Atherosclerotic plaque characterization by CT angiography for identification of high-risk coronary artery lesions: a comparison to optical coherence tomography

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Aims
Adverse plaque characteristics (APCs) by coronary computed tomography (CT) angiography (CTA) are associated with myocardial ischaemia and future acute coronary syndromes. The overall objective was to determine whether APCs on non-invasive CTA are associated with vulnerable plaque features by invasive optical coherence tomography (OCT).

Methods and results
Sixty-eight coronary plaques in 45 patients were evaluated by CTA and OCT. APCs by CTA were: positive remodelling (PR), remodelling index \( \geq 1.10 \); low attenuation plaque (LAP), any intraplaque voxel, \( \leq 30 \) Hounsfield units; spotty calcification (SC), intraplaque calcification \( \leq 3 \) mm; and ‘napkin-ring’ sign, low intraplaque attenuation surrounded by a higher attenuation rim. OCT evaluated plaques for thin-cap fibroatheroma (TCFA, \( \leq 65 \) \( \mu \text{m} \), lipid arch \( > 90^\circ \)) and macrophage infiltration. Increasing plaque vulnerability was graded by OCT as having no TCFA, TCFA without macrophage infiltration, and TCFA with macrophage infiltration. OCT lesions included those with no TCFA (\( n = 44 \)), TCFA without macrophage infiltration (\( n = 7 \)), and TCFA with macrophage infiltration (\( n = 17 \)). Increasing plaque vulnerability grade by OCT was associated with higher diameter stenosis (43.6 vs. 40.7 vs. 57.3%, \( P = 0.01 \)), and greater prevalence of PR (11 vs. 43 vs. 71%, \( P < 0.001 \)), LAP (11 vs. 29 vs. 59%, \( P = 0.001 \)), and SC (2 vs. 29 vs. 18%, \( P = 0.02 \)), but not for napkin-ring sign (\( P = 0.18 \)). In multivariable analysis, PR (odds ratio (OR) 16.9, 95% confidence interval (CI) 3.9–73.3, \( P < 0.001 \)) and LAP (OR 11.2, 95% CI 2.8–44.3, \( P = 0.001 \)) predicted TCFA with macrophage infiltration, whereas SC and napkin-ring sign did not.

Conclusion
Plaques demonstrating PR and LAP by CTA are associated with TCFA with macrophage infiltration by OCT.

Keywords
Thin-cap fibroatheroma • Plaque • Computed tomography angiography • Optical coherence tomography

Introduction
Histopathological studies on subjects who have experienced sudden cardiac death suggest the pathogenesis of the majority of acute coronary events to be related to occlusive thrombus formation after disruption of a thin-cap fibroatheroma (TCFA) overlying a large necrotic lipid core.¹² These ‘vulnerable plaques’ are also often characterized by both intraplaque and systemic inflammation that are critical to this process.³ Extensive ex vivo and in vitro evidence link local macrophage infiltration with vulnerable plaque characteristics,¹²⁴ with

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histopathological evidence of intense macrophage infiltration localized at the site of the thin fibrous cap.5,6

Optical coherence tomography (OCT) is an intravascular imaging method that enables coronary artery plaque characterization by the highest achievable in vivo spatial resolution at 10–20 μm, a resolution of ~10-fold higher than that of intravascular ultrasound (IVUS).7,8 A prior study has demonstrated OCT to be a reliable and accurate for characterization of high-risk plaque features, including thickness of fibrous cap and intraplaque lipid arcs.9 Macrophages can also be visualized by OCT and are seen as signal-rich, distinct, or confluent punctate regions that exceed the intensity of background speckle noise.8,10

Coronary computed tomography (CT) angiography (CTA) is a non-invasive test that enables direct visualization of coronary artery disease (CAD) and correlates favourably with invasive angiography for measures of stenosis severity.11 CTA also permits assessment of coronary atherosclerotic plaque morphology and composition in general concordance with intravascular ultrasonography.12,13 Coronary plaque characteristics visualized by CTA—including positive remodelling (PR), low attenuation plaque (LAP), spotty calcification (SC), and a ‘napkin-ring’ sign—have been associated with myocardial ischaemia and markers of future acute coronary syndromes (ACS).14,15 Whether these adverse plaque characteristics (APCs) are associated with high-risk plaque features by OCT has not been adequately examined to date. Furthermore, it is difficult to routinely perform intravascular assessment of coronary plaque in a large number of patients. Thus, the overall objective was to determine whether APCs on non-invasive CTA are associated with high-risk plaque features when compared with an invasive OCT reference standard.

### Methods

Consecutive patients who underwent clinically indicated CTA and were observed to have at least one CTA-determined ≥50% stenosis in the proximal or mid portion of a major epicardial coronary artery were referred for invasive coronary angiography (ICA). At ICA, OCT was prospectively performed in CTA-determined lesions (between 25 and 90% stenosis) for research purpose. Exclusion criteria included: chronic kidney disease, left main CAD; vessel tortuosity ≥90°; and ST-segment elevation myocardial infarction. Patients presenting with unstable angina or non-ST-segment elevation myocardial infarction were eligible for study entry. Study patients underwent OCT within 3 months of CTA without an intervening coronary event and change in medications. In 45 patients, 68 lesions were evaluated by CTA and OCT. Baseline characteristics of the study population are listed in Table 1. The mean interval between CTA and OCT was 31 ± 23 days.

Prior to CTA, we prospectively ascertained the presence of CAD risk factors. Hypertension was defined as blood pressure ≥140/90 mmHg or use of anti-hypertensive drugs. Hyperlipidaemia was defined as a past or present history of low-density lipoprotein-cholesterol level ≥140 mg/dL, or use of cholesterol-lowering medications. Diabetes mellitus was defined as a fasting blood glucose >126 mg/dL or haemoglobin A1C ≥6.5%, or use of anti-diabetic medications. The present study was performed at two centres (Kobe University Graduate School of Medicine and Kobe Circulation Clinic). The Institutional Review Board of the study centres approved the study and all patients provided written informed consent.

CTA was performed using 128-detector row CT (Somatom Definition AS+™, Forchheim, Germany) or 320-detector row CT (Toshiba Aquilion One™, Otawara, Japan) in accordance with societal guidelines.16 An intravenous bolus (30–90 mL) of contrast agent (Omnipaque™ 350 mg/dL, Daiichi-Sankyo, Tokyo, Japan or Iomeron™ 350 mg/dL, Eizai, Tokyo, Japan) was injected at a flow rate of 0.07 mL/kg/s. The scan parameters included 64 × 0.5 mm collimation, tube current time product of 300–400 ms per rotation, tube voltage 100 or 120 kVp for 320-detector row CT; 64 × 0.6 mm collimation, tube current time product of 300 ms per rotation, tube voltage 100 or 120 kVp for 128-detector row CT. Scans were performed using ECG-based tube current modulation whenever possible, or sequential image acquisition. Transaxial images were reconstructed with 0.75–0.5-mm slice thickness and 0.3–0.5-mm slice increment using a medium-smooth convolution kernel. An estimated effective radiation dose for CTA ranged from 2 to 10 mSv.17

Each CTA-identified plaque was quantified manually by an experienced imager (initial experience for Level 3 by the Society of Cardiovascular Computed Tomography) blinded to OCT results in accordance with societal guidelines.18 To ensure that CTA-identified plaques were those identical to OCT, an independent cardiologist identified anatomic landmarks (e.g. side branches and bifurcations) to select the proximal and distal fiduciary points for CTA and OCT analysis. After identification of plaques referenced to fiduciary markers, contiguous cross-sectional reconstructions were rendered along a vessel centreline using a slice thickness of 1.0 mm and an increment of 0.5 mm on a dedicated 3D workstation (AW Advantage; GE Healthcare, Waukesha, WI, USA).19

In order to enable optimal and consistent detection of plaque and outer vessel boundaries, window width was set at 155% of the mean intensity within the lumen and window level was set at 65% of the mean intensity for each lesion, as we have previously described.20 Diameter stenosis (%) and area stenosis (%) were calculated using proximal and distal reference segments, respectively, which were selected to be adjacent to the maximal stenosis in which there was minimal or no plaque. Minimum luminal diameter [MLD (mm)] and minimum luminal area [MLA (mm²)] were measured from the long-axis and short-axis views of double-oblique reconstructions, respectively, at the site of the

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline patient characteristics</th>
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<tr>
<td>Age (years)</td>
<td>68 ± 10</td>
</tr>
<tr>
<td>Male</td>
<td>36 (80)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.7 ± 4.2</td>
</tr>
</tbody>
</table>

### Risk factors

- Hypertension: 33 (73)
- Diabetes mellitus: 17 (38)
- Dyslipidaemia: 33 (73)
- Current smoker: 8 (18)
- Stable angina pectoris: 32 (78)
- Acute coronary syndrome: 8 (18)
- Prior percutaneous coronary intervention: 18 (40)
- Statin therapy: 28 (62)
- Total cholesterol (mg/dL): 181.1 ± 45.2
- Low-density lipoprotein-cholesterol (mg/dL): 105.3 ± 41.7
- High-density lipoprotein-cholesterol (mg/dL): 50.0 ± 11.4
- Triglyceride (mg/dL): 140.8 ± 69.1
- Fasting blood glucose (mg/dL): 110.0 ± 24.9
- Haemoglobin A1C (%): 6.1 ± 0.8

Values are mean ± SD or n (%).
maximum stenosis. We evaluated the CT attenuation values in each plaque lesions on cross-sectional images. For each plaque, greater than or equal to three rounded regions of interest (ROIs) of 0.5 mm² were placed within the target lesions, and the lowest CT density value (Hounsfield units, HU) was recorded as a CT attenuation value. For plaques with calcified components, ROIs were placed within non-calcified regions.

The outer vessel contour was defined as the visualized border, with lumen areas traced in each cross-section. A remodelling index was defined as the ratio of the outer vessel area at the most stenotic segment divided by the outer vessel area at a proximal reference defined as the ratio of the outer vessel area at the most stenotic calcified components, ROIs were placed within non-calcified regions.

Field units, HU) was recorded as a CT attenuation value. For plaques with placed within the target lesions, and the lowest CT density value (Hounsfield attenuation in the centre of a plaque close to the lumen circumscribed by a rim area with higher attenuation.15

Images were acquired using a commercially available frequency-domain OCT system (C7-XR OCT Intravascular Imaging System, St Jude Medical, St Paul, MN, USA), and performed in a standard fashion.26 In brief, a 2.7-Fr OCT imaging catheter (Dragonfly, LightLab Imaging, Inc.) was advanced distal to the lesion, with automatic pullback initiated concordantly with blood clearance. Each coronary vessel was imaged with automated pullback at 15 mm/s, and OCT data were recorded on a CD-ROM for off-line analysis.

A signal-rich homogenous lesion overlying lipid content was diagnosed as a fibrous cap.7,24,25 The thinnest part of the fibrous cap was measured as a function of plaque vulnerability grade by OCT (0.85 to 1.16, P = 0.01). Prevalence of OCT plaque features was evaluated by the χ² test for trend. Inter- and intraobserver variability for OCT-derived macrophage detection was assessed by the kappa test. Uni- and multivariable logistic regression analyses were performed to evaluate the relationships between CT parameters and OCT plaque features. To examine discrimination, area under the receiver operating characteristic (AUC) curves were constructed and compared for different OCT parameters.24 Associations and differences with P-values of < 0.05 were considered significant. Statistical analyses were performed using the STATA software (version 11, StataCorp LP, College Station, TX, USA).

## Results

By OCT, lesions were: those without TCFA (n = 44), TCFA without macrophage infiltration (n = 7), and TCFA with macrophage infiltration (n = 17; Table 2). Increasing OCT plaque vulnerability was associated with higher CTA % diameter stenosis (43.6 vs. 40.7 vs. 57.3%, P = 0.01), but not for MLA. Arterial remodelling indices increased as a function of plaque vulnerability grade by OCT (0.85 vs. 1.05 vs. 1.16, P < 0.0001). CT attenuation values decreased across lesions with no TCFA, TCFA without macrophages, and

<table>
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<tr>
<th>Table 2</th>
<th>Comparison of OCT and CT parameters among three groups</th>
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<tr>
<td></td>
<td>Non-TCFA (n = 44)</td>
</tr>
<tr>
<td>CT parameters</td>
<td></td>
</tr>
<tr>
<td>Diameter stenosis (%)</td>
<td>43.6 ± 13.7</td>
</tr>
<tr>
<td>Area stenosis (%)</td>
<td>58.3 ± 21.4</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>2.0 ± 0.6</td>
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<tr>
<td>MLA (mm²)</td>
<td>4.5 ± 2.4</td>
</tr>
<tr>
<td>Remodelling index</td>
<td>0.85 ± 0.24</td>
</tr>
<tr>
<td>CT attenuation value (HU)</td>
<td>107.9 ± 58.1</td>
</tr>
<tr>
<td>PR, n (%)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>LAP, n (%)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>SC, n (%)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Napkin-ring sign, n (%)</td>
<td>4 (9)</td>
</tr>
<tr>
<td>OCT parameters</td>
<td></td>
</tr>
<tr>
<td>Fibrous cap thickness (µm)</td>
<td>253 ± 132</td>
</tr>
<tr>
<td>Lipid angle (°)</td>
<td>65.5 ± 75.7</td>
</tr>
<tr>
<td>Lipid length (mm)</td>
<td>3.3 ± 3.9</td>
</tr>
<tr>
<td>MLD (mm)</td>
<td>1.7 ± 0.7</td>
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</table>

TCFA: thin-cap fibroatheroma; MLD, minimal lumen diameter; MLA, minimal lumen area; PR, positive remodelling; LAP, low attenuation plaque; SC, spotty calcification; OCT, optical coherence tomography.

*P < 0.05 vs. non-TCFA (Scheffe).
TCFA with macrophage groups (107.9 vs. 114.0 vs. 55.6 HU, P = 0.01). A napkin-ring sign was not significantly different among three groups. By OCT, there was a stepwise increase in lipid length for lesions without TCFA, with TCFA but no macrophages, and TCFA with macrophages (3.3 vs. 6.9 vs. 11.6 mm, P < 0.001). TCFA with macrophage infiltration was associated with an increased number of APCs (Figure 1). With regard to the macrophage detection by OCT, inter- and intraobserver (±90 days apart) variability for a randomly selected 44% [n = 30 (with macrophage n = 12, without macrophage n = 18)] of lesions demonstrated good agreement (κ = 0.932 and 0.932, respectively).

By univariable analysis, CTA parameters associated with TCFA and macrophages are listed in Table 3, which included PR or LAP, increasing remodelling index, lower CT attenuation value, greater diameter stenosis, and smaller MLD. The napkin-ring sign was not an independent predictor for TCFA with macrophage. In multivariable models considering age and gender, PR [odds ratio (OR) 16.9, 95% confidence interval (CI) 3.9–73.3, P < 0.001] or LAP (OR 11.2, 95% CI 2.8–44.3, P = 0.001) were strongly associated with TCFA with macrophage (Table 3). Furthermore, in multivariable logistic regression analysis also considering % diameter stenosis, PR (OR 12.3, 95% CI 2.4–62.5, P = 0.002) or LAP (OR 6.9, 95% CI 1.2–39.4, P = 0.03), higher remodelling index (OR 1.1, 95% CI 1.0–1.2, P = 0.006), and lower CT attenuation values (OR 0.9, 95% CI 0.97–0.99, P = 0.04) were independent predictors of TCFA with macrophage.

AUC for TCFA with macrophage was highest for higher remodelling index was 0.85 (95% CI 0.75–0.94, P < 0.001). AUC was 0.77 (95% CI 0.63–0.90, P < 0.001) for a decreasing CT attenuation value, 0.75 (95% CI 0.57–0.92, P = 0.003) for % diameter stenosis; 0.62 (95% CI 0.46–0.78, P = 0.06) for % area stenosis; 0.69 (95% CI 0.52–0.87, P = 0.01) for MLD; and 0.59 (95% CI 0.44–0.74, P = 0.12) for MLA. AUC was 0.77 (95% CI 0.65–0.90, P = 0.001) for PR; 0.73 (95% CI 0.60–0.86, P = 0.0003) for LAP; 0.56 (95% CI 0.46–0.66, P = 0.12) for SC; and 0.56 (95% CI 0.45–0.67, P = 0.15) for napkin-ring sign. Figure 2 represents the example of CTA and OCT image for a lesion of TCFA with macrophage.

**Table 3** Logistic regression analysis for predicting TCFA with macrophage

<table>
<thead>
<tr>
<th>CT parameters</th>
<th>Univariable OR (95% CI)</th>
<th>Standardized OR</th>
<th>P-value</th>
<th>Multivariable OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PR</td>
<td>12.9 (3.6–46.8)</td>
<td>3.2</td>
<td>&lt;0.001</td>
<td>16.9 (3.9–73.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LAP</td>
<td>9.0 (2.6–31.4)</td>
<td>2.6</td>
<td>0.001</td>
<td>11.2 (2.8–44.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>SC</td>
<td>3.4 (0.7–18.9)</td>
<td>1.4</td>
<td>0.16</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Napkin-ring sign</td>
<td>2.3 (0.6–9.4)</td>
<td>1.3</td>
<td>0.24</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Remodelling index</td>
<td>1.1 (1.0–1.1)</td>
<td>7.4</td>
<td>0.001</td>
<td>1.1 (1.0–1.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>CT attenuation value</td>
<td>0.98 (0.97–0.99)</td>
<td>0.31</td>
<td>0.003</td>
<td>0.98 (0.97–0.99)</td>
<td>0.004</td>
</tr>
<tr>
<td>% Diameter stenosis</td>
<td>1.1 (1.0–1.1)</td>
<td>3.1</td>
<td>0.006</td>
<td>1.1 (1.0–1.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>Area stenosis</td>
<td>1.0 (0.9–1.1)</td>
<td>1.6</td>
<td>0.15</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>MLD</td>
<td>0.4 (0.1–0.9)</td>
<td>0.5</td>
<td>0.04</td>
<td>0.3 (0.1–0.9)</td>
<td>0.03</td>
</tr>
<tr>
<td>MLA</td>
<td>0.9 (0.7–1.1)</td>
<td>0.7</td>
<td>0.29</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>OCT parameters</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid length</td>
<td>1.3 (1.1–1.5)</td>
<td>4.6</td>
<td>&lt;0.001</td>
<td>–</td>
<td>–</td>
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</table>

**Discussion**

In the current study of individuals undergoing CTA, ICA, and OCT, we observed that increasing plaque vulnerability grade by OCT was associated with an increasing number of APCs as well as individual APCs by CTA, including PR and LAP. We observed a particularly strong relationship between PR and LAP by CTA to TCFA with macrophage, both for diagnosis and for discrimination. Even when adjusted for conventional angiographic measures of CAD severity—including % diameter stenosis—these relations remained independent and additive. Collectively, these present results suggest the utility of APCs as an effective method for CTA evaluation.
of CAD beyond stenosis severity for enhanced identification of high-risk coronary plaques.

By virtual histology IVUS, the PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) study evaluated coronary lesions in the proximal-to-mid-portions of major epicardial arteries from patients undergoing uncomplicated percutaneous coronary intervention after presentation of ACS.27 At a 3-year follow-up, nearly half of subsequent ACS events were associated with non-culprit lesions. The majority of these lesions were observed to be angiographically mild, confirming previous data presented by Falk et al.28 In PROSPECT, numerous atherosclerotic plaque characteristics beyond stenosis severity were observed to be important in the ACS process, including large plaque burden, smaller MLA, and TCFA. Note, however, that the positive predictive value of plaque characteristics remains very low in absolute terms in the PROSPECT study.

CTA enables a non-invasive assessment of atherosclerotic plaque characteristics within arterial walls, with general agreement to invasive methods. Several prior reports have evaluated the value of CT-based APC identification—including PR, LAP, and SC—for identification of culprit lesions at the time of presentation of ACS. Hoffmann et al.29 first reported that culprit lesions identified at the time of ACS demonstrated higher rates of PR and non-calcified plaque, when compared with culprit lesions in patients with stable angina pectoris. These findings were confirmed by Motoyama et al.14, in a large retrospective CTA study that culprit lesions of ACS possessed a higher prevalence of PR, LAP, and typically had SC; findings confirmed by Kitagawa et al.30 In the sole prospective CTA study to date, Motoyama et al.31 reported that the PR and LAP conferred a >20-fold higher hazards for subsequent ACS in a 27-month follow-up. The data from the present study both confirm as well as add to these important investigations by use of an intravascular ‘gold’ standard method with the highest achievable in vivo spatial resolution to permit the association of CTA APCs to TCFA, lipid angles, and macrophage infiltration.

Interestingly, preliminary studies that have employed CTA to identify OCT-identified plaque morphologies for lesions that do vs. do not possess TCFA have reported conflicting findings.32–34 Kashiwagi et al.32 reported that a ‘ring-like’ enhancement, or ‘napkin-ring’ sign, was associated with TCFA, but that increasing remodelling indexes or decreasing CT attenuation values were not. Soeda et al.33 analysed 162 coronary plaque segments in 17 patients in order to differentiate tissue characteristics of plaques by CTA in comparison with OCT. In this study, CTA was not observed to be capable for adequate differentiation between lipid-rich plaques with a thin fibrous cap from those with a thick fibrous cap. In a subsequent study, Ito et al.34 compared by both CTA and OCT coronary lesions targeted for percutaneous coronary intervention vs. non-target lesions causing luminal diameter narrowing >50%. Contrary to the results of Kashiwagi, these investigators identified lower CT attenuation values, higher

Figure 2 Example case. (A) Multiplanar reformat and short-axis view of the CTA in the proximal left anterior descending coronary artery. CTA demonstrates mild diameter stenosis with PR (remodelling index 1.15) and LAP (yellow circle, 24 HU). Corresponding images of ICA (B) and OCT (C and D). (D) Yellow arrow shows macrophage infiltration (superficial high-intensity signal band underlying a low signal area), and yellow circle shows thin fibrous cap, indicating TCFA with macrophage. CTA, coronary CT angiography; LAP, low attenuation plaque; OCT, optical coherence tomography; PR, positive arterial remodelling.
remodelling indexes, and a ‘ring-like’ enhancement appearance of coronary plaques to be predictors of TCFA. Our present study results are more consistent with the latter of these studies, but are directly additive to their important results by evaluating intravascular imaging criteria of intraplaque inflammation in addition to CTA.

We observed the strongest relation of CTA-identified PR to TCFA by OCT, findings that are in agreement with those reported by Raffel et al. Many potential mechanisms exist to explain these findings, including PR to be potentially associated with higher atheroma volume or a compensatory state that promotes endothelial dysfunction. It appears likely that these morphological APCs— that is, PR and LAP— identified by CTA are, in fact, inter-related. We observed not only a strong association between individual APCs and plaque vulnerability grade by OCT, but also a dose-response relationship as well wherein multiple APCs appeared to confer a higher probability of vulnerable plaque by OCT when compared with a single APC.

Our study findings are in contradistinction with a recent ex vivo study by Maurovich-Horvat, who reported that a napkin-ring sign has significantly improved diagnostic accuracy for the detection of TCFA as adjudicated by histopathology. In our study, napkin-ring sign was not associated with TCFA with macrophage by OCT. There are a number of potential explanations for our findings. Given the need for fixation of arterial specimens in prior ex vivo studies, the preparation process may have influenced the CT appearance of the studied atherosclerotic plaques. In contrast, in our in vivo study, we employed a standardized method for the evaluation of coronary plaques in order to ensure uniformity of assessment. We have previously described this method to be that which demonstrates the highest diagnostic accuracy compared with IVUS. Yet, additional differences in study performance—including differences in iodinated contrast opacification of coronary plaques, or calcified plaque components— may exist. Future studies evaluating the diagnostic performance of CTA to identify ‘napkin-ring’ signs, as well as their prognostic potential, now appear warranted and are currently being pursued by our laboratory.

The findings of the present study carry high clinical import. Current interpretation methods of CTA endorsed by societal guidelines generally limit recommendations of CTA reporting to findings related to angiographic measures of stenosis severity. Yet, in addition to our present study findings, CTA assessment of the morphological components of coronary plaques has been demonstrated to be associated with myocardial ischaemia and future ACS. The findings of the present study provide insights into the anatomical and inflammatory mechanisms that may explain these findings wherein these plaque features—including PR and LAP—are strongly and directly associated with OCT plaque characteristics that are well accepted as ‘vulnerable’ in nature. It seems reasonable to consider extending CTA interpretation to include these features, with routine reporting of these findings in addition to measures of stenosis severity.

Limitations

This study is not without limitations. The present study sample was small owing to the invasive nature of evaluation by OCT, which emphasizes the need for more non-invasive methods for coronary plaque assessment that permit evaluation of greater sample sizes. It is, in part, for this reason that we are aiming to determine the relationship of a non-invasive method (CT) to the invasive reference standard (OCT). Furthermore, we examined a consecutive cohort of patients for plaque features that are generally associated with plaque rupture. As such, the findings of study should be applied to other potential mechanisms of ACS with caution, as recent evidence suggests that the plaque morphologies by CTA for ACS may not be routinely detectable. Although there were no intervening coronary events or changes on medications between CTA and OCT, the change in the nature of characteristics (such as macrophage) could not be excluded. Finally, the endpoints examined in the present study were for atherosclerotic plaque features considered to be high risk. Thus, the clinical outcomes evidence is lacking and the clinical value of the present findings is a bit limited. Although our study findings may enhance the diagnostic potential of CTA for identification of these anatomically high-risk characteristics, future large-scale prospective studies examining the relationship of APCs to incident adverse outcomes should be performed, and our laboratory is currently pursuing such investigations.

Conclusion

Atherosclerotic plaque features by CTA, including positive arterial remodelling and LAP, are associated with coronary lesions that possess TCFA and macrophage infiltration. CTA may serve a role as a potential non-invasive method to identify high-risk plaques.

Conflict of interest: All authors have reported that they have no relationships relevant to the contents of this paper to disclose.

References


