Features of Disrupted Plaques by Coronary Computed Tomographic Angiography Correlates With Invasively Proven Complex Lesions

Ryan D. Madder, MD; Kavitha M. Chinnaiyan, MD; Anna M. Marandici, MD; James A. Goldstein, MD

**Background**—This study was designed as a “proof-of-concept” to establish whether coronary computed tomographic angiography (CTA) has the capability to identify morphological features of plaque disruption.

**Methods and Results**—In patients with unstable angina undergoing CTA and invasive coronary angiography within 30 days, quantitative CTA analysis was performed on all plaques for percent stenosis, volume, remodeling index, and volume of low-attenuation plaque (<50 Hounsfield units). Plaques with >25% stenosis were evaluated for CTA features of disruption, including ulceration and intraplaque dye penetration. Using invasive coronary angiography complex plaque as the reference standard for disruption, the sensitivity and specificity of ulceration and intraplaque dye penetration by CTA were determined. In 60 patients, 294 plaques were identified by CTA, of which 109 (37%) had features of disruption, including ulceration in 53 (18%) lesions and intraplaque dye penetration in 80 (27%). Compared with nondisrupted lesions, plaques with ulceration or intraplaque dye penetration by CTA were more voluminous (313 ± 356 mm$^3$ versus 118 ± 93 mm$^3$, $P<0.0001$), more often positively remodeled (94.5% versus 44.3%, $P<0.0001$), contained more low-attenuation plaque (99 ± 161 mm$^3$ versus 19 ± 18 mm$^3$, $P<0.0001$), and were more often complex by ICA (57.8% versus 8.1%, $P<0.0001$). CTA features of disruption demonstrated modest to good sensitivity (53% to 81%) and good specificity (82% to 95%) for complex plaque by invasive coronary angiography.

**Conclusions**—In this highly selected group of patients with unstable angina, CTA can delineate features of plaque disruption, including ulceration and intraplaque dye penetration, which are specific markers of invasively identified complex plaque. Further studies are needed to confirm the generalizability of the results and to explore the clinical and prognostic implications of these findings. (Circ Cardiovasc Imaging. 2011;4:105-113.)

**Key Words:** complex plaque ▪ coronary CT angiography ▪ acute coronary syndrome

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Plaque disruption with superimposed thrombus formation is the proximate cause of acute coronary syndromes (ACS). Invasive coronary imaging is the gold standard for detection of disrupted plaques, the angiographic hallmark a “complex” lesion characterized by “Ambrose criteria” including haziness, ulceration, intraplaque dye penetration and intraluminal filling defects. These angiographic features correlate with plaque rupture and thrombosis by direct imaging with intravascular ultrasound (IVUS) and at pathological examination.

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Coronary computed tomographic angiography (CTA) can accurately detect the presence of coronary atherosclerosis and assess its impact on luminal narrowing. CTA also has plaque characterization capabilities. Previous CTA studies demonstrate that ACS patients typically harbor lesions that are low attenuation and positively remodeled; however, there are only scant data regarding the ability of CTA to delineate features of frank plaque disruption. Given the utilization of CTA for the evaluation of patients with acute chest pain, identifying features indicative of complex ruptured plaque has considerable clinical implications. This study was designed as a “proof-of-concept” to establish whether CTA has the capability to identify morphological features of plaque disruption and to validate these findings using invasive coronary angiography (ICA) as the reference standard.

**Methods**

**Study Population**

From an existing data base of patients undergoing CTA at a single institution, we retrospectively identified those who underwent CTA and subsequent ICA within 30 days. Patients were included in this study if (1) CTA was performed for the evaluation of unstable...
angina, defined according to American College of Cardiology/American Heart Association guidelines as either rest angina, new-onset angina, or increasing angina26; (2) ICA was performed for the clinical evaluation of coronary artery disease ≥30 days after the index CTA; and (3) there was no history of prior coronary revascularization. Patients were further classified according to temporal presentation as either acute chest pain presenting to the emergency center with acute chest pain, certain "low-risk" criteria had to be met to undergo CTA, including a "nonischemic" ECG, normal cardiac enzymes, and no history of coronary artery disease. Patients having inadequate CTA image quality, including those with ≥1 uninterpretable segment in a major epicardial coronary artery, and/or those with a history of revascularization or chronic total coronary occlusion(s) were excluded from the analysis.

CTA Scanning Techniques
In patients undergoing CTA before July 1, 2006, imaging was performed on a 64-slice scanner (Sensation 64, Siemens Medical Systems, Forchheim, Germany), and thereafter on a dual-source system (Somatom Definition, Siemens Healthcare, Forchheim, Germany). β-Blockers and sublingual nitroglycerin (0.4 mg) were administered according to standard institutional protocols. Typical scan parameters included a tube voltage of 100 to 120 kV, tube current of 425 mAs/rotation, gantry rotation time of 0.330 seconds, pitch of 0.2 to 0.43 (adapted to heart rate), and ECG current modulation with full current between 40 and 70% of the cardiac cycle. Using a medium soft convolution kernel (B36), 0.75-mm multiphase axial reconstructions were performed at 0% to 90% of the R-R interval. Additional reconstruction windows were used as necessary to minimize motion artifacts.

CTA Analysis
We performed an analysis of all plaques seen by CTA that were >25% diameter stenosis by quantitative analysis. CTA interpretation was performed by 2 independent observers blinded to the clinical presentation and invasive angiographic results. Images were analyzed on a 3-dimensional workstation (Aquarius, TeraRecon, San Mateo, CA). Quantitative lesion analysis was performed according to established methods17–20,21,22 and using software that facilitates calculation of lesion geometry and density (SUREPlaque, Vital Images, Minnetonka, MN). Parameters assessed included (1) plaque volume, obtained by the aforementioned automated software system after manually marking the proximal and distal boundaries of the plaque along the long axis of the vessel; lesions spanning more than 1 coronary segment were analyzed as 2 separate plaques on a per-segment basis; (2) remodeling index, calculated as the ratio of R1/R2 (R1 being the area of the vessel at the level of the lesion and R2 being the mean area of the nearest normal proximal and distal reference segments); plaques with a remodeling index ≥1.10 were considered positively-remodeled; (3) plaque attenuation, using an automated software system that analyzes each pixel within the entire lesion; “low-attenuation plaque” (LAP) was defined as plaque with density <50 Hounsfield units. Rather than reporting plaque attenuation for a limited region of interest,21,22,27 we report plaque density as both the total volume and proportionate volume of LAP within the entire plaque. This approach was taken to fully represent the character of plaque contents and to quantify the volume of LAP. All plaques were also analyzed for the presence or absence of calcification.

Plaques were qualitatively assessed for features indicative of plaque disruption including (1) ulceration, defined as contrast extending beyond the vessel lumen but contiguous with it; or (2) intraplaque dye penetration, defined as a contrast pool within the plaque not contiguous with an overlying ulceration. A plaque was considered to be disrupted by CTA if either of these features was present. Designations of disrupted features by the 2 independent readers were compared to determine interobserver variability. When disagreement existed, a final decision was reached by consensus.

For those patients having a coronary artery calcium score performed immediately before CTA, calcium scores were measured in Agatston units using the SYNCGo software (Siemens Medical Systems). We report the frequency of plaques having ulceration and intraplaque dye penetration within vessels having a calcium score of zero.

Invasive Coronary Angiography
Invasive angiograms were performed according to standard methods and images were stored digitally. Angiograms were evaluated by 2 independent observers blinded to each other as well as to clinical findings and CTA results. Angiographic plaque morphology was analyzed according to established invasive criteria.4–6 Lesions were considered “complex” if they exhibited either (1) ulceration, defined as the presence of contrast beyond the vessel lumen; (2) intraluminal filling defect consistent with thrombus; or (3) a combination of haziness, irregular margins, or fissuring, defined as overhanging edges. All other lesions not fulfilling these criteria were considered “noncomplex.” When disagreement existed between the two observers in regard to designation of a plaque as complex, a final decision was made through consensus. ICA was also analyzed to determine “culprit” status of all plaques identified by CTA. Plaques were deemed culprit lesions if they were labeled as ≥70% stenosis by the physician performing the catheterization and which underwent revascularization.

Statistical Analysis
To determine whether CTA features of disruption were predictive of complex plaque by invasive angiography, all plaques by CTA were compared with ICA lesions. Using ICA complex plaque as the reference standard, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of CTA features of plaque disruption were determined. PPV and NPV were calculated based on a prevalence of 37%, 18%, and 27% for any feature of disruption, ulceration, and intraplaque dye penetration by CTA, respectively.

A comparison of the morphological characteristics of plaques with and without features of disruption by CTA was performed using a repeated measures analysis. To perform a repeated-measures analysis adjusting for plaques within the same patient, the data needed to be normally distributed. Various transformations were made on nonnormally distributed variables and the analysis was completed on the best-fitted transformation. For categorical variables, repeated-measures analysis was performed using generalized estimating equations with an exchangeable correlation model. For continuous variables, repeated-measures analysis was performed using mixed effects models with plaque type as a fixed effect.

Categorical variables are reported as counts and percentage of frequencies. Continuous variables are shown as means±standard deviation, and, where appropriate, median±standard deviation was used. To describe the reproducibility of quantitatively determined CTA morphological features, the correlation coefficient, absolute and relative coefficients of variability, and Bland-Altman plots were generated. To describe the reproducibility of qualitative CTA features, plaque disruption, agreement rates and k values were calculated. All analyses used The SAS System for Windows version 9.2 (Cary, NC).

Results
Clinical Characteristics
Between May 2004 and January 2008, we identified 529 patients who underwent CTA followed by ICA within 30 days, of whom 206 underwent CTA for symptoms consistent with unstable angina. Patients were excluded for inadequate CTA image quality, prior revascularization, and chronic total occlusions (Figure 1). The present analysis was therefore performed in the remaining cohort of 60 patients. Demographics and risk factors for the study population are dem-
The indication for CTA was acute chest pain in 42 (70.0%) patients who presented to the emergency room, whereas in 18 (30.0%) others, CTA was performed on an outpatient basis to evaluate recent-onset chest pain. All patients underwent ICA within 30 days of CTA (mean, 7.1+/\textpm/8.6 days): 27 (45.0%) within 48 hours, 42 (70.0%) within 7 days, 46 (76.7%) within 14 days, and the remainder (23.3%) between 2 weeks to 1 month. Coronary artery calcium scoring was performed immediately before CTA in 43 (71.7%) patients (calcium score, 316+/\textpm/407 Agatston units).

Prevalence of CTA Features of Plaque Disruption
A total of 294 lesions causing >25% diameter stenosis were identified by CTA. CTA identified at least 1 plaque with evidence of disruption in 53 (88.3%) patients and multiple disrupted plaques in 35 (58.3%). Among all lesions, features of disruption were evident in 109 (37.1%) plaques, including ulceration in 53 (18.0%) and intraplaque dye penetration in 80 (27.2%). Of those plaques having CTA features of disruption, 15 (13.8%) occurred in a vessel with a calcium score of zero (Figure 2). The interobserver agreement for designation of a plaque as disrupted by CTA was 95%. The agreement rate for the presence of ulceration was 96% (κ=0.88; 95% confidence interval, 0.80 to 0.96) and for intraplaque dye penetration was 96% (κ=0.91; 95% confidence interval, 0.85 to 0.97). Of those lesions for which disagreement existed regarding CTA features of disruption, 71.4% were calcified.

Table 1. Baseline Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(n=60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>59.6+/\textpm/11.2</td>
</tr>
<tr>
<td>Male</td>
<td>36 (60)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>43 (72)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>45 (75)</td>
</tr>
<tr>
<td>Smoking</td>
<td>19 (32)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10 (17)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>60 (100)</td>
</tr>
<tr>
<td>Acute chest pain</td>
<td>42 (70)</td>
</tr>
<tr>
<td>Recent-onset chest pain</td>
<td>18 (30)</td>
</tr>
<tr>
<td>Time between CTA and ICA, d</td>
<td>7.1+/\textpm/8.6</td>
</tr>
<tr>
<td>ICA within 48 h of CTA</td>
<td>27 (45)</td>
</tr>
<tr>
<td>ICA within 7 d of CTA</td>
<td>42 (70)</td>
</tr>
<tr>
<td>ICA within 14 d of CTA</td>
<td>46 (77)</td>
</tr>
<tr>
<td>ICA 2 wk to 30 d after CTA</td>
<td>14 (23)</td>
</tr>
</tbody>
</table>

All values are No. (%), except for “Age” and “Time between CTA and ICA,” which are mean+/\textpm/standard deviation.

Table 2. Reproducibility of Plaque Volume, LAP Volume, Remodeling Index, and Percent Stenosis by Quantitative CTA Analysis

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>Absolute CoV</th>
<th>Relative CoV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plaque volume</td>
<td>0.99</td>
<td>1.79</td>
<td>17.3</td>
</tr>
<tr>
<td>LAP volume</td>
<td>0.98</td>
<td>1.97</td>
<td>-8.12</td>
</tr>
<tr>
<td>Remodeling index</td>
<td>0.97</td>
<td>1.29</td>
<td>-13.8</td>
</tr>
<tr>
<td>% Stenosis</td>
<td>0.87</td>
<td>0.93</td>
<td>4.4</td>
</tr>
</tbody>
</table>

CoV indicates coefficient of variability; R, correlation coefficient.
Figure 3. Compared with nondisrupted lesions, plaques having CTA features of disruption were significantly more voluminous (313 ± 356 mm³ versus 118 ± 93 mm³, P < 0.0001) and contained a greater volume of LAP (99 ± 161 mm³ versus 19 ± 18 mm³, P < 0.0001) and a greater proportionate volume of LAP (30 ± 16% versus 16 ± 9%, P < 0.0001) (Table 3). With respect to arterial remodeling, 94.5% of plaques with ulceration or intraplaque dye penetration by CTA were positively remodeled compared with 44.3% of CTA nondisrupted plaques (P < 0.0001). Similarly, the degree of positive remodeling was greater among plaques having CTA features of disruption (1.5 ± 0.4 versus 1.1 ± 0.3, P < 0.0001). Plaques with evidence of disruption by CTA were less often calcified (48.6% versus 76.2%, P = 0.0006).

CTA Features of Disruption and Complex Plaque by Invasive Angiography

Of the 294 lesions analyzed by CTA, 78 (26.5%) plaques were complex by ICA and 216 (73.5%) were noncomplex. ICA complex plaques were characterized by ulceration in 68 (87.2%) lesions, by a filling defect consistent with thrombus in 7 (9.0%) lesions, and concomitant ulceration and filling defect in 4 (5.1%) lesions. Only 7 (9.0%) lesions were

Table 3. Morphologic Characteristics of Plaques With and Without CTA Features of Plaque Disruption

<table>
<thead>
<tr>
<th>Feature</th>
<th>Disrupted (n=109)</th>
<th>Nondisrupted (n=185)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume, mm³</td>
<td>313 ± 356</td>
<td>118 ± 93</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LAP, %</td>
<td>30 ± 16</td>
<td>16 ± 9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Positively remodeled</td>
<td>103 (94.5)</td>
<td>82 (44.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Remodeling index</td>
<td>1.5 ± 0.4</td>
<td>1.1 ± 0.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calcification</td>
<td>53 (48.6)</td>
<td>141 (76.2)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Complex by ICA</td>
<td>63 (57.8)</td>
<td>15 (8.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Culprit by ICA</td>
<td>55 (50.5)</td>
<td>37 (20.0)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

For volume, LAP, and remodeling index, P values were generated using mixed-effects models with plaque type as a fixed effect. For all other variables, P values were obtained using generalized estimating equations with an exchangeable correlation model.
deemed complex by ICA according to a combination of haziness, irregularity, and fissuring. At least 1 ICA complex plaque was found in 46 (76.7%) patients, and multiple complex lesions were identified in 22 (36.7%). Compared with nondisrupted lesions, plaques having CTA features of disruption were more likely to be complex by ICA (57.8% versus 8.1%, \( P < 0.0001 \)). Ulceration and intraplaque dye penetration by CTA were predictive of ICA complex plaque in 79.2% and 51.3% of lesions, respectively (Figure 4 and Figure 5). The presence of both ulceration and intraplaque dye penetration within the same plaque on CTA was predictive of ICA complex plaque in 84.0% of cases. Using plaque complexity by ICA as the reference standard, the sensitivity, specificity, PPV, and NPV for CTA features of plaque disruption are demonstrated in Table 4.

Among all complex lesions by ICA, 80.8% contained features of disruption by CTA. Of the 15 ICA complex lesions in which CTA did not demonstrate ulceration or intraplaque dye penetration, 13 (86.7%) were calcified plaques. In all 7 cases in which a filling defect was identified by invasive angiography, CTA identified a lesion at the corresponding site that contained either ulceration or intraplaque dye penetration. Of the 46 plaques with CTA evidence of disruption that were noncomplex by ICA, 34 (73.9%) had intraplaque dye penetration as the sole feature of disruption.

CTA Features of Disruption and Culprit Status by Invasive Angiography
A total of 92 culprit lesions were identified by ICA, of which 56 (60.9%) met criteria for ICA complex plaques and 55 had
features of disruption by CTA (59.8%), including ulceration in 32 (34.8%) and intraplaque dye penetration in 39 (42.4%). Compared with plaques without CTA features of disruption, plaques with ulceration or intraplaque dye penetration on CTA were more likely culprits at the time of ICA (50.5% versus 20.0%, \( P < 0.0001 \)).

Discussion

The present study demonstrates that coronary CTA has the ability to delineate morphological features of complex plaques in a highly selected group of patients with acute unstable or new-onset angina. These observations are consistent with prior CTA plaque characterization studies demonstrating that lesions in ACS patients are typically low-attenuation, eccentric, and positively remodeled.21,22,28 The present findings extend those of previous reports, demonstrating that CTA can identify features indicative of frank plaque disruption, including ulceration and intraplaque dye penetration on CTA were more likely culprits at the time of ICA (50.5% versus 20.0%, \( P < 0.0001 \)).

A critical step in the process of plaque instability is disruption of the protective fibrous cap, which once breached results in intracoronary thrombus formation.29,30 Plaque rupture is evident by invasive angiography as a “complex” lesion, characterized by luminal irregularity, ulceration, haziness and intraplaque contrast penetration.4–6 By direct imaging with IVUS, unstable plaques are bulky, positively remodeled, low-attenuation, and show signs of disruption, including ulceration and luminal clot.31–33 Similar to these invasive modalities, we demonstrate that in addition to characterizing features of vulnerable plaques, CTA can identify features of plaque disruption among individuals with high CT image quality.

We found ulceration, which marks a loss in the integrity of the plaque-lumen interface, to be a highly predictive CTA marker of invasively identified complex plaque, with a specificity of 95%. Similarly, CTA-documented intraplaque dye penetration was also predictive of complex plaque by ICA. Although we can only speculate as to its mechanism, intraplaque dye penetration by ICA is typically a result of breach of the fibrous cap allowing leakage of intraluminal contrast into intramural plaque. Interestingly, there were some lesions that appeared to be disrupted by CTA but were labeled noncomplex by ICA. In the majority of such lesions, intraplaque dye penetration was the sole CTA feature of disruption. This is consistent with the concept that even in the absence of fibrous cap disruption, other pathophysiologic mechanisms may lead to intraplaque hemorrhage and thus to intraplaque dye penetration.34–36 Up to one-third of cases of acute coronary syndrome may result from plaque erosion with resultant intraplaque hemorrhage,34,35 conditions in which intraluminal contrast dye might be expected to penetrate and accumulate within the plaque and manifest as intraplaque dye penetration by CTA. Intraplaque hemorrhage may also result from leaky or ruptured vasa vasorum,36 a scenario in which intraplaque dye penetration might occur from the adventitial surface inward, despite an intact fibrous cap. Further studies using invasive direct coronary imaging techniques will be necessary to establish whether the present CTA findings reflect such mechanisms.

Although CTA features of disruption were found to be specific markers of complex plaque by ICA, we found features of disruption to have modest to good sensitivity. The lower sensitivity is likely attributable to the lower spatial resolution of CTA compared with ICA. Further, ulceration and intraplaque dye penetration may have been missed on CTA due to the presence of plaque calcification, as suggested by our observation that the majority of cases in which CTA

| Table 4. Diagnostic Performance of CTA Features of Plaque Disruption |
|----------------|----------------|----------------|----------------|----------------|
|                | Sensitivity, % | Specificity, % | PPV, %          | NPV, %          |
|                | (95% CI)       | (95% CI)       | (95% CI)        | (95% CI)        |
| Ulceration or IDP, n=109 | 80.8 (70.3–88.8) | 78.7 (72.6–84.0) | 57.8 (48.0–67.2) | 91.9 (87.0–95.4) |
| Ulceration, n=53 | 53.8 (42.2–65.2) | 94.9 (91.1–97.4) | 79.2 (65.9–89.2) | 85.1 (79.9–89.3) |
| IDP, n=80      | 52.6 (40.9–64.0) | 81.9 (76.2–86.8) | 51.3 (39.8–62.6) | 82.7 (77.0–87.5) |
| Ulceration and IDP, n=25 | 26.9 (17.5–38.2) | 98.1 (95.3–99.5) | 84.0 (63.9–95.5) | 78.8 (73.4–83.5) |

CI indicates confidence interval; IDP, intraplaque dye penetration.
failed to identify complex lesions (false-negatives) occurred in extensively calcified plaques.

We also observed CTA lesions that were bulky, positively remodeled, and low attenuation but lacked any signs of disruption by CTA or ICA. Recent observations suggest that such lesions may represent vulnerable plaques at greater risk for rupture. Furthermore, invasive direct coronary imaging studies suggest such bulky low attenuation lesions may be composed of lipid necrotic core. Interestingly, our analysis showed plaques with CTA features of disruption to be significantly more voluminous, more positively remodeled, and to contain more low attenuation material than similar appearing but nondisrupted plaques. It is beyond the scope of the present results to draw any firm conclusions regarding the pathophysiologic implications of these observed differences in architectural structure; we can only speculate whether incremental volume of low attenuation plaque represents expansion of lipid necrotic core that reflects transition from vulnerable to ruptured plaque. Future studies are needed to explore the clinical and prognostic implications of these CTA findings.

Clinical Implications
Coronary atherosclerosis is a chronic indolent disease punctuated by flares of plaque instability, this process may present clinically as ACS or recent-onset chest pain. Although 1 or more discrete lesions may rupture and emerge as the culprit underlying acute ischemia, such patients typically harbor multiple unstable plaques, as well as other “vulnerable” plaques at risk for rupture. Invasive imaging techniques using angiography and IVUS facilitate detection and characterization of the spectrum of unstable, stable, and potentially “vulnerable” plaques. Similar to these invasive modalities, we demonstrate that in addition to characterizing features of vulnerable plaques, CTA can identify features of plaque disruption among individuals with high CT image quality. Given the utilization of CTA for the evaluation of patients with acute chest pain, identifying features indicative of complex ruptured plaque may have considerable clinical implications. Furthermore, recent observations suggest that plaque characterization by CTA can identify patients at risk for clinical events as well as specific “vulnerable” plaque features of lesions that underlie such events. The present findings are consistent with and support this concept; however, future studies will be necessary to further establish whether CTA can identify “vulnerable” plaques.

Limitations
It is important to emphasize limitations pertinent to the methods of this study. First, this report constitutes a small retrospective study undertaken as a “proof-of-concept” to test the ability of CTA to identify morphological features of plaque disruption. The present study is based on a highly selected patient population, with high image quality (ie, those with inadequate CTA image quality were excluded). Therefore, appropriate caution must be used when extrapolating the diagnostic accuracy and reproducibility reported in the present study to an unselected population undergoing CTA.

Importantly, ulceration and intraplaque dye penetration were the only CTA features of disruption evaluated in this study. Whether other characteristics suggestive of plaque disruption, such as intraluminal thrombus formation, can be accurately detected by CTA requires further study. Second, although the majority of patients underwent CTA for assessment of acute chest pain as part of the emergency center evaluation of ACS, less than one-third of cases were referred for evaluation of recent-onset symptoms (within the prior 30 days). That such patients reflect the spectrum of unstable coronary disease is supported by the finding that all had recent onset symptoms and the majority had at least one complex plaque by invasive angiography. These findings are consistent with the concept that the process of plaque disruption results in a spectrum of temporal presentations which may be acute, crescendo, new onset “stable angina” or may even be clinically “silent.” That we did not observe 100% concordance in complexity between invasive angiography and CTA may be attributable to the lower spatial resolution of CTA and possibly by calcification (evident in nearly all invasively identified complex lesions judged by CTA to be noncomplex). It is important to emphasize that CTA did not delineate intraluminal thrombus in any cases. This may be attributable to the lower resolution capabilities of CTA as well as the fact that ICA and CTA were performed at different times and under different pharmacological regimens, which might influence the presence of coronary thrombus. Regardless, in all 7 cases in which a filling defect consistent with thrombus was identified by ICA, CTA identified a lesion at the corresponding site that exhibited either ulceration or intraplaque dye penetration. Although previous studies have compared and validated IVUS architectural features to CTA findings in nondisrupted plaques, IVUS data were not available in the patients in the present study. In addition, the present data does not provide insight regarding whether various scanner types (64-slice versus dual-source) might influence image interpretation and plaque characterization. Finally, we observed only 50% of plaques having CTA features of disruption to be culprits at the time of invasive angiography. A further limitation is the delay between invasive angiography and cardiac CT as relevant changes in plaque morphology may have occurred during this time. According to the design of this study, all culprit lesions were revascularized; defining the natural history of nonculprit plaques having CTA features of disruption and their clinical and prognostic implications requires further investigation.

Conclusions
In patients with unstable angina, CTA can delineate features of plaque disruption, including ulceration and intraplaque dye penetration, which are specific markers of invasively identified complex plaque. Future studies are needed to explore the clinical and prognostic implications of these findings.

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References
CLINICAL PERSPECTIVE

Coronary computed tomographic angiography (CTA) can accurately detect the presence of coronary atherosclerosis and assess its impact on luminal narrowing. Although CTA also has plaque characterization capabilities, there are only scant data regarding the ability of CTA to delineate features of frank plaque disruption. Given the use of CTA for the evaluation of patients with acute chest pain, identifying features indicative of complex ruptured plaque has considerable clinical implications. This study was designed as a “proof-of-concept” to establish whether CTA has the capability to identify morphologic features of plaque disruption and to validate these findings using invasive coronary angiography as the reference standard. In a highly selected group of patients with unstable angina, this study demonstrates that CTA can delineate features of plaque disruption, including ulceration and intraplaque dye penetration, which were found to be specific markers of invasively identified complex plaque. Further studies are needed to confirm the generalizability of the results and to explore the clinical and prognostic implications of these findings.
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