. Assuming a between-group difference of 15° and a standard deviation of 20° , with a two-sided alpha of 0.05 and 80% power, at least 142 patients per group were required. To account for unusable studies and incomplete measurements, 150 patients were included in each group.

2.2.4 Group definitions

The final cohort included 300 patients: 150 in the RI group and 150 in the non-RI group. Within the RI group, patients were further categorized by RI ostial location as proximal to the LAD ($n = 82$) or proximal to the LCX ($n = 68$). RI CT-FFR positivity was defined as $\text{CT-FFR} \leq 0.80$ [31–36, 40, 45–50].

2.3 CCTA acquisition

CCTA examinations were performed with either a Toshiba Aquilion ONE 320-slice CT scanner or a Siemens SOMATOM Force dual-source CT scanner [4, 27–30, 37–39]. Scanning parameters were adjusted according to scanner type and patient habitus and included tube voltage of 80–120 kV, tube current of 300–400 mAs, gantry rotation time of 0.4–0.6 seconds, and slice thickness of 0.5 or 0.75 mm [4, 30, 37–39]. The scan range extended from 1 cm below the carina to the cardiac diaphragm. Patients

fasted for 4–6 hours and received breath-hold training before image acquisition. When needed, heart rate was controlled with oral beta-blockers (target ≤ 75 beats/min for 320-slice CT and ≤ 90 beats/min for dual-source CT) [37]. Iopromide contrast medium (350 mg I/mL) was injected intravenously at 1.5 mL/kg and 4.5–5.0 mL/s, followed by 40 mL saline at the same rate. Image acquisition was triggered by bolus tracking in the ascending aorta during a single end-inspiratory breath-hold [37].

2.4 Image analysis

2.4.1 Coronary anatomy and vessel measurements

DICOM datasets were first reviewed on a GE AW 4.6 workstation to identify RI presence. Quantitative analyses were then performed with dedicated coronary analysis software (Shukun-FFR, version 1.11.1) [31, 32, 34–36, 38, 45]. The LAD-LCX angle was defined as the take-off angle between the proximal LAD and LCX at the LM bifurcation [16–26]. Vessel diameter and cross-sectional area (CSA) were measured at standardized locations: within 5 mm of the ostium for the LM, LAD, and LCX, and at the RI origin for the RI [38, 39].

Plaque within 5 mm of the distal LM and at the LAD and LCX ostia was classified as calcified, noncalcified, or mixed according to accepted CCTA criteria [30, 38, 39, 51–55]. Stenosis severity was visually assessed and classified as $< 50\%$ or $\geq 50\%$ diameter stenosis [30, 38, 39]. Because a single patient could have more than one diseased segment, plaque type and stenosis burden are summarized at the diseased-segment level where appropriate. Lesion-based counts may therefore exceed the number of patients in a group.

2.4.2 CT-FFR analysis

CT-FFR values were calculated from the CCTA datasets with the same software platform, Shukun-FFR, version 1.11.1 [31, 32, 34–36, 41, 45, 56–62]. Cross-platform validation and independent interobserver or intraobserver reproducibility testing were not performed in this cohort. Semi-automated centerlines were generated for the LM, LAD, LCX, and RI [34, 35]. CT-FFR measurements were obtained 2 cm distal to the ostium of each vessel, in line with prior methodological recommendations [34, 35]. A CT-FFR value ≤ 0.80 was considered functionally significant [31–36, 40, 45–50].

2.4.3 Blinding

The observer who performed anatomic measurements and CT-FFR analysis was blinded to recorded clinical variables during image processing. RI-specific subgroup classification was based on anatomic findings from the CCTA dataset.

2.5 Statistical analysis

Continuous variables were assessed for normality with the Shapiro-Wilk test. Normally distributed variables are presented as mean $\pm$ standard deviation and were compared with the independent-samples t test. Non-normally distributed variables are presented as median (interquartile range) and were

compared with the Mann-Whitney U test. Categorical variables are reported as n/N (%). RI CT-FFR values were compared between RI diameter categories with the Mann-Whitney U test; the RI diameter cutoff was based on the cohort mean of 2.48 mm. Primary comparisons between the RI and non-RI groups were performed at the patient level for geometric measures. Plaque and stenosis summaries were analyzed separately as diseased-segment-level comparisons. Analyses of RI ostial location, RI diameter, and RI CT-FFR were restricted to the RI subgroup because these variables are not defined in patients without an RI. All tests were two sided, and $P < 0.05$ was considered statistically significant for the primary geometric comparison [42–44]. Baseline imbalance was additionally described with standardized mean differences (SMDs); BMI was used as the available body-size metric, and age was controlled at the design stage by 1:1 matching. Because only 10 patients had RI CT-FFR ≤ 0.80 , comparisons that stratified patients by RI CT-FFR-positive versus RI CT-FFR-negative status (Table 10) were summarized descriptively with absolute counts and percentages and were not used for inferential claims.

Table 4

Plaque composition and stenosis severity in diseased LM, LAD, and LCX segments by RI status.

Variable	RI group	Non-RI group	Test statistic	P value
Diseased segments, n	208	189	—	—
Plaque composition: calcified	71/208 (34.1%)	72/189 (38.1%)	$\chi^2 = 4.371^*$	0.112*
Plaque composition: noncalcified	48/208 (23.1%)	28/189 (14.8%)	—	—
Plaque composition: mixed	89/208 (42.8%)	89/189 (47.1%)	—	—
Stenosis severity: <50% diameter stenosis	166/208 (79.8%)	145/189 (76.7%)	$\chi^2 = 0.556^\dagger$	0.456†
Stenosis severity: $\geq 50\%$ diameter stenosis	42/208 (20.2%)	44/189 (23.3%)	—	—

Note. This is a lesion-based summary of combined diseased LM, LAD, and LCX segments rather than a patient-level analysis; therefore, the number of diseased segments may exceed the number of patients. Percentages are based on the number of diseased segments in each group (RI group, n = 208; non-RI group, n = 189). *P values for plaque composition compare the overall 3-category distribution (calcified, noncalcified, mixed). †P values for stenosis severity compare the 2-category distribution of diameter stenosis (< 50% vs $\geq 50\%$).

3.3 RI ostial location and associated anatomic and functional findings

Among the 150 patients in the RI group, 82 had an RI ostium proximal to the LAD and 68 had an RI ostium proximal to the LCX. RI location corresponded to different geometric and lesion patterns. On nominal testing, the RI-LAD subgroup had smaller LM, LAD, and LCX CSA values than the RI-LCX subgroup. After Benjamini-Hochberg FDR correction across the eight geometry/dimension comparisons, only the LAD CSA difference remained below $q = 0.05$ ($P < 0.001$; $q < 0.008$); the LM and LCX CSA findings were attenuated to $q = 0.056$ (Table 5). Sex distribution also differed between the RI-location subgroups (absolute SMD = 0.37) and is summarized in Table 6. Representative anatomic and CT-FFR images according to RI ostial location are shown in Fig. 2.

Table 6
Sex distribution according to RI ostial location among patients with an RI.

Variable	RI-LAD subgroup (n = 82)	RI-LCX subgroup (n = 68)	P value
Male	58/82 (70.7%)	36/68 (52.9%)	0.025
Female	24/82 (29.3%)	32/68 (47.1%)	—
Note. Values are presented as n/N (%). The reported P value corresponds to the overall comparison of sex distribution between the two RI-location subgroups. Values are unadjusted subgroup comparisons. Sex distribution differed between RI-location subgroups (absolute SMD = 0.37) and may have introduced residual confounding.			

Table 10

Descriptive plaque and stenosis findings according to RI CT-FFR status among patients with an RI.

Variable	RI CT-FFR positive (≤ 0.80; n = 10)	RI CT-FFR negative (> 0.80; n = 140)
LM plaque positive	7/10 (70.0%)	47/140 (33.6%)
LM stenosis positive	1/10 (10.0%)	0/140 (0.0%)
LAD plaque positive	10/10 (100.0%)	99/140 (70.7%)
LAD stenosis positive	6/10 (60.0%)	26/140 (18.6%)
LCX plaque positive	5/10 (50.0%)	40/140 (28.6%)
LCX stenosis positive	3/10 (30.0%)	9/140 (6.4%)

Variable	RI CT-FFR positive (≤ 0.80 ; n = 10)	RI CT-FFR negative (> 0.80 ; n = 140)
Note. This table is descriptive because only 10 patients had RI CT-FFR positivity. Values are presented as n/N (%). No hypothesis tests, P values, or multiplicity-adjusted q values are reported for this CT-FFR-positive versus CT-FFR-negative comparison, and the observed numerical differences should not be interpreted as confirmatory associations. All CT-FFR values were generated using the same software platform described in the Methods; measurement reproducibility was not separately assessed.		
4. Discussion		
This retrospective single-center study observed that RI presence was associated with a wider LAD-LCX angle and larger LM dimensions on CCTA [10–17, 24–26]. The primary LAD-LCX angle contrast was large (mean difference, 30.13°; 95% CI, 25.11°–35.15°). Because the groups differed markedly in sex distribution, we added a summary-data tipping-point analysis: under the specified additive model, sex imbalance alone would reduce the observed angle contrast to zero only if the male-female difference in LAD-LCX angle were approximately 105.1°. Age was controlled by matching and BMI imbalance was small (absolute SMD = 0.07). This aggregate calculation indicates that a very large sex-related angle difference would be required under the specified model, but it does not establish covariate-adjusted robustness and cannot replace patient-level multivariable analysis. Within the RI subgroup, FDR correction materially narrowed the set of findings remaining below $q = 0.05$: proximal-LAD RI origin retained associations with smaller LAD CSA and higher LAD CT-FFR positivity, whereas several other nominal CSA and stenosis signals were attenuated. Findings based on the 10 RI CT-FFR-positive cases were presented descriptively and were not treated as inferential evidence. Taken together, the data support a cautious imaging-based interpretation and do not establish a causal mechanism [4, 10–15, 27–41, 45].		
The primary anatomic observation was the wider LAD-LCX angle and larger LM dimensions in patients with an RI [10–17, 24–26]. Previous studies have linked LM bifurcation geometry with plaque distribution and lesion assessment [10, 13–26]. In the present study, RI anatomy corresponded to a trifurcation pattern, and CCTA quantified the associated widening of the LAD-LCX angle and enlargement of the LM luminal profile [4–15, 24–26]. These findings are most appropriately framed as CCTA-detectable anatomic variation rather than evidence of a specific hemodynamic pathway [3–26]. Recent data also suggest an association between RI anatomy and plaque deposition in the LM bifurcation region [10–15], but the present study measured imaging associations only.		
The RI ostial location analyses add information beyond RI presence or absence [9–15]. On nominal testing, patients with an RI arising proximal to the LAD had smaller LM, LAD, and LCX CSA values and higher frequencies of CT-FFR abnormality and stenosis than patients with an RI arising proximal to the LCX [10–15, 26, 31–36]. After Benjamini-Hochberg correction within the relevant outcome families, the LAD CSA difference ($q < 0.008$) and LAD CT-FFR positivity ($q = 0.009$) remained below $q = 0.05$. The RI and LAD/LCX anatomic stenosis comparisons were attenuated to $q = 0.051$, and the sparse-event RI CT-FFR positivity comparison to $q = 0.069$. These corrected results support a narrower interpretation than the nominal P values alone. Because local hemodynamic parameters were not measured and computational fluid dynamics was not performed, the RI-location findings should be interpreted as exploratory anatomic-functional associations rather than mechanistic validation [3, 16–26].		
The descriptive RI CT-FFR-status analysis is particularly limited by subgroup size [31–36, 45, 59, 60]. Only 10 RI CT-FFR-positive cases were available, so plaque and stenosis frequencies in Table 10 were summarized with absolute counts and percentages without hypothesis testing. Numerically higher frequencies in the positive subgroup may be sensitive to the classification of only one or two patients and therefore do not provide stable effect estimates or confirmatory evidence. These observations are retained only to describe the cohort and to generate hypotheses for validation in larger samples [31–36, 51–55].		

Variable	RI CT-FFR positive (≤ 0.80 ; n = 10)	RI CT-FFR negative (> 0.80 ; n = 140)
	From an imaging perspective, RI ostial location, especially origin proximal to the LAD, may be worth describing in CCTA reports because selected associations with LAD geometry and LAD CT-FFR positivity persisted after FDR correction in this cohort [9–15, 24–26, 30, 37–39]. Other nominal associations, particularly the anatomic stenosis comparisons, were weakened after multiplicity adjustment. CT-FFR provided complementary functional information to anatomic assessment in this study [31–36, 45, 59, 60]. These observations may have exploratory value for image-based phenotyping, but they should not be read as evidence that the RI directly remodels the LM bifurcation or independently causes atherosclerosis [3–26, 51–55].	
	Future work should test these findings in larger, multicenter prospective cohorts and use standardized lesion- or segment-level reporting with complete absolute counts [30, 38, 39, 42–44]. Additional imaging studies should assess whether RI ostial location and RI diameter improve CCTA-based description of LM trifurcation anatomy and whether CT-FFR provides incremental functional information beyond morphology [9–15, 24–26, 31–36]. Studies integrating CCTA, CT-FFR, and intravascular imaging, such as optical coherence tomography, could further evaluate plaque characteristics in patients with proximal-LAD RI or low RI CT-FFR [51–55, 64–66].	
5. Conclusions		
	In this retrospective CCTA study, ramus intermedius presence was associated with a wider LM bifurcation angle and larger LM dimensions. The large unadjusted LAD-LCX angle difference was not readily explained by the specified aggregate sex-imbalance sensitivity model, but no patient-level multivariable or sex-stratified model was available and residual confounding cannot be excluded. Within the RI subgroup, FDR correction narrowed the findings: proximal-LAD RI origin remained associated with smaller LAD CSA and more frequent LAD CT-FFR positivity, while several other nominal subgroup associations were attenuated. Findings among the 10 RI CT-FFR-positive patients were reported descriptively only. These data support a cautious imaging-based conclusion and do not prove a direct causal remodeling effect.	
6. Limitations		
	This study has several limitations. First, it was retrospective and conducted at a single center. Although patients were matched by age and BMI imbalance between the RI and non-RI groups was small, sex distribution differed substantially between groups and also between RI-location subgroups. A summary-data tipping-point analysis was added for the primary LAD-LCX angle comparison, but no patient-level multivariable or sex-stratified model was performed; the primary estimate should therefore be interpreted as an unadjusted association supplemented by an aggregate sensitivity calculation, and residual confounding by sex and other covariates cannot be excluded [42–44]. Second, RI-specific analyses were exploratory and included small subgroups. In particular, only 10 patients had RI CT-FFR ≤ 0.80; comparisons stratified by this status were therefore limited to descriptive counts and percentages rather than inferential testing. Third, Benjamini-Hochberg FDR correction was applied within clinically coherent RI-specific outcome families for Tables 5 and 7–9, but multiplicity remains relevant because the analyses were exploratory and some families contained sparse events; q values should not be interpreted as confirmatory evidence. Fourth, CT-FFR was generated with a single software platform, and interobserver/intraobserver reproducibility or cross-platform consistency of CT-FFR measurements was not assessed [31–36, 45, 59, 60]. Fifth, lesion analyses were partly diseased-segment based, whereas geometric analyses were patient based; this distinction matters when lesion counts exceed patient counts in the tables [30, 38, 39]. Sixth, RI diameter analyses were limited to patients with complete RI-specific data and used a cohort-derived diameter cutoff [42–44]. Seventh, BMI was the body-size metric available in the baseline analysis; body-surface-area or other anthropometric adjustment was not modeled. Eighth, the study assessed conventional plaque classification and stenosis severity but did not evaluate high-risk plaque markers or directly quantify local hemodynamic parameters [3, 16–26, 51–55]. Finally, medication use, interval treatment information, and other unmeasured clinical factors were not incorporated into subgroup analyses and may have influenced the observed associations [1, 2, 28, 29, 63]. These constraints indicate that the observed associations should be validated in larger,	

Variable	RI CT-FFR positive (≤ 0.80 ; n = 10)	RI CT-FFR negative (> 0.80 ; n = 140)
multicenter prospective cohorts with patient-level multivariable analysis, standardized patient-level and lesion-level reporting, reproducibility testing of CT-FFR, and integration of hemodynamic and high-risk plaque assessments.		
Abbreviations		
BMI: body mass index; CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CSA: cross-sectional area; CT-FFR: computed tomography-derived fractional flow reserve; LAD: left anterior descending artery; LCX: left circumflex artery; LM: left main coronary artery; RI: ramus intermedius.		

Because sex distribution differed substantially between the RI and non-RI groups, a summary-data tipping-point sensitivity analysis was added for the primary LAD-LCX angle comparison. Under a simple additive bias model, the observed group mean difference was expressed as $\Delta_{\text{obs}} = \Delta_{\text{RI}} + (p_{\text{male,RI}} - p_{\text{male,non-RI}}) \times \delta_{\text{sex}}$, where δ_{sex} denotes the unknown male-female mean difference in LAD-LCX angle. We report the value of δ_{sex} required to reduce the observed RI-group contrast to zero. This is an aggregate sensitivity calculation only and does not substitute for patient-level multivariable regression or establish a sex-adjusted treatment or exposure effect. For RI-specific subgroup analyses other than the descriptive Table 10 comparison, Benjamini-Hochberg FDR correction was applied separately within clinically coherent outcome families: coronary geometry and vessel dimensions (Table 5), CT-FFR positivity by territory (Table 7), anatomic stenosis positivity by territory (Table 8), and RI-diameter-related outcomes (Table 9). Endpoints with no estimable between-group test were excluded from the corresponding FDR family. Both nominal P values and FDR-adjusted q values are reported for these inferential subgroup families. For categorical comparisons, Pearson's chi-square test was used when expected cell counts were adequate; continuity-corrected chi-square testing or Fisher's exact test was used for sparse 2×2 tables, as appropriate. When both groups had zero events for a given endpoint, no between-group test was performed and the P value was reported as not estimable. Analyses were performed using IBM SPSS Statistics, version 26.0 (IBM Corp., Armonk, NY, USA); FDR q values and summary-data sensitivity calculations were derived from the reported test results and aggregate summaries.

Table 5

Coronary geometry and vessel dimensions according to RI ostial location among patients with an RI.

Parameter	RI-LAD subgroup (n = 82)	RI-LCX subgroup (n = 68)	Test statistic	Nominal P; BH-FDR q
LM diameter (mm)	4.42 ± 0.75	4.45 ± 0.84	t = -0.221	0.825; 0.973
LM CSA (mm ²)	11.67 (9.00, 14.84)	13.91 (10.19, 16.35)	Z = -2.305	0.021; 0.056
RI diameter (mm)	2.47 (2.16, 2.77)	2.29 (2.16, 2.79)	Z = -0.566	0.571; 0.914
RI CSA (mm ²)	2.28 (1.53, 3.04)	2.12 (1.60, 2.98)	Z = -0.140	0.889; 0.973
LAD diameter (mm)	3.48 (3.04, 3.91)	3.43 (3.06, 3.93)	Z = -0.034	0.973; 0.973
LAD CSA (mm ²)	5.76 (4.69, 7.76)	7.70 (6.27, 9.98)	Z = -3.798	< 0.001; <0.008
LCX diameter (mm)	3.00 (2.55, 3.35)	3.10 (2.58, 3.44)	Z = -0.714	0.476; 0.914
LCX CSA (mm ²)	4.89 (3.56, 6.57)	6.02 (3.91, 8.77)	Z = -2.360	0.018; 0.056

Note. This table is restricted to patients with an RI. RI-LAD denotes an RI ostium located proximal to the LAD; RI-LCX denotes an RI ostium located proximal to the LCX. Values are presented as mean ± SD or median (Q1, Q3), as appropriate. The final column reports the nominal P value followed by the Benjamini-Hochberg FDR-adjusted q value, calculated across the eight geometry/dimension comparisons in this table. Because the exact nominal P value for LAD CSA was reported only as P < 0.001, its q value is conservatively reported as q < 0.008. Abbreviations: CSA, cross-sectional area; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main coronary artery; RI, ramus intermedius.

Table 7

CT-FFR positivity according to RI ostial location among patients with an RI.

Territory	RI-LAD subgroup (n = 82)	RI-LCX subgroup (n = 68)	Nominal P; BH-FDR q
LM	0/82 (0.0%)	0/68 (0.0%)	NA; NA
RI	9/82 (11.0%)	1/68 (1.5%)	0.046; 0.069
LAD	19/82 (23.2%)	4/68 (5.9%)	0.003; 0.009
LCX	5/82 (6.1%)	0/68 (0.0%)	0.106; 0.106

Note. Values are presented as n/N (%). CT-FFR positivity was defined as CT-FFR ≤ 0.80. P values were calculated using Pearson's chi-square test, continuity-corrected chi-square test, or Fisher's exact test, as appropriate. "NA" indicates that no between-group test was performed because both groups had zero positive findings. The final column reports the nominal P value followed by the Benjamini-Hochberg FDR-adjusted q value, calculated across the three estimable CT-FFR territory comparisons. The RI-specific row is a sparse-event comparison because only 10 RI CT-FFR-positive cases occurred overall and should be interpreted as exploratory rather than confirmatory. All CT-FFR values were generated using the same software platform described in the Methods; measurement reproducibility was not separately assessed.

Table 8

Anatomic stenosis positivity according to RI ostial location among patients with an RI.

Territory	RI-LAD subgroup (n = 82)	RI-LCX subgroup (n = 68)	Nominal P; BH-FDR q
LM	1/82 (1.2%)	0/68 (0.0%)	1.000; 1.000
RI	16/82 (19.5%)	4/68 (5.9%)	0.015; 0.051
LAD	23/82 (28.0%)	9/68 (13.2%)	0.027; 0.051
LCX	10/82 (12.2%)	2/68 (2.9%)	0.038; 0.051

Note. Values are presented as n/N (%). Stenosis positivity was defined as luminal diameter stenosis $\geq 50\%$ on CCTA. P values were calculated using Pearson's chi-square test, continuity-corrected chi-square test, or Fisher's exact test, as appropriate. For the LM row, Fisher's exact test was used for the comparison of 1/82 versus 0/68. The final column reports the nominal P value followed by the Benjamini-Hochberg FDR-adjusted q value, calculated across the four stenosis territory comparisons. The three nominal RI/LAD/LCX stenosis signals each yielded $q = 0.051$ and should therefore be interpreted as borderline exploratory findings rather than FDR-supported associations.

3.4 RI diameter and lesion patterns

RI CT-FFR values were nominally lower in the small-RI subgroup than in the large-RI subgroup (0.96 [0.93, 0.97] vs. 0.97 [0.95, 0.98], $P = 0.043$). In the subset with complete RI diameter and plaque data ($n = 111$), patients were categorized as small RI (< 2.48 mm; $n = 71$) or large RI (≥ 2.48 mm; $n = 40$). LCX plaque was nominally more common in the small-RI subgroup than in the large-RI subgroup (17/71 [23.9%] vs. 3/40 [7.5%], $P = 0.030$). After Benjamini-Hochberg FDR correction across the six estimable comparisons in this outcome family, neither signal remained below $q = 0.05$ (both $q = 0.129$); the remaining comparisons were also not FDR-supported (Table 9).

Table 9
RI CT-FFR and lesion findings by RI diameter category in complete cases.

Variable	Small RI (< 2.48 mm; n = 71)	Large RI (≥ 2.48 mm; n = 40)	Nominal P; BH-FDR q
RI CT-FFR value	0.96 (0.93, 0.97)	0.97 (0.95, 0.98)	0.043; 0.129
LM plaque positive	22/71 (31.0%)	11/40 (27.5%)	0.700; 0.809
LM stenosis positive	0/71 (0.0%)	0/40 (0.0%)	NA; NA
LAD plaque positive	46/71 (64.8%)	25/40 (62.5%)	0.809; 0.809
LAD stenosis positive	8/71 (11.3%)	2/40 (5.0%)	0.446; 0.719
LCX plaque positive	17/71 (23.9%)	3/40 (7.5%)	0.030; 0.129
LCX stenosis positive	3/71 (4.2%)	0/40 (0.0%)	0.479; 0.719

Note. This analysis is restricted to the subset with complete RI diameter and plaque data (n = 111). Values are presented as median (Q1, Q3) for RI CT-FFR and as n/N (%) for categorical outcomes. The RI diameter cutoff of 2.48 mm corresponds to the cohort mean. “NA” indicates that no between-group test was performed because both groups had zero events. The final column reports the nominal P value followed by the Benjamini-Hochberg FDR-adjusted q value, calculated across the six estimable RI-diameter-related comparisons. This subgroup analysis remains exploratory because it was restricted to patients with complete RI diameter and plaque data and the cutoff was cohort-derived. All CT-FFR values were generated using the same software platform described in the Methods; measurement reproducibility was not separately assessed.

3.5 Descriptive exploratory findings according to RI CT-FFR positivity

Only 10 of the 150 patients in the RI group had RI CT-FFR ≤ 0.80. Because this positive subgroup was too small to support stable inferential estimates, comparisons stratified by RI CT-FFR status are presented descriptively only. LM plaque was present in 7/10 (70.0%) RI CT-FFR-positive patients and 47/140 (33.6%) RI CT-FFR-negative patients; LAD stenosis was present in 6/10 (60.0%) and 26/140 (18.6%), respectively; and LCX stenosis was present in 3/10 (30.0%) and 9/140 (6.4%), respectively. These numerical differences were not treated as statistically supported associations and should be regarded solely as hypothesis-generating observations (Table 10).

2.6 Use of artificial intelligence-assisted technology

Artificial intelligence-assisted technology was used only for language editing and manuscript-revision support after the study analyses had been completed. It was not used for image generation, data collection, statistical analysis, or interpretation of the study data. All AI-assisted edits were reviewed and approved by the authors, who take responsibility for the final manuscript.

2.7 Ethics approval

The study was approved by the Ethics Committee of Cangzhou Central Hospital (approval number: 2023-329-01) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was waived because of the retrospective design.

3. Results

3.1 Cohort characteristics

Consecutive CCTA examinations were screened as described in the Methods, and the final matched analytic cohort included 300 patients, with 150 patients in the RI group and 150 age-matched patients in the non-RI group. The overall mean age was 60.71 ± 11.77 years, and 145 patients were male. Baseline clinical characteristics other than age and sex are shown in Table 1; sex distribution is presented separately in Table 2 because of the marked between-group imbalance, and imaging-derived vessel dimensions are reported with the geometric outcomes in Table 3. Body mass index, smoking status, alcohol consumption, hypertension, hyperlipidemia, and diabetes mellitus did not differ significantly between groups (all $P > 0.05$). Age was controlled by the 1:1 matching design. BMI showed only small imbalance between groups (25.26 ± 2.85 vs. 25.47 ± 3.19 kg/m²; absolute SMD = 0.07), whereas sex distribution differed substantially (male, 62.7% vs. 34.0%; absolute SMD = 0.60) (Table 2).

Table 1

Baseline clinical characteristics other than age and sex according to ramus intermedius status.

Variable	Overall cohort (N = 300)	RI group (n = 150)	Non-RI group (n = 150)	P value
BMI (kg/m ²)	25.37 ± 3.02	25.26 ± 2.85	25.47 ± 3.19	0.542
Smoking	40/300 (13.3%)	24/150 (16.0%)	16/150 (10.7%)	0.174
Alcohol consumption	22/300 (7.3%)	14/150 (9.3%)	8/150 (5.3%)	0.184
Hypertension	175/300 (58.3%)	94/150 (62.7%)	81/150 (54.0%)	0.128
Hyperlipidemia	156/300 (52.0%)	77/150 (51.3%)	79/150 (52.7%)	0.817
Diabetes mellitus	76/300 (25.3%)	42/150 (28.0%)	34/150 (22.7%)	0.288

Note. Values are presented as mean $\pm$ SD or n/N (%), as appropriate. P values compare the RI and non-RI groups. Age is summarized in the text because the comparison group was selected by 1:1 age matching; sex is reported separately in Table 2 because of the marked imbalance. Imaging-derived vessel diameter and cross-sectional area measurements are reported in Table 3. For BMI, the absolute standardized mean difference between groups was 0.07.

Table 2
Sex distribution according to ramus intermedius status in the study cohort.

Sex	RI group (n = 150)	Non-RI group (n = 150)	P value
Male	94/150 (62.7%)	51/150 (34.0%)	< 0.001
Female	56/150 (37.3%)	99/150 (66.0%)	—
Note. Values are presented as n/N (%). Percentages are column-based, using the number of patients in each group as the denominator. The reported P value corresponds to the overall comparison of sex distribution between the RI and non-RI groups. Sex distribution differed substantially despite age matching (absolute SMD = 0.60). The resulting potential confounding was explored only with an aggregate tipping-point sensitivity calculation for the primary LAD-LCX angle comparison; no patient-level sex-adjusted model was available.			
3.2 Comparison of LM bifurcation geometry between RI and non-RI groups			
Patients with an RI had a larger LAD-LCX angle than patients without an RI ($99.35^\circ \pm 25.61^\circ$ vs. $69.22^\circ \pm 17.83^\circ$, $t = 11.825$, $P < 0.001$). The unadjusted mean difference was 30.13° (95% CI, 25.11°-35.15°). The RI group also had larger LM diameter (median 4.38 mm vs. 4.08 mm, $P < 0.001$) and LM CSA (median 12.58 mm² vs. 10.82 mm², $P < 0.001$). LAD and LCX diameter and CSA did not differ significantly between the two groups (all $P > 0.05$) (Table 3). In the sex-imbalance tipping-point analysis, the male proportion differed by 28.7 percentage points (62.7% vs. 34.0%); under the specified additive model, a male-female mean difference of approximately 105.1° in LAD-LCX angle would be required for sex imbalance alone to reduce the observed 30.13° RI-group contrast to zero. This aggregate sensitivity calculation does not provide patient-level adjustment, and residual confounding by sex or other covariates cannot be excluded. Representative examples of LM bifurcation geometry according to RI status are shown in Fig. 1.			

Table 3
Comparison of left main bifurcation geometry and vessel dimensions between the RI and non-RI groups.

Parameter	RI group (n = 150)	Non-RI group (n = 150)	Test statistic	P value
LAD-LCX angle (°)	99.35 ± 25.61	69.22 ± 17.83	$t = 11.825$	< 0.001
LM diameter (mm)	4.38 (3.92, 4.94)	4.08 (3.65, 4.58)	$Z = -3.296$	< 0.001
LM CSA (mm ²)	12.58 (9.51, 15.93)	10.82 (8.65, 13.35)	$Z = -3.458$	< 0.001
LAD diameter (mm)	3.46 (3.06, 3.92)	3.33 (3.03, 3.68)	$Z = -1.865$	0.062
LAD CSA (mm ²)	6.68 (4.93, 8.93)	6.50 (5.14, 8.62)	$Z = -0.054$	0.957
LCX diameter (mm)	3.02 (2.56, 3.40)	2.95 (2.64, 3.29)	$Z = -0.541$	0.588
LCX CSA (mm ²)	5.30 (3.79, 7.65)	5.52 (3.80, 7.00)	$Z = -0.467$	0.641
Note. Values are presented as mean $\pm$ SD or median (Q1, Q3), as appropriate. Abbreviations: CSA, cross-sectional area; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main coronary artery; RI, ramus intermedius.				

4. Discussion

This retrospective single-center study observed that RI presence was associated with a wider LAD-LCX angle and larger LM dimensions on CCTA [10–17,24–26]. The primary LAD-LCX angle contrast was large (mean difference, 30.13°; 95% CI, 25.11°–35.15°). Because the groups differed markedly in sex distribution, we added a summary-data tipping-point analysis: under the specified additive model, sex imbalance alone would reduce the observed angle contrast to zero only if the male-female difference in LAD-LCX angle were approximately 105.1°. Age was controlled by matching and BMI imbalance was small (absolute SMD = 0.07). This aggregate calculation indicates that a very large sex-related angle difference would be required under the specified model, but it does not establish covariate-adjusted robustness and cannot replace patient-level multivariable analysis. Within the RI subgroup, FDR correction materially narrowed the set of findings remaining below $q = 0.05$: proximal-LAD RI origin retained associations with smaller LAD CSA and higher LAD CT-FFR positivity, whereas several other nominal CSA and stenosis signals were attenuated. Findings based on the 10 RI CT-FFR-positive cases were presented descriptively and were not treated as inferential evidence. Taken together, the data support a cautious imaging-based interpretation and do not establish a causal mechanism [4,10–15,27–41,45].

The primary anatomic observation was the wider LAD-LCX angle and larger LM dimensions in patients with an RI [10–17,24–26]. Previous studies have linked LM bifurcation geometry with plaque distribution and lesion assessment [10,13–26]. In the present study, RI anatomy corresponded to a trifurcation pattern, and CCTA quantified the associated widening of the LAD-LCX angle and enlargement of the LM luminal profile [4–15,24–26]. These findings are most appropriately framed as CCTA-detectable anatomic variation rather than evidence of a specific hemodynamic pathway [3–26]. Recent data also suggest an association between RI anatomy and plaque deposition in the LM bifurcation region [10–15], but the present study measured imaging associations only.

The RI ostial location analyses add information beyond RI presence or absence [9–15]. On nominal testing, patients with an RI arising proximal to the LAD had smaller LM, LAD, and LCX CSA values and higher frequencies of CT-FFR abnormality and stenosis than patients with an RI arising proximal to the LCX [10–15,26,31–36]. After Benjamini-Hochberg correction within the relevant outcome families, the LAD CSA difference ($q < 0.008$) and LAD CT-FFR positivity ($q = 0.009$) remained below $q = 0.05$. The RI and LAD/LCX anatomic stenosis comparisons were attenuated to $q = 0.051$, and the sparse-event RI CT-FFR positivity comparison to $q = 0.069$. These corrected results support a narrower interpretation than the nominal P values alone. Because local hemodynamic parameters were not measured and computational fluid dynamics was not performed, the RI-location findings should be interpreted as exploratory anatomic-functional associations rather than mechanistic validation [3,16–26].

The descriptive RI CT-FFR-status analysis is particularly limited by subgroup size [31–36,45,59,60]. Only 10 RI CT-FFR-positive cases were available, so plaque and stenosis frequencies in Table 10 were summarized with absolute counts and percentages without hypothesis testing. Numerically higher frequencies in the positive subgroup may be sensitive to the classification of only one or two patients and therefore do not provide stable effect estimates or confirmatory evidence. These observations are

retained only to describe the cohort and to generate hypotheses for validation in larger samples [31–36,51–55].

From an imaging perspective, RI ostial location, especially origin proximal to the LAD, may be worth describing in CCTA reports because selected associations with LAD geometry and LAD CT-FFR positivity persisted after FDR correction in this cohort [9–15,24–26,30,37–39]. Other nominal associations, particularly the anatomic stenosis comparisons, were weakened after multiplicity adjustment. CT-FFR provided complementary functional information to anatomic assessment in this study [31–36,45,59,60]. These observations may have exploratory value for image-based phenotyping, but they should not be read as evidence that the RI directly remodels the LM bifurcation or independently causes atherosclerosis [3–26,51–55].

Future work should test these findings in larger, multicenter prospective cohorts and use standardized lesion- or segment-level reporting with complete absolute counts [30,38,39,42–44]. Additional imaging studies should assess whether RI ostial location and RI diameter improve CCTA-based description of LM trifurcation anatomy and whether CT-FFR provides incremental functional information beyond morphology [9–15,24–26,31–36]. Studies integrating CCTA, CT-FFR, and intravascular imaging, such as optical coherence tomography, could further evaluate plaque characteristics in patients with proximal-LAD RI or low RI CT-FFR [51–55,64–66].

5. Conclusions

In this retrospective CCTA study, ramus intermedius presence was associated with a wider LM bifurcation angle and larger LM dimensions. The large unadjusted LAD-LCX angle difference was not readily explained by the specified aggregate sex-imbalance sensitivity model, but no patient-level multivariable or sex-stratified model was available and residual confounding cannot be excluded. Within the RI subgroup, FDR correction narrowed the findings: proximal-LAD RI origin remained associated with smaller LAD CSA and more frequent LAD CT-FFR positivity, while several other nominal subgroup associations were attenuated. Findings among the 10 RI CT-FFR-positive patients were reported descriptively only. These data support a cautious imaging-based conclusion and do not prove a direct causal remodeling effect.

Limitations

This study has several limitations. First, it was retrospective and conducted at a single center. Although patients were matched by age and BMI imbalance between the RI and non-RI groups was small, sex distribution differed substantially between groups and also between RI-location subgroups. A summary-data tipping-point analysis was added for the primary LAD-LCX angle comparison, but no patient-level multivariable or sex-stratified model was performed; the primary estimate should therefore be interpreted as an unadjusted association supplemented by an aggregate sensitivity calculation, and residual confounding by sex and other covariates cannot be excluded [42–44]. Second, RI-specific analyses were exploratory and included small subgroups. In particular, only 10 patients had RI CT-FFR

≤ 0.80 ; comparisons stratified by this status were therefore limited to descriptive counts and percentages rather than inferential testing. Third, Benjamini-Hochberg FDR correction was applied within clinically coherent RI-specific outcome families for Tables 5 and 7–9, but multiplicity remains relevant because the analyses were exploratory and some families contained sparse events; q values should not be interpreted as confirmatory evidence. Fourth, CT-FFR was generated with a single software platform, and interobserver/intraobserver reproducibility or cross-platform consistency of CT-FFR measurements was not assessed [31–36,45,59,60]. Fifth, lesion analyses were partly diseased-segment based, whereas geometric analyses were patient based; this distinction matters when lesion counts exceed patient counts in the tables [30,38,39]. Sixth, RI diameter analyses were limited to patients with complete RI-specific data and used a cohort-derived diameter cutoff [42–44]. Seventh, BMI was the body-size metric available in the baseline analysis; body-surface-area or other anthropometric adjustment was not modeled. Eighth, the study assessed conventional plaque classification and stenosis severity but did not evaluate high-risk plaque markers or directly quantify local hemodynamic parameters [3,16–26,51–55]. Finally, medication use, interval treatment information, and other unmeasured clinical factors were not incorporated into subgroup analyses and may have influenced the observed associations [1,2,28,29,63]. These constraints indicate that the observed associations should be validated in larger, multicenter prospective cohorts with patient-level multivariable analysis, standardized patient-level and lesion-level reporting, reproducibility testing of CT-FFR, and integration of hemodynamic and high-risk plaque assessments.

Abbreviations

BMI: body mass index; CAD: coronary artery disease; CCTA: coronary computed tomography angiography; CSA: cross-sectional area; CT-FFR: computed tomography-derived fractional flow reserve; LAD: left anterior descending artery; LCX: left circumflex artery; LM: left main coronary artery; RI: ramus intermedius.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Cangzhou Central Hospital (approval number: 2023-329-01) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was waived because of the retrospective design.

Consent for publication

Not applicable. All displayed CCTA and CT-FFR images were de-identified and contain no directly or indirectly identifying participant information.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

H.L. contributed to conceptualization, data curation, formal analysis, and writing of the original draft. X.L. contributed to investigation and methodology. Y.D. contributed to resources and validation. L.Z. contributed to data collection. S.Y. contributed to software. Y.X. contributed to funding acquisition, supervision, and manuscript review and editing. All authors read and approved the final manuscript.

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Data Availability

The datasets generated and/or analysed during the current study are not publicly available because they contain potentially identifiable clinical information. De-identified data are available from the corresponding author on reasonable request, subject to institutional regulations and approval by the Ethics Committee of Cangzhou Central Hospital.

References

1. Vaduganathan M, Mensah GA, Turco JV, Fuster V, Roth GA. The global burden of cardiovascular diseases and risk: a compass for future health. *J Am Coll Cardiol.* 2022;80(25):2361–2371. doi: 10.1016/j.jacc.2022.11.005. PMID: 36368511.
2. Mensah GA, Fuster V, Murray CJL, Roth GA. Global Burden of Cardiovascular Diseases and Risks Collaborators. Global burden of cardiovascular diseases and risks, 1990–2022. *J Am Coll Cardiol.* 2023;82(25):2350–2473. doi: 10.1016/j.jacc.2023.11.007. PMID: 38092509.
3. Brown AJ, Teng Z, Evans PC, Gillard JH, Samady H, Bennett MR. Role of biomechanical forces in the natural history of coronary atherosclerosis. *Nat Rev Cardiol.* 2016;13(4):210–220.

- 10.1038/nrcardio.2015.203. PMID: 26822720.
4. Narula J, Chandrashekar Y, Ahmadi A, Abbata S, Berman DS, Blankstein R, Leipsic J, Newby D, Nicol ED, Nieman K, Shaw L, Villines TC, Williams M, Hecht HS. SCCT 2021 expert consensus document on coronary computed tomographic angiography: a report of the Society of Cardiovascular Computed Tomography. *J Cardiovasc Comput Tomogr*. 2021;15(3):192–217. 10.1016/j.jcct.2020.11.001. PMID: 33303384.
 5. Bazzocchi G, Romagnoli A, Sperandio M, Simonetti G. Evaluation with 64-slice CT of the prevalence of coronary artery variants and congenital anomalies: a retrospective study of 3,236 patients. *Radiol Med*. 2011;116(5):675–689. 10.1007/s11547-011-0627-3. PMID: 21293945.
 6. Koşar P, Ergun E, Öztürk C, Koşar U. Anatomic variations and anomalies of the coronary arteries: 64-slice CT angiographic appearance. *Diagn Interv Radiol*. 2009;15(4):275–283. 10.4261/1305-3825.DIR.2550-09.1. PMID: 19957241.
 7. Ghadri JR, Kazakauskaitė E, Braunschweig S, Burger IA, Frank M, Fiechter M, Gebhard C, Fuchs TA, Templin C, Gaemperli O, Lüscher TF, Schmied C, Kaufmann PA. Congenital coronary anomalies detected by coronary computed tomography compared to invasive coronary angiography. *BMC Cardiovasc Disord*. 2014;14:81. 10.1186/1471-2261-14-81. PMID: 25004927.
 8. Dodd JD, Ferencik M, Liberthson RR, Cury RC, Hoffmann U, Brady TJ, Abbata S. Congenital anomalies of coronary artery origin in adults: 64-MDCT appearance. *AJR Am J Roentgenol*. 2007;188(2):W138-W146. 10.2214/AJR.05.2098. PMID: 17242219.
 9. Dai Y, Costantini S, Montalbano MJ, Loukas M. A meta-analysis and simplified nomenclature for diagonal coronary artery and ramus intermedius across adult and pediatric hearts. *Clin Anat*. 2026;39(3):305–324. 10.1002/ca.70034. PMID: 41175009.
 10. Zhang DQ, Xu YF, Dong YP, Yu SJ. Coronary computed tomography angiography study on the relationship between the ramus intermedius and atherosclerosis in the bifurcation of the left main coronary artery. *BMC Med Imaging*. 2023;23(1):53. 10.1186/s12880-023-01009-2. PMID: 37041479.
 11. Rosani NS, Zamin RM, Raja Aman RRA, Mahmood Zuhdi AS, Danaee M. The influence of the presence of the ramus intermedius on atherosclerotic plaque deposition in the left bifurcation region in low-risk individuals. *Rev Cardiovasc Med*. 2025;26(2):25252. 10.31083/RCM25252. PMID: 40026505.
 12. Bekirçavuşoğlu AF, Bekirçavuşoğlu S, Turan Özsoy HG, Erkan M. Coronary computed tomography angiography evaluation of ramus intermedius and left coronary atherosclerosis: presence, distribution, and plaque characteristics. *Clin Radiol*. 2026;96:107299. 10.1016/j.crad.2026.107299. PMID: 41962318.
 13. Galbraith EM, McDaniel MC, Jeroudi AM, Kashlan OR, Suo J, Giddens DP, Samady H. Comparison of location of culprit lesions in left anterior descending coronary artery among patients with anterior wall ST-segment elevation myocardial infarction. *Am J Cardiol*. 2010;106(2):162–166. doi: 10.1016/j.amjcard.2010.02.027. PMID: 20598997.

14. El Zayat A, Eldeeb M, Gad M, Ibrahim IM. Effect of presence of ramus intermedius artery on location of culprit lesions in acute left circumflex coronary artery occlusion. *J Saudi Heart Assoc.* 2021;33(1):35–40. 10.37616/2212-5043.1238.
15. Pourafkari L, Ansari S, Kinninger A, Budoff MJ. Association of ramus intermedius with increased atherosclerotic plaque in the left main stem. *Int J Cardiovasc Imaging.* 2026. Epub 2026 Feb 18. 10.1007/s10554-026-03656-2. PMID: 41706392.
16. Sun Z, Chaichana T. An investigation of correlation between left coronary bifurcation angle and hemodynamic changes in coronary stenosis by coronary computed tomography angiography-derived computational fluid dynamics. *Quant Imaging Med Surg.* 2017;7(5):537–548. 10.21037/qims.2017.10.03. PMID: 29184766.
17. Cui Y, Zeng W, Yu J, Lu J, Hu Y, Diao N, Liang B, Han P, Shi H. Quantification of left coronary bifurcation angles and plaques by coronary computed tomography angiography for prediction of significant coronary stenosis: a preliminary study with dual-source CT. *PLoS One.* 2017;12(3):e0174352. 10.1371/journal.pone.0174352. PMID: 28346530.
18. Yahia M, Farid W, Lotfy M, Osama M, El Deep HA. Association between bifurcation angle of the left main coronary artery and severity of stenosis of the proximal left anterior descending artery. *Cardiovasc J Afr.* 2023;34(2):93–97. 10.5830/CVJA-2022-031. PMID: 35976685.
19. Chaichana T, Sun Z, Jewkes J. Computation of hemodynamics in the left coronary artery with variable angulations. *J Biomech.* 2011;44(10):1869–1878. 10.1016/j.jbiomech.2011.04.033. PMID: 21550611.
20. Chaichana T, Sun Z, Jewkes J. Hemodynamic impacts of various types of stenosis in the left coronary artery bifurcation: a patient-specific analysis. *Phys Med.* 2013;29(5):447–452. doi: 10.1016/j.ejmp.2013.02.001. PMID: 23453845.
21. Chaichana T, Sun Z, Jewkes J. Hemodynamic impacts of left coronary stenosis: a patient-specific analysis. *Acta Bioeng Biomech.* 2013;15(3):107–112. 10.5277/abb130313. PMID: 24215177.
22. Ziyrek M, Sertdemir AL, Duran M. Effect of coronary artery bifurcation angle on atherosclerotic lesion localization distance to the bifurcation site. *J Saudi Heart Assoc.* 2020;32(3):399–407. 10.37616/2212-5043.1071. PMID: 33299782.
23. Kamangar S, Anjum Badruddin I, Anqi AE, Ahamed Saleel C, Tirth V, Yunus Khan TM, Khan MA, Mallick Z, Salman Ahmed NJ. Influence of bifurcation angle in left coronary artery with stenosis: a CFD analysis. *Biomed Mater Eng.* 2020;31(6):339–349. 10.3233/BME-201107. PMID: 33252058.
24. Geerlings-Batt J, Sun Z. Evaluation of the relationship between left coronary artery bifurcation angle and coronary artery disease: a systematic review. *J Clin Med.* 2022;11(17):5143. 10.3390/jcm11175143. PMID: 36079071.
25. Mansouri P, Nematipour E, Rajablou N, Ghorashi SM, Azari S, Omid N. Left anterior descending coronary artery-left circumflex coronary artery bifurcation angle and severity of coronary artery disease; is there any correlation? A cross-sectional study. *Health Sci Rep.* 2024;7(6):e2182. 10.1002/hsr2.2182. PMID: 38868537.

26. Tsugu T, Tanaka K, Nagatomo Y, De Mey J. Impact of coronary bifurcation angle on computed tomography derived fractional flow reserve in coronary vessels with no apparent coronary artery disease. *Eur Radiol.* 2023;33(2):1277–1285. 10.1007/s00330-022-09125-3. PMID: 36114847.
27. Moss AJ, Williams MC, Newby DE, Nicol ED. The updated NICE guidelines: cardiac CT as the first-line test for coronary artery disease. *Curr Cardiovasc Imaging Rep.* 2017;10(5):15. 10.1007/s12410-017-9412-6. PMID: 28446943.
28. Knuuti J, Wijns W, Saraste A, Capodanno D, Barbato E, Funck-Brentano C, Prescott E, Storey RF, Deaton C, Cuisset T, Agewall S, Dickstein K, Edvardsen T, Escaned J, Gersh BJ, Svitil P, Gilard M, Hasdai D, Hatala R, Mahfoud F, Masip J, Muneretto C, Cillaj; Valgimigli M, Achenbach S, Bax JJ, ESC Scientific Document Group. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J.* 2020;41(3):407–477. 10.1093/eurheartj/ehz425. PMID: 31504439.
29. Gulati M, Levy PD, Mukherjee D, Amsterdam E, Bhatt DL, Birtcher KK, Blankstein R, Boyd J, Bullock-Palmer RP, Conejo T, Diercks DB, Gentile F, Greenwood JP, Hess EP, Hollenberg SM, Jaber WA, Jneid H, Joglar JA, Morrow DA, O'Connor RE, Ross MA, Shaw LJ. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain. *Circulation.* 2021;144(22):e368-e454. 10.1161/CIR.0000000000001029. PMID: 34709879.
30. Cury RC, Leipsic J, Abbara S, Achenbach S, Berman D, Bittencourt M, Budoff M, Chinnaiyan K, Choi AD, Ghoshhajra B, Jacobs J, Kowek L, Lesser J, Maroules C, Rubin GD, Rybicki FJ, Shaw LJ, Williams MC, Williamson E, White CS, Villines TC, Blankstein R. CAD-RADS 2.0–2022 Coronary Artery Disease-Reporting and Data System: an expert consensus document. *J Cardiovasc Comput Tomogr.* 2022;16(6):536–557. 10.1016/j.jcct.2022.07.002. PMID: 35864070.
31. Nørgaard BL, Leipsic J, Gaur S, Seneviratne S, Ko BS, Ito H, Jensen JM, Mauri L, De Bruyne B, Bezerra H, Osawa K, Marwan M, Naber C, Erglis A, Park SJ, Christiansen EH, Kaltoft A, Lassen JF, Bøtker HE, Achenbach S, NXT Trial Study Group. Diagnostic performance of noninvasive fractional flow reserve derived from coronary computed tomography angiography in suspected coronary artery disease: the NXT trial. *J Am Coll Cardiol.* 2014;63(12):1145–1155. 10.1016/j.jacc.2013.11.043. PMID: 24486266.
32. Rajiah P, Cummings KW, Williamson E, Young PM. CT fractional flow reserve: a practical guide to application, interpretation, and problem solving. *Radiographics.* 2022;42(2):340–358. 10.1148/rg.210097. PMID: 35119968.
33. Min JK, Leipsic J, Pencina MJ, Berman DS, Koo BK, van Mieghem C, Erglis A, Lin FY, Dunning AM, Apruzzese P, Budoff MJ, Cole JH, Jaffer FA, Leon MB, Malpeso J, Mancini GB, Park SJ, Schwartz RS, Shaw LJ, Mauri L. Diagnostic accuracy of fractional flow reserve from anatomic CT angiography. *JAMA.* 2012;308(12):1237–1245. 10.1001/2012.jama.11274. PMID: 22922562.
34. Zhang LJ, Tang C, Xu P, Guo B, Zhou F, Xue Y, Zhang J, Zheng M, Xu L, Hou Y, Lu B, Guo Y, Cheng J, Liang C, Song B, Zhang H, Hong N, Wang P, Chen M, Xu K, Liu S, Jin Z, Lu G. Chinese Society of Radiology. Coronary computed tomography angiography-derived fractional flow reserve: an expert consensus document of Chinese Society of Radiology. *J Thorac Imaging.* 2022;37(6):385–400. 10.1097/RTI.0000000000000679. PMID: 36162081.

35. Chen YC, Zhou F, Wang YN, Zhang JY, Yu MM, Hou Y, Xu PP, Zhang XL, Xue Y, Zheng MW, Zhang B, Zhang DM, Hu XH, Xu L, Liu H, Lu GM, Tang CX, Zhang LJ. Optimal measurement sites of coronary computed tomography angiography-derived fractional flow reserve: the insight from China CT-FFR Study. *J Thorac Imaging*. 2023;38(3):194–202. 10.1097/RTI.0000000000000687. PMID: 36469852.
36. Guo B, Jiang M, Guo X, Tang C, Zhong J, Lu M, Liu C, Zhang X, Qiao H, Zhou F, Xu P, Xue Y, Zheng M, Hou Y, Wang Y, Zhang J, Zhang B, Zhang D, Xu L, Hu X, Zhou C, Li J, Yang Z, Mao X, Lu G, Zhang L. Diagnostic and prognostic performance of artificial intelligence-based fully automated on-site CT-FFR in patients with CAD. *Sci Bull (Beijing)*. 2024;69(10):1472–1485. 10.1016/j.scib.2024.03.053. PMID: 38637226.
37. Abbara S, Blanke P, Maroules CD, Cheezum M, Choi AD, Han BK, Marwan M, Naoum C, Nørgaard BL, Rubinshtein R, Schoenhagen P, Villines T, Leipsic J. SCCT guidelines for the performance and acquisition of coronary computed tomographic angiography. *J Cardiovasc Comput Tomogr*. 2016;10(6):435–449. 10.1016/j.jcct.2016.10.002. PMID: 27780758.
38. Nieman K, Garcia-Garcia HM, Hideo-Kajita A, Collet C, Dey D, Pugliese F, Weissman G, Tijssen JGP, Leipsic J, Opolski MP, Ferencik M, Lu MT, Williams MC, Bruining N, Blanco PJ, Maurovich-Horvat P, Achenbach S. Standards for quantitative assessments by coronary computed tomography angiography: an expert consensus document of the Society of Cardiovascular Computed Tomography. *J Cardiovasc Comput Tomogr*. 2024;18(5):429–443. 10.1016/j.jcct.2024.05.232. PMID: 38849237.
39. Kim C, Park CH, Lee BY, Park CH, Kang EJ, Koo HJ, Kitagawa K, Cha MJ, Krittayaphong R, Choi SI, Yong HS, Ko SM, Kim SM, Hwang SH, Trang NN, Lee W, Kim YJ, Lee J, Yang DH. 2024 consensus statement on coronary stenosis and plaque evaluation in CT angiography from the Asian Society of Cardiovascular Imaging-Practical Tutorial. *Korean J Radiol*. 2024;25(4):331–342. 10.3348/kjr.2024.0112. PMID: 38528691.
40. Nørgaard BL, Gaur S, Leipsic J, Ito H, Miyoshi T, Park SJ, Zvaigzne L, Tzemos N, Jensen JM, Hansson N, Ko B, Bezerra H, Christiansen EH, Kaltoft A, Lassen JF, Bøtker HE, Achenbach S. Influence of coronary calcification on the diagnostic performance of CT angiography-derived FFR in coronary artery disease. *JACC Cardiovasc Imaging*. 2015;8(9):1045–1055. 10.1016/j.jcmg.2015.06.003. PMID: 26298072.
41. Mickley H, Veien KT, Gerke O, Lambrechtsen J, Rohold A, Steffensen FH, Husic M, Akkan D, Busk M, Jessen LB, Jensen LO, Diederichsen A, Øvrehus KA. Diagnostic and clinical value of FFRCT in stable chest pain patients with extensive coronary calcification: the FACC Study. *JACC Cardiovasc Imaging*. 2022;15(6):1046–1058. 10.1016/j.jcmg.2021.12.010. PMID: 35680213.
42. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, STROBE Initiative. The Strengthening the Reporting of Observational Studies in Epidemiology statement: guidelines for reporting observational studies. *BMJ*. 2007;335(7624):806–808. 10.1136/bmj.39335.541782.AD. PMID: 17947786.
43. White IR, Carlin JB. Bias and efficiency of multiple imputation compared with complete-case analysis for missing covariate values. *Stat Med*. 2010;29(28):2920–2931. 10.1002/sim.3944. PMID:

20842622.

44. Heymans MW, Twisk JWR. Handling missing data in clinical research. *J Clin Epidemiol*. 2022;151:185–188. 10.1016/j.jclinepi.2022.08.016. PMID: 36150546.
45. Tesche C, De Cecco CN, Baumann S, Renker M, McLaurin TW, Duguay TM, Bayer RR 2nd, Steinberg DH, Grant KL, Canstein C, Schwemmer C, Schoebinger M, Itu LM, Rapaka S, Sharma P, Schoepf UJ. Coronary CT angiography-derived fractional flow reserve: machine learning algorithm versus computational fluid dynamics modeling. *Radiology*. 2018;288(1):64–72. 10.1148/radiol.2018171291. PMID: 29634438.
46. Pijls NH, De Bruyne B, Peels K, Van Der Voort PH, Bonnier HJRM, Bartunek JK, Koolen JJ. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. *N Engl J Med*. 1996;334(26):1703–1708. 10.1056/NEJM199606273342604. PMID: 8637515.
47. Pijls NH, Van Gelder B, Van der Voort P, Peels K, Bracke FA, Bonnier HJRM, el Gamal MI. Fractional flow reserve: a useful index to evaluate the influence of an epicardial coronary stenosis on myocardial blood flow. *Circulation*. 1995;92(11):3183–3193. doi: 10.1161/01.CIR.92.11.3183. PMID: 7586302.
48. Tonino PAL, De Bruyne B, Pijls NHJ, Siebert U, Ikeno F, van't Veer M, Klauss V, Manoharan G, Engstrøm T, Oldroyd KG, Ver Lee PN, MacCarthy PA, Fearon WF. FAME Study Investigators. Fractional flow reserve versus angiography for guiding percutaneous coronary intervention. *N Engl J Med*. 2009;360(3):213–224. 10.1056/NEJMoa0807611. PMID: 19144937.
49. De Bruyne B, Pijls NHJ, Kalesan B, Barbato E, Tonino PAL, Piroth Z, Jagic N, Möbius-Winkler S, Rioufol G, Witt N, Kala P, MacCarthy P, Engström T, Oldroyd KG, Mavromatis K, Manoharan G, Verlee P, Frobert O, Curzen N, Johnson JB, Jüni P, Fearon WF. FAME 2 Trial Investigators. Fractional flow reserve-guided PCI versus medical therapy in stable coronary disease. *N Engl J Med*. 2012;367(11):991–1001. 10.1056/NEJMoa1205361. PMID: 22924638.
50. Fearon WF, Zimmermann FM, De Bruyne B, Piroth Z, van Straten AHM, Szekely L, Davidavicius G, Kalinauskas G, Mansour S, Kharbada R, Östlund-Papadogeorgos N, Aminian A, Oldroyd KG, Al-Attar N, Jagic N, Dambrink JE, Kala P, Angerås O, MacCarthy P, Wendler O, Casselman F, Witt N, Mavromatis K, Miner SES, Sarma J, Engstrøm T, Christiansen EH, Tonino PAL, Reardon MJ, Lu D, Ding VY, Kobayashi Y, Hlatky MA, Mahaffey KW, Desai M, Woo YJ, Yeung AC, Pijls NHJ. FAME 3 Investigators. Fractional flow reserve-guided PCI as compared with coronary bypass surgery. *N Engl J Med*. 2022;386(2):128–137. 10.1056/NEJMoa2112299. PMID: 34735046.
51. Williams MC, Moss AJ, Dweck M, Adamson PD, Alam S, Hunter A, Shah ASV, Pawade T, Weir-McCall JR, Roditi G, van Beek EJR, Newby DE, Nicol ED. Coronary artery plaque characteristics associated with adverse outcomes in the SCOT-HEART study. *J Am Coll Cardiol*. 2019;73(3):291–301. 10.1016/j.jacc.2018.10.066. PMID: 30678759.
52. Motoyama S, Ito H, Sarai M, Kondo T, Kawai H, Nagahara Y, Harigaya H, Kan S, Anno H, Takahashi H, Naruse H, Ishii J, Hecht H, Shaw LJ, Ozaki Y, Narula J. Plaque characterization by coronary

- computed tomography angiography and the likelihood of acute coronary events in mid-term follow-up. *J Am Coll Cardiol.* 2015;66(4):337–346. 10.1016/j.jacc.2015.05.069. PMID: 26205589.
53. Puchner SB, Liu T, Mayrhofer T, Truong QA, Lee H, Fleg JL, Nagurney JT, Udelson JE, Hoffmann U, Ferencik M. High-risk plaque detected on coronary CT angiography predicts acute coronary syndromes independent of significant stenosis in acute chest pain. *J Am Coll Cardiol.* 2014;64(7):684–692. 10.1016/j.jacc.2014.05.039. PMID: 25125300.
 54. Maurovich-Horvat P, Ferencik M, Voros S, Merkely B, Hoffmann U. Comprehensive plaque assessment by coronary CT angiography. *Nat Rev Cardiol.* 2014;11(7):390–402. 10.1038/nrcardio.2014.60. PMID: 24755916.
 55. Yang S, Koo BK. Coronary physiology-based approaches for plaque vulnerability: implications for risk prediction and treatment strategies. *Korean Circ J.* 2023;53(9):581–593. 10.4070/kcj.2023.0117. PMID: 37653694.
 56. Tesche C, De Cecco CN, Albrecht MH, Duguay TM, Bayer RR 2nd, Litwin SE, Steinberg DH, Schoepf UJ. Coronary CT angiography-derived fractional flow reserve. *Radiology.* 2017;285(1):17–33. 10.1148/radiol.2017162641. PMID: 28926310.
 57. Zhuang B, Wang S, Zhao S, Lu M. Computed tomography angiography-derived fractional flow reserve (CT-FFR) for the detection of myocardial ischemia with invasive fractional flow reserve as reference: systematic review and meta-analysis. *Eur Radiol.* 2020;30(2):712–725. 10.1007/s00330-019-06470-8. PMID: 31696294.
 58. Yi D, Zhou F, Liang Q, Liu T, Bao X, Cai J, Tang C, Zhang L. Coronary computed tomography angiography-derived fractional flow reserve: a comprehensive review. *Rev Cardiovasc Med.* 2025;26(9):39717. 10.31083/RCM39717. PMID: 41089771.
 59. Tang CX, Qiao HY, Zhang XL, Di Jiang M, Schoepf UJ, Rudziński PN, Giovagnoli DP, Lu MJ, Li JH, Wang YN, Zhang JY, Hou Y, Zheng MW, Zhang B, Zhang DM, Hu XH, Xu L, Liu H, Lu GM, Zhang LJ. Functional CAD-RADS using FFRCT on therapeutic management and prognosis in patients with coronary artery disease. *Eur Radiol.* 2022;32(8):5210–5221. 10.1007/s00330-022-08618-5. PMID: 35258672.
 60. Fairbairn TA, Nieman K, Akasaka T, Nørgaard BL, Berman DS, Raff G, Hurwitz-Kowek LM, Pontone G, Kawasaki T, Sand NP, Jensen JM, Amano T, Poon M, Øvrehus K, Sonck J, Rabbat M, Mullen S, De Bruyne B, Rogers C, Matsuo H, Bax JJ, Leipsic J, Patel MR. Real-world clinical utility and impact on clinical decision-making of coronary computed tomography angiography-derived fractional flow reserve: lessons from the ADVANCE Registry. *Eur Heart J.* 2018;39(41):3701–3711. 10.1093/eurheartj/ehy530. PMID: 30165613.
 61. Nørgaard BL, Gaur S, Fairbairn TA, Douglas PS, Jensen JM, Patel MR, Ihsdayhid AR, Ko BSH, Sellers SL, Weir-McCall J, Matsuo H, Sand NPR, Øvrehus KA, Rogers C, Mullen S, Nieman K, Parner E, Leipsic J, Abdulla J. Prognostic value of coronary computed tomography angiographic derived fractional flow reserve: a systematic review and meta-analysis. *Heart.* 2022;108(3):194–202. 10.1136/heartjnl-2021-319773. PMID: 34686567.

62. Argacha JF, Motoc A, Lammens J, Vandeloo B, Tanaka K, Belsack D, Michiels V, Lochy S, Tsugu T, De Potter T, Thorrez Y, Magne J, De Mey J, Cosyns B. Clinical and prognostic incremental value of FFRCT in screening of patients with obstructive coronary artery disease. *J Cardiovasc Comput Tomogr.* 2024;18(1):62–68. doi: 10.1016/j.jcct.2023.11.078. PMID: 38072710.
63. Maron DJ, Hochman JS, Reynolds HR, Bangalore S, O'Brien SM, Boden WE, Chaitman BR, Senior R, López-Sendón J, Alexander KP, Lopes RD, Shaw LJ, Berger JS, Newman JD, Sidhu MS, Goodman SG, Ruzyllo W, Gosselin G, Maggioni AP, White HD, Bhargava B, Min JK, Mancini GBJ, Berman DS, Picard MH, Kwong RY, Ali ZA, Mark DB, Spertus JA, Krishnan MN, Elghamazi A, Moorthy N, Hueb WA, Demkow M, Mavromatis K, Bockeria O, Peteiro J, Miller TD, Szwed H, Doerr R, Keltai M, Selvanayagam JB, Steg PG, Held C, Kohsaka S, Mavromichalis S, Kirby R, Jeffries NO, Harrell FE Jr, Rockhold FW, Broderick S, Ferguson TB Jr, Williams DO, Harrington RA, Stone GW, Rosenberg Y. ISCHEMIA Research Group. Initial invasive or conservative strategy for stable coronary disease. *N Engl J Med.* 2020;382(15):1395–1407. 10.1056/NEJMoa1915922. PMID: 32227755.
64. Jang IK, Bouma BE, Kang DH, Park SJ, Park SW, Seung KB, Choi KB, Shishkov M, Schlendorf K, Pomerantsev E, Houser SL, Aretz HT, Tearney GJ. Visualization of coronary atherosclerotic plaques in patients using optical coherence tomography: comparison with intravascular ultrasound. *J Am Coll Cardiol.* 2002;39(4):604–609. 10.1016/S0735-1097(01)01799-5. PMID: 11849858.
65. Araki M, Park SJ, Dauerman HL, Uemura S, Kim JS, Di Mario C, Johnson TW, Guagliumi G, Kastrati A, Joner M, Holm NR, Alfonso F, Wijns W, Adriaenssens T, Nef H, Rioufol G, Amabile N, Souteyrand G, Meneveau N, Gerbaud E, Opolski MP, Gonzalo N, Tearney GJ, Bouma B, Aguirre AD, Mintz GS, Stone GW, Bourantas CV, Räber L, Gili S, Mizuno K, Kimura S, Shinke T, Hong MK, Jang Y, Cho JM, Yan BP, Porto I, Niccoli G, Montone RA, Thondapu V, Papafaklis MI, Michalis LK, Reynolds H, Saw J, Libby P, Weisz G, Iannaccone M, Gori T, Toutouzas K, Yonetsu T, Minami Y, Takano M, Raffel OC, Kurihara O, Soeda T, Sugiyama T, Kim HO, Lee T, Higuma T, Nakajima A, Yamamoto E, Bryniarski KL, Di Vito L, Vergallo R, Fracassi F, Russo M, Seegers LM, McNulty I, Park S, Feldman M, Escaned J, Prati F, Arbustini E, Pinto FJ, Waksman R, Garcia-Garcia HM, Maehara A, Ali Z, Finn AV, Virmani R, Kini AS, Daemen J, Kume T, Hibi K, Tanaka A, Akasaka T, Kubo T, Yasuda S, Croce K, Granada JF, Lerman A, Prasad A, Regar E, Saito Y, Sankardas MA, Subban V, Weissman NJ, Chen Y, Yu B, Nicholls SJ, Barlis P, West NEJ, Arbab-Zadeh A, Ye JC, Dijkstra J, Lee H, Narula J, Crea F, Nakamura S, Kakuta T, Fujimoto J, Fuster V, Jang IK. Optical coherence tomography in coronary atherosclerosis assessment and intervention. *Nat Rev Cardiol.* 2022;19(10):684–703. 10.1038/s41569-022-00687-9. PMID: 35449407.
66. Sinclair H, Bourantas C, Bagnall A, Mintz GS, Kunadian V. OCT for the identification of vulnerable plaque in acute coronary syndrome. *JACC Cardiovasc Imaging.* 2015;8(2):198–209. doi: 10.1016/j.jcmg.2014.12.005. PMID: 25677892.

Figures

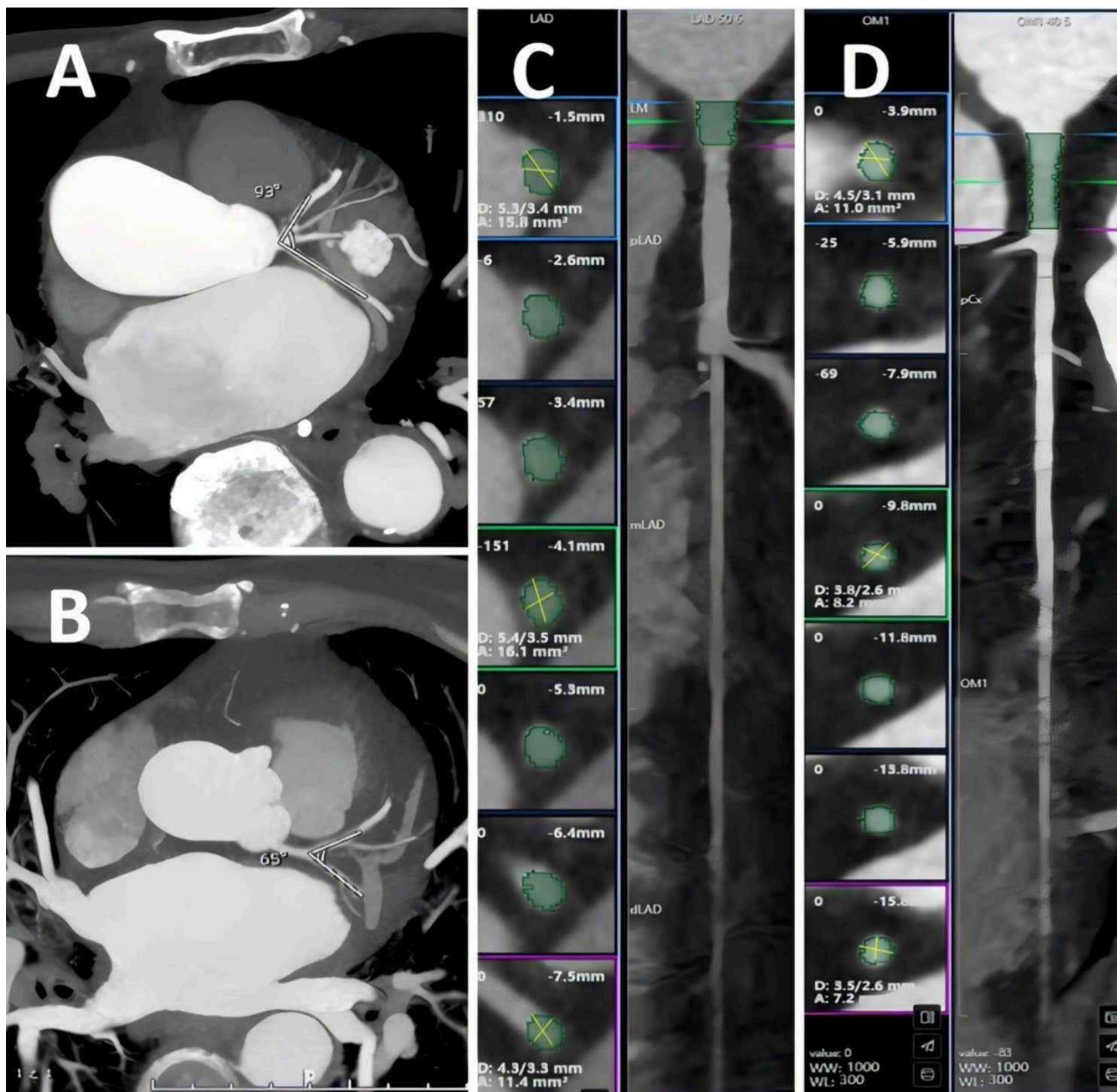


Figure 1

Left main bifurcation geometry according to ramus intermedius status. (A) Representative CCTA image showing a widened LAD-LCX angle in a patient with an RI. (B) Representative CCTA image showing a narrower LAD-LCX angle in a patient without an RI. (C) Representative cross-sectional image showing larger LM diameter and CSA in a patient with an RI. (D) Representative cross-sectional image showing smaller LM diameter and CSA in a patient without an RI. These panels are illustrative and do not represent group means or medians.

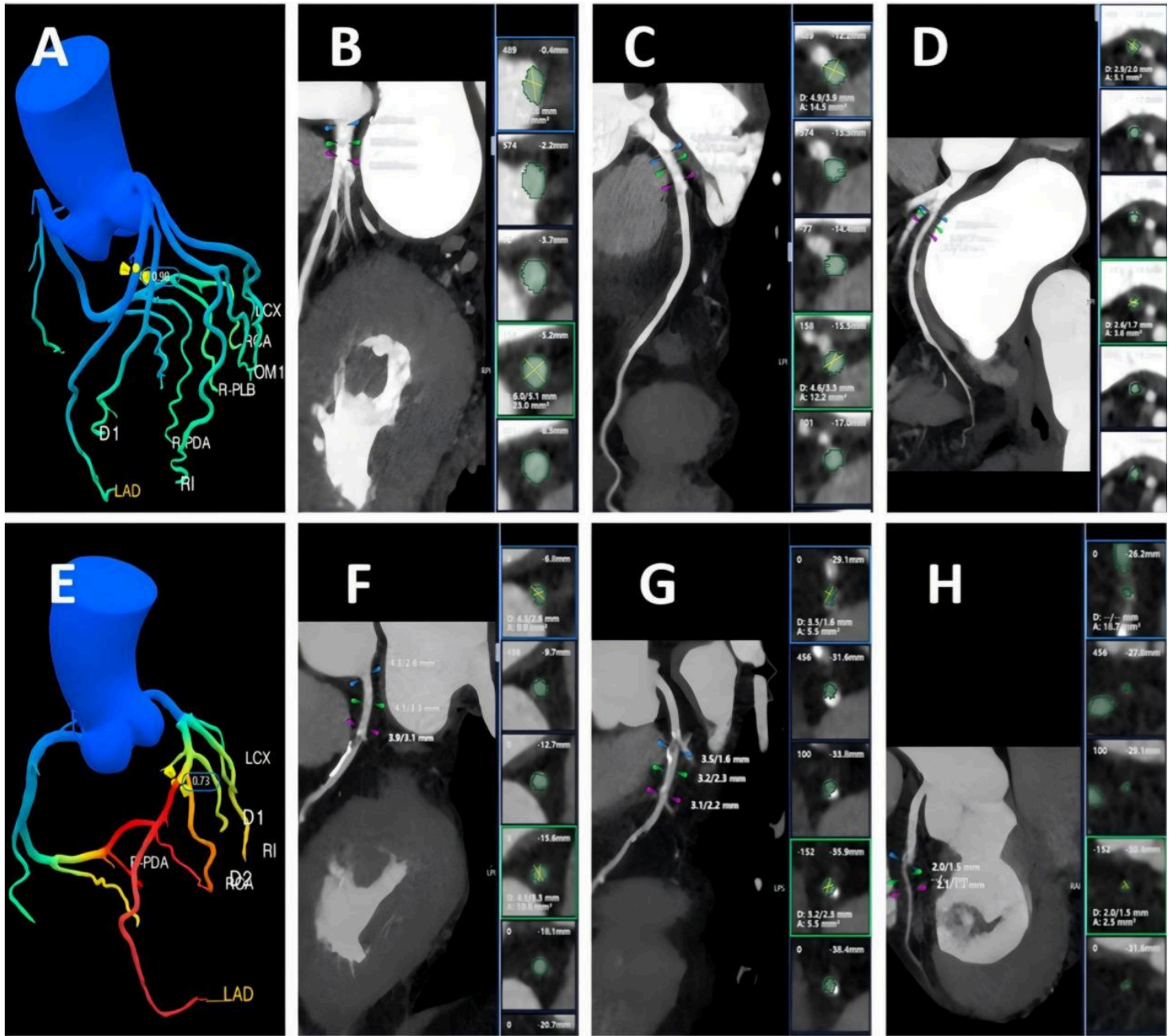


Figure 2

Anatomic and functional findings according to RI ostial location. (A) CT-FFR map showing no CT-FFR-defined LAD functional abnormality in a patient with an RI arising proximal to the LCX. (B-D) Representative cross-sectional images showing relatively larger LM, LAD, and LCX CSA values in the RI-LCX configuration. (E) CT-FFR map showing a CT-FFR-defined LAD functional abnormality in a patient with an RI arising proximal to the LAD. (F-H) Representative cross-sectional images showing relatively smaller LM, LAD, and LCX CSA values in the RI-LAD configuration. These panels are illustrative and do not represent group means or medians.