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Moving Beyond Binary Grading of Coronary Arterial Stenoses on Coronary Computed Tomographic Angiography

Insights for the Imager and Referring Clinician

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OBJECTIVES We evaluated the technical and clinical utility of visual 5-point coronary stenosis grading on coronary computed tomographic angiography (CCTA).

BACKGROUND The binary approach used to assess coronary stenoses on CCTA does not adequately describe borderline obstructive lesions and limits full expression of clinically useful information.

METHODS From 84 patients who underwent CCTA and invasive angiography, we identified 278 native coronary segments with ≥25% stenosis on CCTA after excluding all <25% stenotic, stented, and uninterpretable segments. Fifty <25% stenotic segments were randomly selected as controls. Segmental stenosis severity on CCTA was consensually graded using a 0 to 5 scale (grade 0 = none, grade 1 = 1% to 24%, grade 2 = 25% to 49%, grade 3 = 50% to 69%, grade 4 = 70% to 89%, grade 5 = 90% to 100%) by 2 readers, using visual inspection and computed tomography–based quantification (CTQCA). Invasive angiography–based stenosis quantification (IQCA) was performed for all segments, using the same 0 to 5 scale to score stenosis severity.

RESULTS On CCTA, 185 (56%) segments had intermediate stenoses (grade 2 or grade 3). Stenosis severity by IQCA increased significantly with each step-up in CCTA grade ($p < 0.001$). CTQCA did not perform better than visual inspection. Visual CCTA stenosis grading differed from IQCA by >1 grade in only 4% of grade 2 to grade 5 segments (10 of 278; 2% of CCTA grade 2 segments, 4% of grade 3, 8% of grade 4, 2% of grade 5). Overall quantitative correlation was strong ($r = 0.82$) with high variability in agreement between CTQCA and IQCA for individual segments (95% of differences between 27.2% and 34.6%).

CONCLUSIONS With current CCTA technology, experienced readers should consider adopting a visually based, multitiered grading approach to evaluate coronary stenoses. A ≤49% lesion on CCTA can be considered virtually exclusive of ≥70% stenosis by invasive angiography. (J Am Coll Cardiol Img 2008;1:460–71) © 2008 by the American College of Cardiology Foundation

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To date, studies comparing coronary computed tomographic angiography (CCTA) and invasive coronary angiography (ICA) have uniformly defined *significant coronary stenosis* as stenosis of ≥50% of arterial diameter (1–9). There are at least 2 potential disadvantages of this binary approach. First, the strong negative predictive value documented for 16- and 64-slice CCTA has been driven by excellent accuracy in large numbers of non- and minimally diseased coronary segments (1–4,6) and generally has not distinguished the "intermediate" stenosis (appearing to

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cause slightly more or <50% narrowing) for which application of the sole ≥50% criterion is more difficult. Second, a binary approach potentially limits expression of useful information regarding stenosis severity gained from CCTA. Although several multitiered stenosis grading systems for CCTA have been previously suggested, none has yet been validated (3,10–12).

Due to limited spatial resolution, quantifying coronary stenosis by CCTA remains challenging, and its value controversial. Although 2 initial reports of 16-slice CCTA stenosis quantification by Cury et al. (11,13) showed excellent correlation with ICA, this success has not been replicated with 64-slice CCTA. Analysis of 130 coronary lesions by Raff et al. (3) and 141 lesions by Leber et al. (12) found significant variability between CCTA and ICA quantification, with greatest variability in lesions causing 25% to 70% obstruction (3,12), thereby questioning the benefit of quantifying and categorizing intermediate stenoses on CCTA.

By using ICA stenosis quantification as the "gold standard," our aim in this study was to evaluate a multitiered grading system for coronary stenoses and to help clarify the value of defining intermediate stenoses on CCTA.

METHODS

Patient and coronary segment selection. We identified 102 consecutive patients who underwent ICA within 35 days of CCTA (on average ICA occurred 6.8 days after CCTA; in 6 patients, ICA occurred before CCTA). Only native coronary segments were eligible for analysis. Patients with bypass grafts remained eligible; however, bypass grafts were not analyzed. A coronary segment was analyzed if it showed ≥1.5 mm absolute luminal diameter and ≥25% maximal luminal diameter stenosis by visual inspection on CCTA. Segments that showed <25% stenosis, were uninterpretable, or contained a stent were initially excluded. In 18 patients, all native coronary segments met exclusion criteria (Fig. 1), and our final study population consisted of the remaining 84 patients. In these 84 patients, 50 additional segments exhibiting <25% diameter stenosis on visual CCTA inspection were then randomly selected as control segments. We used a 17-segment modification of the American Heart Association 15-segment coronary tree model (14), including left main, proximal, mid, and distal left anterior descending, first and second diagonal, proximal, mid, and distal left circumflex, first and second obtuse marginal, proximal, mid, and distal right coronary, posterior descending, posterolateral, and ramus intermedius segments.

CCTA image acquisition. CCTA was performed on the SOMATOM Definition dual-source computed tomography scanner (Siemens Medical Systems, Forchheim, Germany). Dual-source computed tomography employs a flying focus along the z-axis with 2 different focal spots, uses 2 32-detector rows to acquire 64 overlapping 0.6-mm image slices, and has a temporal resolution of 83 ms (15).

Before imaging, patients with heart rates ≥70 beats/min and no contraindications to beta-blockade (documented allergy, active bronchospastic disease, or systolic blood pressure <100 mm Hg) were administered oral metoprolol (25 to 100 mg) and/or intravenous metoprolol (5 mg injection every 1 to 2 min up to 30 mg) to attain a heart rate <70 beats/min. Imaging proceeded even if heart rate remained ≥70 beats/min despite maximal beta-blockade.

Unless contraindicated, a sublingual spray of 0.4 mg nitroglycerin (Sciele Pharma, Alpharetta, Georgia) was then given, followed by power-injection of 92 ml of intravenous contrast (Omnipaque or Visipaque if serum creatinine was >1.5 g/dl, GE Healthcare, Princeton, New Jersey) into the antecubital vein at 5 ml/s, chased by 80 ml of saline at 5 ml/s. Upon detection of ≥100 HU in the ascending aorta, the patient was instructed to hold respiration for 10 to 12 s, during which time electrocardiogram (ECG)-gated scanning was performed, from 1 cm below tracheal bifurcation to the diaphragm. Scanning parameters included heart-rate–dependent pitch (0.2 to 0.45), 330 ms gantry

ABBREVIATIONS AND ACRONYMS

BMI = body mass index

CCTA = coronary computed tomographic angiography

CI = confidence interval

CTQCA = computed tomography–based quantitative coronary analysis

ICA = invasive coronary angiography

IQCA = invasive angiography–based quantitative coronary analysis

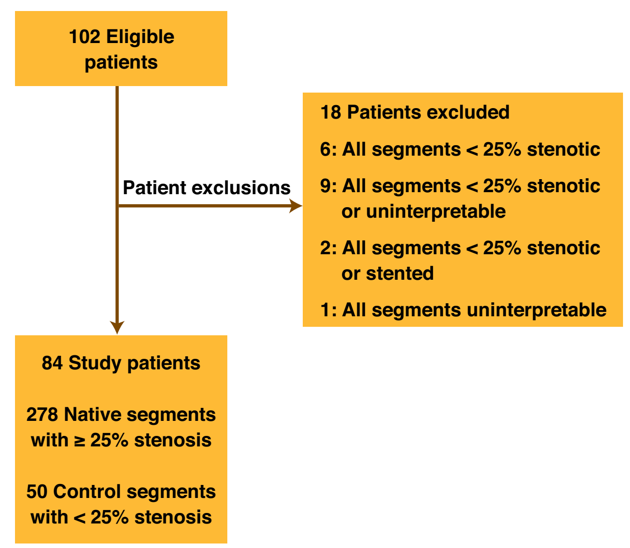

Figure 1. Patient and Coronary Segment Selection Flow Chart

Only diagnostically evaluable, unstented native coronary segments ≥1.5 mm in luminal diameter and exhibiting ≥25% stenosis on visual inspection of coronary computed tomographic angiography images were initially included, resulting in exclusion of 18 patients. One patient had a completely uninterpretable study due to inappropriate contrast timing. Of the 289 segments with ≥25% stenosis from the remaining 84 patients, 11 were incompletely visualized on invasive coronary angiography, leaving 278 such segments for analysis. Fifty <25% stenotic segments were also randomly selected as control segments.

rotation time, 100 or 120 kVp tube voltage, and 600 mAs tube current. Lower tube voltage (100 kVp) was utilized in patients with body mass index (BMI) <30 kg/m^2, weight <85 kg, and no more than mild calcification in the proximal coronary arteries on the calcium-scoring scan. In 77 patients, ECG-based dose modulation was used.

CCTA image reconstruction. Retrospectively gated reconstruction of raw CCTA data was routinely performed at 40%, 65%, 70%, 75%, and 80% of the R-R interval using the following parameters: 0.6-mm slice thickness (0.75 mm if BMI >35 kg/m^2), 0.3-mm slice increment, 250-mm field-of-view, 512 × 512 matrix, and B26f "medium smooth" kernel. The B46f "sharp" kernel was also used in patients with coronary stents or dense coronary calcium (calcium score >100). Whenever image quality from routine reconstruction was degraded due to arrhythmia or motion, reconstruction of additional cardiac phases and/or by manual ECG editing was performed.

CCTA image evaluation. Reconstructed data were transferred to a Hewlett-Packard workstation (Palo Alto, California) that utilized the Vitrea 2 software package (Vital Images, Minnetonka, Minnesota) for coronary artery analysis. Without knowledge of clinical and ICA findings, 2 experienced CCTA readers (A.G. and Y.S.) visually assessed each coronary segment using standard axial images, oblique multiplanar longitudinal and cross-sectional reconstructions, and oblique maximum intensity longitudinal and cross-sectional projections (16). To reduce artifact from coronary calcification, readers increased window width to 1,600 to 2,000, adjusted contrast to allow continued visualization of vessel lumen, and limited evaluation to thinnest axial slices and oblique multiplanar reconstructions. Maximal diameter stenosis severity was visually determined and graded from 0 to 5 (0 = 0%, 1 = 1% to 24%, 2 = 25% to 49%, 3 = 50% to 69%, 4 = 70% to 89%, 5 = 90% to 100%) (Table 1), and a segment graded 2 or 3 was considered intermediately stenotic. To estimate reproducibility of this scoring system, each CCTA reader first independently graded 58 coronary segments from 16 patients randomly selected from the study population. Results showed excellent interobserver (kappa = 0.82, weighted kappa = 0.91 with 95% confidence interval [CI] of 0.83 to 0.97) and intraobserver (kappa = 0.87, weighted kappa = 0.93 with 95% CI of 0.86 to 0.98) agreements. Both readers then officially graded all study segments, resolving disagreements by consensus. Stenosis grading examples are shown in Figure 2. Readers also consensually graded degree of plaque calcification from 0 to 3 (0 = no calcification, 1 = less than one-third of plaque, 2 = one-third to two-thirds of plaque, 3 = greater than two-thirds of plaque) (Fig. 3). Whenever applicable, artifacts were attributed to arrhythmia, respiratory/patient motion, coronary calcium (causing adjacent hypodense tissue appearance or overestimation of plaque size) (17–19), contrast underenhancement, and interference from metallic devices.

Table 1. Five-Point System for Grading of the Severity of Coronary Artery Luminal Diameter Stenosis by CT Angiography

CCTA Grade	
0	No stenosis
1	<25% stenosis
2	25%–49% stenosis
3	50%–69% stenosis
4	70%–89% stenosis
5	≥90% stenosis

CCTA = coronary computed tomographic angiography; CT = computed tomography.

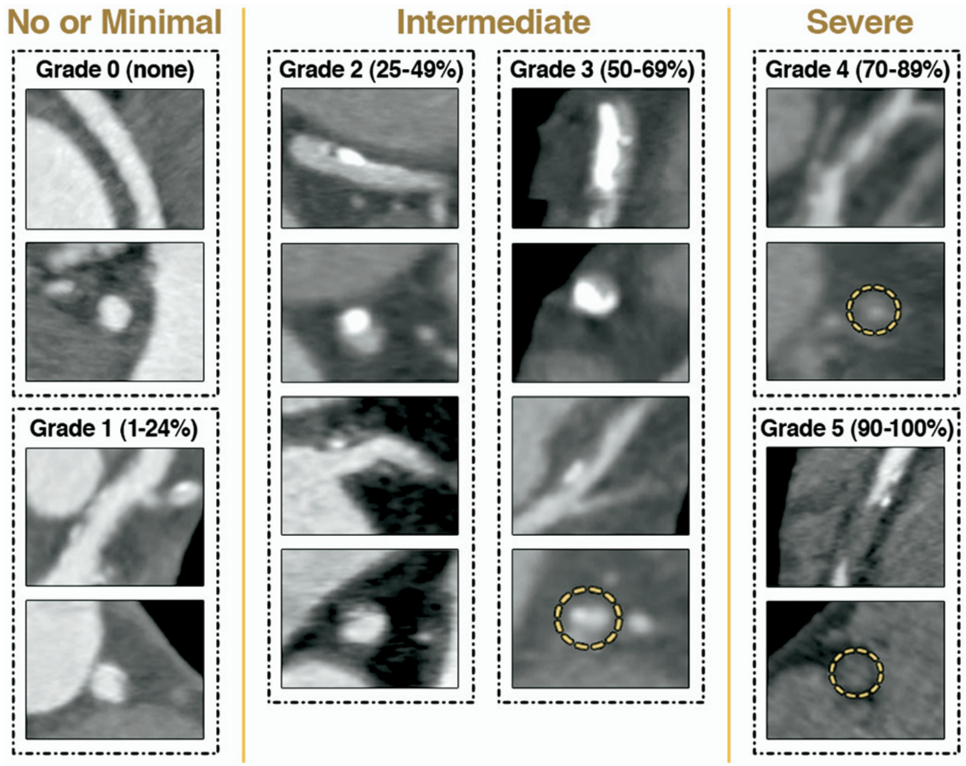

Figure 2. Representative Examples of Coronary Segment Stenosis Severity by Visual Grading on CCTA

All images are 0.6 mm in slice thickness and obtained by manipulation of oblique multiplanar reconstructions. Each example is shown with longitudinal view on top and short-axis view on bottom. **Dotted orange circles** outline short-axis location of the vessel in more stenotic segments. The darker vessel lumen appearance in the top grade 2 and grade 3 examples is due to windowing changes to reduce artifact from heavily calcified plaque. Coronary computed tomographic angiography (CCTA) readers assigned a grade between 0 and 5 for each segment by assessing plaque morphology in both longitudinal and short-axis views.

After completing visual assessment of each segment, one reader (A.G.) performed manual computed tomography–based quantitative coronary analysis (CTQCA) using the most representative longitudinal image and a simplified calculation that estimates normal tapering of the coronary artery based on the initial method described by Reiber et al. (20). This reader made the following measurements: reference vessel diameter proximal to the stenosis (D_{prox}), reference vessel diameter distal to the stenosis (D_{dis}), luminal diameter at the site of stenosis (D_{sten}), distance between proximal refer-

Figure 3. Representative Examples of Qualitative Lesion Calcification Grading

All images are 0.6 mm in slice thickness and obtained by manipulation of oblique multiplanar reconstructions. Visual grading of plaque calcification was obtained by consensus from the same coronary computed tomographic angiography readers who graded stenosis severity. Grade 1 = calcified plaque makes up less than one-third of total plaque; grade 2 = calcified plaque makes up one-third to two-thirds of total plaque; grade 3 = calcified plaque makes up greater than two-thirds of total plaque. Because of artifacts associated with dense calcification, stenoses of plaques with grade 2 or grade 3 calcification may be less accurately characterized on coronary computed tomographic angiography.

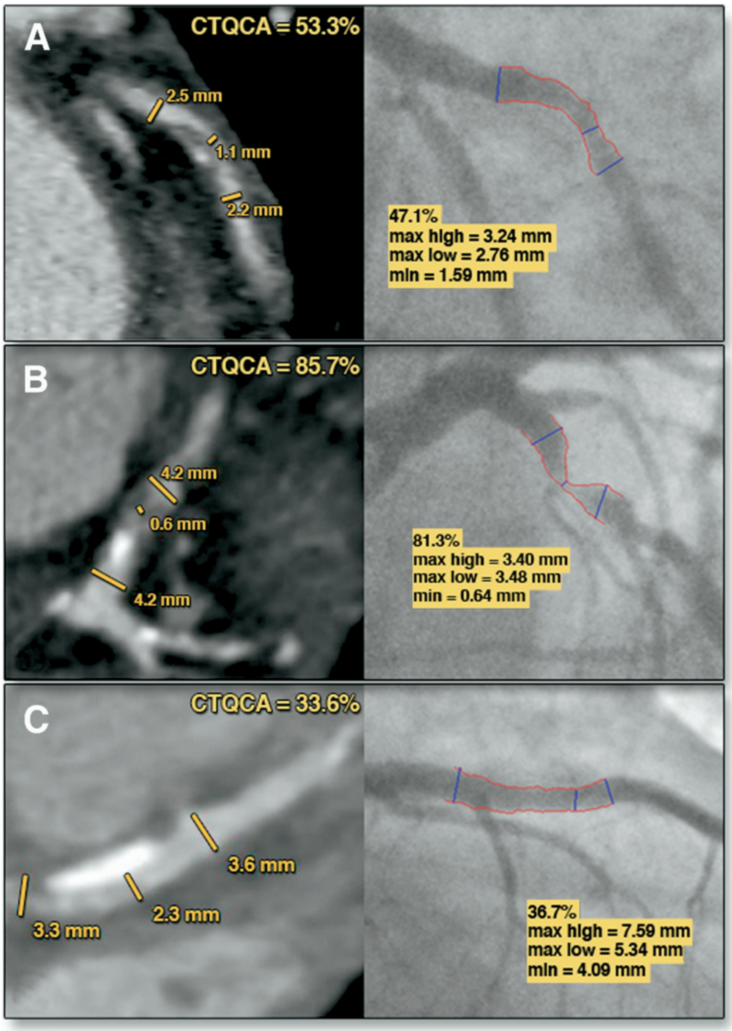

Figure 4. Examples of CCTA-Based and ICA-Based Stenosis Quantification

Coronary computed tomographic angiography (CCTA) images are on the **left**, and invasive coronary angiography (ICA) images are on the **right**. Computed tomography–based quantitative coronary analysis (CTQCA) was performed on the thinnest possible image slice by using a simplified formula based on the technique described by Reiber et al. (20) (see Methods section). This simplified formula may be useful for future investigations requiring routine stenosis calculation on CCTA. **(A)** Quantification of an intermediately stenotic noncalcified plaque in the midleft circumflex artery. **(B)** Quantification of a severely occlusive noncalcified plaque in the proximal left anterior descending artery. **(C)** Quantification of mild stenosis from a calcified plaque in the proximal left anterior descending artery.

ence site and distal reference site (X_1), and distance between proximal reference site and maximally stenotic site (X_2). Maximal degree of stenosis was calculated using the following formula (Fig. 4):

$$\text{Stenosis (\%)} = [1 - (D_{sten})/(D_{prox} - ((X_1/X_2) * (D_{prox} - D_{dis})))]$$

Before use in this study, we compared this formula to the Reiber computerized automated technique on ICA images of 20 randomly selected stenoses. Given the same proximal reference, distal reference, and stenosis site positions, both methods produced nearly identical results (Pearson r = 0.998, bias of −0.01% with 95% CI of −0.60% to 0.57%). Initial visual grading could not be altered after calculation of stenosis % by CTQCA.

ICA image acquisition. ICA was performed using the Inova digital X-ray system from GE Healthcare (Buckinghamshire, United Kingdom). Standard cardiac catheterization technique was employed. Nitrates were not routinely used during ICA. Acquired images were transferred to an AGFA Heartlab workstation (Greenville, South Carolina) for analysis.

ICA image evaluation. CCTA readers (A.G. and Y.S.) compiled a list of all 278 visually ≥grade 2 segments and the 50 control segments. A separate blinded investigator (V.C.) independently performed invasive coronary angiography–based quantitative coronary analysis (IQCA) for all segments in this list. For each coronary segment, the IQCA investigator first assessed ICA images to identify the projection in which the segment appeared most stenotic. Reference luminal positions proximal and distal to the stenosis were then defined in this projection. Quantitative coronary analysis software on the workstation was then used to detect luminal edges, locate site of maximal stenosis, and quantify the degree of maximal stenosis (20). Whenever automatic edge detection failed, manual edge tracing was performed. Each IQCA-determined stenosis was given an ordinal score of 0 to 5 by applying the same grading criteria used by CCTA readers.

Statistical methods. Continuous variables were described with mean ± SD. CCTA and IQCA grades were analyzed as ordinal variables. The chi-square test was used to compare distribution of ordinal IQCA grading between different CCTA grades and differences in ordinal IQCA grading between visual and quantitative CCTA assessment. For 5 different CCTA grades (0 and 1 were combined), 10 total Bonferroni-corrected pairwise comparisons were made for both visual and quantitative CCTA grading, with a p value <0.005 necessary for statistical significance. Correlations of visual and quantitative CCTA grading to IQCA grading were further evaluated by calculating Kendall's tau-b (adjusted for ties) and linearly weighted kappa estimates for inter-rater agreement, with bias-corrected 95% CI obtained by nonparametric bootstrapping (21). To assess differences in IQCA results between different CCTA grades, pairwise, Bonferroni-corrected analysis of variance comparisons were performed. Agreement between CTQCA and IQCA stenosis quantification (continuous variables) was determined by calculating the Pearson correlation coefficient and generating a bias plot from the Bland-Altman test (22). To determine predictors of discrepancy between CCTA and IQCA grading, multivariate logistic regression was performed, with clustering on each individual patient. At baseline, the regression model contained variables already shown to affect CCTA quality: age, BMI, and average heart rate and heart rate variation at time of scanning (3,23,24). Pre-specified candidate predictors, including reference vessel diameter, length of stenotic lesion, luminal diameter at stenotic site, degree of lesion calcification, and presence of artifact from lesion calcification were then added to the model while controlling for baseline variables. Artifact from arrhythmia, patient motion, contrast underenhancement, and metallic devices occurred rarely and were not considered candidate variables. Total coronary calcium score was not used in this model as it did not necessarily represent calcium burden in individual segments. Significance was set at the level of 0.05. A goodness-of-fit test was performed and verified stability of logistic regression. Statistical analyses were performed using Analyse-it, standard edition (Leeds, England) and STATA 8.2 for Windows (College Station, Texas).

RESULTS

Our study population was predominantly male gender (76%), with a mean age of 66 ± 11 years and BMI of 27.8 ± 5.0 kg/m^2. Prevalences of risk factors were: diabetes 23%, hypertension 63%, cigarette smoking history 27%, dyslipidemia 74%, and family coronary artery disease history 38%. Sixty-three patients (75%) underwent CCTA for chest pain or dyspnea. Prevalence of prior myocardial infarction or coronary revascularization was 38%. Mean coronary calcium score was 752. Mean scan heart rate was 57 beats/min. CCTA detected ≥grade 3 stenosis in 71 patients (85%) and ≥grade 4 stenosis in 51 patients (61%).

Of the 339 total coronary segments (including 50 control segments) identified on CCTA, 11 visually ≥grade 2 segments were excluded from analysis due to inadequate ICA visualization. Table 2 shows characteristics of the remaining 278 ≥grade 2 segments. By visual CCTA evaluation, 105 segments were grade 2, 80 were grade 3, 52 were grade 4, and 41 were grade 5. By CCTA quantification, 102 segments were grade 2, 105 were grade 3, 60 were grade 4, and 24 were grade 5. All 50 control segments were grade 0 or grade 1 on CCTA by both visual and quantitative evaluation.

Ordinal stenosis grading on CCTA compared with that of IQCA. Distributions of IQCA coronary stenosis grading as functions of visual and quantitative CCTA evaluation are shown in the top and bottom graphs of Figure 5. Any increase in CCTA grade tracked a significant increase in IQCA stenosis severity ($p < 0.0001$), quantified in Table 3. IQCA results differed between visual and quantitative CCTA evaluation only for grade 5 stenoses, found more frequently in segments determined grade 4 by CCTA quantification than visual CCTA inspection (21% to 6%, $p = 0.016$). Overall correlation of

Table 2. Characteristics of Coronary Segments With ≥Grade 2 Stenosis on CCTA

	n	(%)
Main epicardial artery	219	(79)
LM	11	(4)
LAD	126	(45)
LCX	36	(13)
RCA	46	(17)
Branches*	59	(21)
Segment diameter		
<2.5 mm	27	(10)
2.5–2.9 mm	42	(15)
3.0–3.4 mm	66	(24)
≥3.5 mm	143	(51)
Degree of calcification		
None	100	(36)
Mild (less than one-third of plaque)	56	(20)
Moderate (one-third to two-thirds of plaque)	52	(19)
Severe (greater than two-thirds of plaque)	70	(25)
Observed artifacts		
Arrhythmia	3	(1)
Patient motion	5	(2)
Calcium related	132	(47)
Contrast underenhancement	11	(4)

*Branches include diagonal, obtuse marginal, posterior descending, posterolateral, and ramus intermedius arteries.
CCTA = coronary computed tomographic angiography; LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main coronary artery; RCA = right coronary artery.

ordinal grading between CCTA and IQCA was good, as shown in Table 4.

While difference of 1 grade between CCTA and IQCA occurred frequently, difference of >1 grade was rare, especially with visual CCTA inspection (Fig. 5). Two such cases (2%) occurred among CCTA grade 2 segments; 3 (4%) among grade 3 segments; 4 (8%) among grade 4 segments; and 1 (2%) among grade 5 segments. In total, visual CCTA inspection underestimated 3 segments (1%) and overestimated 7 segments (2%) by >1 grade, while quantitative CCTA evaluation underestimated 4 segments (1%) and overestimated 16 segments (5%) by >1 grade. Table 5 describes the 10 segments with >1 grade "misses" on visual CCTA inspection. The site of stenosis was noncalcified in 2 of 3 underestimated segments and severely calcified in 6 of 7 overestimated segments.

Twenty-four segments were 100% occluded on ICA. By visual CCTA inspection, 23 of these segments were grade 5, and 1 was grade 3. By quantitative CCTA evaluation, 16 were grade 5, 7 were grade 4, and 1 was grade 2. Complete occlusions made up 56% and 67% of grade 5 segments by visual CCTA inspection and quantitative CCTA evaluation, respectively. All control segments (grade 0 or grade 1 by CCTA) were grade 0 or grade 1 by IQCA.

Quantitative stenosis grading on CCTA compared with that of IQCA. Correlation and bias plots of CTQCA and IQCA results from 328 coronary segments are shown in Figure 6 (20 segments without plaque or stenosis on both CCTA and ICA were assigned 0% stenosis). The Pearson r-coefficient was 0.82 (95% CI: 0.79 to 0.86), indicating very good overall correlation. Quantitative correlation was strong in segments with minimal stenoses ($r = 0.80$) and moderate in segments with intermediate and severe stenoses ($r = 0.52$ and 0.51, respectively). In the 308 segments with visible plaque, correlation was higher for cases in which the stenotic plaque contained less than one-third calcified component ($n = 172$, $r = 0.81$, 95% CI: 0.76 to 0.86) than when the stenotic plaque contained greater than one-third calcification ($n = 136$, $r = 0.66$, 95% CI: 0.55 to 0.75); this difference in correlation was statistically significant based on nonoverlapping CIs. Bland-Altman analysis showed high variability in agreement between CTQCA and IQCA for individual segments. On average, CTQCA was higher than IQCA by 3.70 (95% CI: 2.0 to 5.4), with 95% of differences falling between −27.2 to 34.6, corresponding to roughly ±1 ordinal grade deviation from IQCA.

Predictors of grading discrepancy. Multivariate logistic regression analysis of BMI, mean heart rate during CCTA, heart rate variation during CCTA, and candidate variables described earlier (see Methods section) revealed only 1 significant predictor of discrepancy between visual CCTA and IQCA grading: increased luminal diameter at the stenotic site was associated with an increased likelihood of visual CCTA grade being lower than IQCA grade ("undercalling," odds ratio 1.66 for each millimeter increase in luminal diameter, 95% CI: 1.14 to 2.42, $p = 0.009$). Degree of lesion calcification was not significantly associated with grading discrepancy between CCTA and IQCA.

DISCUSSION

We performed this study to address 2 potential limitations of the currently commonplace binary (< or ≥50%) approach in evaluating coronary stenoses on CCTA. We addressed the first limitation—that intermediate stenoses on CCTA had not been well represented in prior studies—by studying a population with high coronary disease burden and in whom the majority of diseased coronary segments

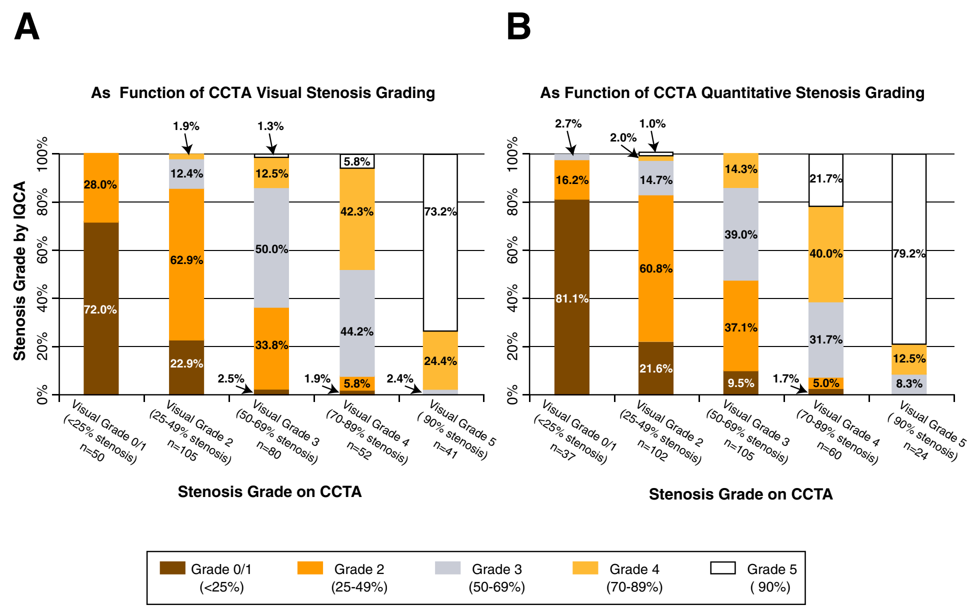

Figure 5. Distribution of IQCA Stenosis Grading Results for Each Group of Segments With the Same Stenosis Grading by Visual CCTA Inspection and Quantitative CCTA Evaluation

Components of each bar total 100%. Each stepwise increase in coronary computed tomographic angiography (CCTA) grading is accompanied by an increase in frequency of higher grade stenoses on invasive coronary angiography–based stenosis quantification (IQCA) ($p < 0.001$). Frequency of IQCA grade 5 stenoses was higher in segments determined grade 4 by CCTA quantification **(B)** (21.7%) than by visual inspection **(A)** (5.8%, $p = 0.016$). A grading discrepancy of >1 between CCTA and IQCA occurred rarely. For example **(A)**, only 1.9% visual CCTA grade 2 segments were grade 4 on IQCA, indicating that when maximal stenosis within a segment is determined at 25% to 49% on CCTA, ≥70% stenosis by IQCA can be excluded.

were intermediately stenotic on CCTA (56% by visual inspection and 63% by quantification were grade 2 or grade 3). We addressed the second limitation—that a binary grading system may conceal useful information generated by CCTA regarding coronary stenoses—by using both an ordinal, 0-to-5-point approach (Table 1) and a quantitative approach to grade stenosis severity on CCTA. To our knowledge, this represents the largest group of diseased coronary segments quantified on CCTA and ICA to date and is also the first work to evaluate a multitiered, ordinal stenosis grading system for CCTA.

Findings from our study are 2-fold: *technical*—more directly applicable to the CCTA imaging physician; and *clinical*—more directly applicable to the clinician managing the patient after receiving CCTA results.

Table 3. Mean and Range of IQCA Stenosis Severity for Each Visually and Quantitatively Determined CCTA Grade

CCTA Grade	n	Mean IQCA ± SD	IQCA Range
Visual grade 0/1 (<25% stenotic)	50	15.6 ± 15.6*	0.0–46.3
Visual grade 2 (25%–49% stenotic)	105	37.2 ± 13.2*	9.0–80.0
Visual grade 3 (50%–69% stenotic)	80	54.5 ± 15.7*	15.0–100.0
Visual grade 4 (70%–89% stenotic)	52	67.1 ± 14.6*	20.6–95.3
Visual grade 5 (≥90% stenotic)	41	92.2 ± 11.4*	63.2–100.0
Quantitative grade 0/1 (<25% stenotic)	37	11.2 ± 15.3†	0.0–55.0
Quantitative grade 2 (25%–49% stenotic)	102	38.0 ± 15.2†	11.9–100.0
Quantitative grade 3 (50%–69% stenotic)	105	51.6 ± 16.7†	16.4–91.0
Quantitative grade 4 (70%–89% stenotic)	60	72.5 ± 18.1†	22.4–100.0
Quantitative grade 5 (≥90% stenotic)	24	94.3 ± 11.9†	53.5–100.0

*$p < 0.0001$ for any pairwise comparison of visual grading; †$p < 0.0001$ for any pairwise comparison of quantitative grading.
CCTA = coronary computed tomographic angiography; IQCA = invasive coronary angiography–based quantitative coronary analysis; SD = standard deviation.

Table 4. Correlation of Quantitative and Ordinal Assessment of Coronary Stenoses Between CCTA and IQCA

	Visual CCTA vs. IQCA (95% CI)	CTQCA vs. IQCA (95% CI)
Quantitative correlation (Pearson)		
Overall	n/a*	0.82 (0.79–0.86)
IQCA grades 0 or 1 ("minimal")	n/a*	0.80 (0.69–0.88)
IQCA grades 2 or 3 ("intermediate")	n/a*	0.52 (0.40–0.61)
IQCA grades 4 or 5 ("severe")	n/a*	0.51 (0.32–0.65)
Ordinal correlation		
Overall (Kendall's tau-b)	0.76 (0.71–0.81)	0.69 (0.62–0.75)
Overall (weighted kappa)	0.70 (0.64–0.76)	0.63 (0.56–0.69)

*n/a = not applicable (visual CCTA evaluation was not quantitative).
CI = confidence interval; CTQCA = computed tomography–based quantitative coronary analysis; other abbreviations as in Table 3.

Technical considerations: for the cardiac computed tomography imaging physician. Based on the method described by Reiber et al. (20), we devised and validated a simplified approach for estimating linear vessel tapering and calculating luminal stenosis severity on CCTA. Our method showed strong correlation to IQCA; the Pearson r-coefficient of 0.82 is similar to that reported by Raff et al. (3) ($r = 0.76$) and higher than that reported by Leber et al. (12) ($r = 0.54$). In the latter study, quantification of CCTA stenosis was based on the luminal diameter ratio of the stenotic site to proximal "healthy" vessel (12). Our method may have achieved higher correlation with IQCA in part by accounting for reference points proximal and distal to the stenosis and by assessing strictly luminal stenosis rather than accounting for positive remodeling. That our quantitative correlation was nearly identical to Raff et al. (3) ($p = 0.94$) despite studying older patients (mean age of 66 vs. 59 years) with higher global coronary calcification (mean coronary calcium score of 752 vs. 326) potentially reflects interim refinements in hardware, software, and CCTA interpretation technique.

We showed that, with current 64-slice CCTA spatial resolution, any increase in CCTA grading was strongly associated with increased IQCA stenosis severity, indicating that a 5-point approach to evaluating coronary stenoses is well within capabilities of contemporary CCTA. We found significantly better quantitative correlation between CCTA and IQCA for relatively noncalcified stenoses, confirming previous work quantifying stenoses from noncalcified plaque using 16-slice CCTA (11,13). Interestingly, multivariable regression analysis did not yield a significant association between ordinal grading accuracy and lesion calcification, suggesting that our readers may have implicitly compensated for calcification-related artifact when grading calcified lesions.

In addition, we demonstrated that quantification of stenosis severity on CCTA did not perform

Table 5. Details of the 10 Coronary Segments for Which Visual CCTA Inspection Differed From IQCA by >1 Grade

	Patient Age (yrs)	Patient Gender	Segment Location	Size (mm)	Lesion Calcification	Agatston Score	Visual CCTA Grade	IQCA Grade	IQCA Result
Under by >1									
Segment 1	79	Male	Proximal LAD	3.1	None	200	2	4	80%
Segment 2	80	Male	D1	3.4	None	362	2	4	95%
Segment 3	44	Male	PLB	1.6	Moderate	932	3	5	100%
Over by >1									
Segment 1	77	Female	Mid-LAD	2.6	Severe	269	3	1	19%
Segment 2	68	Male	Proximal LAD	4.8	Severe	948	3	1	15%
Segment 3	78	Male	Mid-LAD	3.3	Severe	1,467	4	2	41%
Segment 4	71	Male	Proximal LAD	2.8	Mild	303	4	2	46%
Segment 5	66	Male	Mid-LCX	3.5	Severe	5,201	4	2	29%
Segment 6	44	Female	Mid-RCA	5.0	Severe	2,270	4	1	21%
Segment 7	63	Female	Mid-LAD	3.0	Severe	396	5	3	63%

D1 = first diagonal artery; IQCA = invasive coronary angiography–based quantitative coronary analysis; PLB = posterolateral branch artery; other abbreviations as in Table 1.

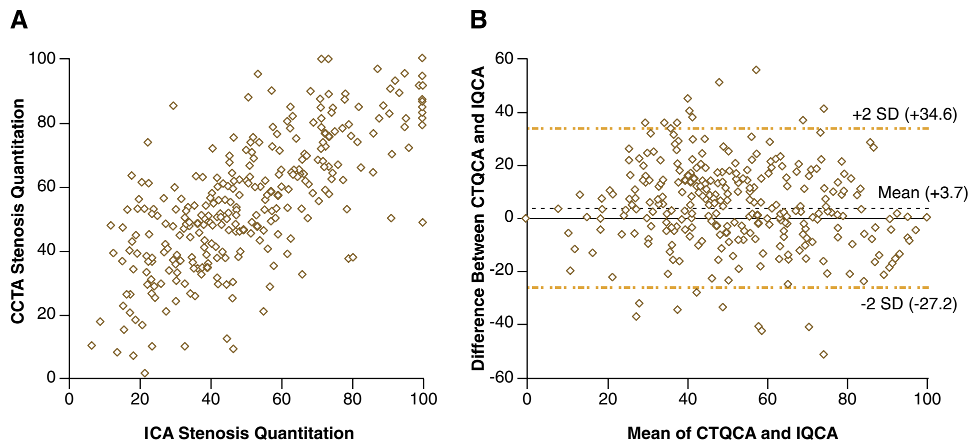

Figure 6. Plots of Correlation and Agreement Between IQCA and CTQCA

Overall Pearson r-coefficient is 0.82, indicating very good correlation (**A**). However, Bland-Altman analysis (**B**) showed CTQCA to have an average bias of +3.70, with 95% of the differences between invasive coronary angiography–based quantitative coronary analysis (IQCA) and CTQCA falling between −27.2 and 34.6, indicating high variability in CTQCA accuracy for individual lesions. SD = standard deviation; other abbreviations as in Figure 4.

better than careful visual inspection when using an ordinal grading system. In fact, severe (>1 grade) discrepancy with IQCA occurred less frequently with visual CCTA inspection. Stenosis quantification by CCTA is currently hampered by wide variability when compared with quantification by IQCA, and, in the hands of an experienced visual reader, routine stenosis quantification on CCTA is unlikely to provide additional information.

Finally, we described 2 findings associated with discrepant ordinal stenosis grading between CCTA and ICA. First, marked overestimation of stenosis grade (by ≥2) on CCTA tended to occur with heavily calcified lesions. In our data, 6 of 7 segments in which marked "overcalling" occurred were severely calcified, consistent with current understanding that lesion calcification can reduce visibility of vessel lumen through creation of artifacts on CCTA (19–21). Second, larger luminal diameter at the stenotic site was associated with CCTA "undercalling." This phenomenon may be related to vasodilation from routine nitroglycerin use during CCTA.

Clinical considerations: for the referring clinician. Perhaps the most important clinical finding from our data is that the degree of stenosis determined by visual CCTA evaluation rarely differed from IQCA by more than 1 grade. This concept can be used to significantly narrow the range of probable IQCA findings given a certain CCTA grade. Importantly, when maximal segmental narrowing by CCTA is ≤49%, IQCA is very unlikely to reveal ≥70% stenosis. When CCTA shows ≥90% stenosis, IQCA of the segment will rarely be <70%. Of note, had a 4-point grading system been employed, with the highest CCTA grade indicating ≥70% stenosis, 30% of such lesions would have been associated with <70% stenosis by IQCA; with the 5-point system, rate of such occurrence was only 2%.

If confirmed in future studies, our findings can be of significant utility when managing patients with chronic coronary artery disease in the contemporary clinical paradigm, which adopts 70% luminal diameter obstruction as angiographic criteria for consideration of revascularization on the strength of several landmark clinical trials (25–28). Under this paradigm, our data show that lesions causing ≤49% narrowing on CCTA are highly unlikely to merit consideration for revascularization. For lesions causing 50% to 69% stenoses on CCTA, which are associated with an approximate 15% rate of ≥70% stenosis by IQCA, additional assessment of myocardial ischemia may significantly impact patient management. Lesions causing ≥70% visual stenosis on CCTA can be expected to meet invasive angiographic criteria for revascularization approximately 50% of the time; whether additional ischemia testing or invasive angiography would be appropriate in these cases needs further study. Lesions causing ≥90% stenosis on CCTA are virtually diagnostic of severe coronary occlusion and suggest that invasive angiography should be considered the most appropriate next step.

Study limitations. Segment selection in this study depended on CCTA identification of coronary disease and does not provide full accuracy assessment of CCTA in detecting intermediate stenoses. Coronary segments <2 mm in diameter were not well represented, limiting applicability of our findings to such segments. Inter- and intraobserver variability assessment was not performed for grading of plaque calcification. Our study patients had higher coronary disease burden compared with previous populations evaluated with CCTA and ICA; however, our findings should still be applicable to a broad population since study design and analyses were strictly segment based. Because image acquisition by ICA was not standardized, optimal views of some coronary segments were not obtained, possibly accentuating differences in stenosis quantification between computed tomography and invasive angiography. Although ≥70% diameter stenosis on ICA was used as criteria for revascularization in recent landmark trials, it is not the sole criterion in clinical practice. In lesions of borderline angiographic significance, invasive functional studies, such as coronary flow reserve measurement, can be performed to obtain more information regarding stenosis severity.

CONCLUSIONS

In summary, we described a systematic 5-grade approach for assessing coronary stenoses on CCTA and, by comparing visual and quantitative CCTA evaluation to ICA, showed that such a multitiered system provides useful clinical information not attainable by a binary approach. At the current state of CCTA technology, experienced readers should consider routine use of a multitiered grading system when assessing and reporting coronary stenosis severity.

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