Detection and characterization of coronary bifurcation lesions with 64-slice computed tomography coronary angiography

Carlos A.G. Van Mieghem1,2, Attila Thury1, Willem B. Meijboom1,2, Filippo Cademartiri1,2, Nico R. Mollet1,2, Annick C. Weustink1,2, Georgios Sianos1, Peter P.T. de Jaegere1, Patrick W. Serruys1, and Pim de Feyter1,2*

1Department of Cardiology, Thoraxcenter, Erasmus MC, Ba 589, Dr Molewaterplein 40, 3015 GD Rotterdam, The Netherlands
and 2Department of Radiology, Erasmus MC, Rotterdam, The Netherlands

Aims To compare the performance of 64-slice computed tomography coronary angiography (CTCA) and invasive coronary angiography (ICA) in the detection and classification (according to the Medina system) of bifurcation lesions (BLs).

Methods and results We studied 323 consecutive patients undergoing 64-slice CTCA prior to ICA. All coronary segments ≥2 mm in diameter were evaluated for the presence of a significant (≥50% diameter reduction on quantitative coronary angiography) BL. Evaluation of BL by CTCA included the assessment of significant lumen obstruction in both main and side branch vessels. Forty-one out of 43 patients (46/48 lesions) with significant BL were identified by CTCA. Excluding coronary segments with non-diagnostic image quality (5%), the sensitivity, specificity, and positive and negative predictive values of CTCA for detecting significant BL were 96, 99, and 85 and 99%, respectively. In 39 of these 41 patients, CTCA assessment was concordant with the Medina lesion classification on ICA.

Conclusion Sixty-four-slice CTCA allows accurate assessment of complex BL.

KEYWORDS
Bifurcations; Coronary atherosclerosis; Computed tomography coronary angiography; Percutaneous coronary intervention

Introduction
Invasive coronary angiography (ICA) is regarded as the reference standard for the diagnosis of significant coronary artery disease (CAD) and to plan and guide percutaneous coronary intervention (PCI). However, coronary angiography has major limitations. Factors such as vessel overlap and foreshortening may make it difficult to accurately assess the severity and extent of coronary artery lesions.1 Furthermore, as angiography only visualizes the lumen, it cannot identify plaque accumulation related to positive remodeling, a ubiquitous phenomenon at bifurcation sites.2

The high diagnostic accuracy of computed tomography coronary angiography (CTCA) in the non-invasive detection of significant CAD is well established.3,4 However, the potential role of CTCA in the detection and characterization of coronary bifurcations is unclear. CTCA allows three-dimensional evaluation of both the lumen and the wall of the vessel; thus, it has potential to provide a more comprehensive assessment of the complex geometry of bifurcation lesions (BLS). The purpose of the present study is to evaluate the diagnostic accuracy of CTCA in patients with bifurcation pathology. Furthermore, we provide a detailed comparison with conventional angiographic data by categorizing each BL according to a simplified classification system (Medina).5

Methods
Patient selection
The study population comprised 323 consecutive patients who underwent 64-slice CTCA, within a 2-week period prior to ICA between March and December 2005. In patients with prior PCI or coronary artery bypass graft surgery (CABG), only the non-intervened coronary artery segments were included in the analysis. Contraindications for CTCA were an irregular heart rhythm, inability to hold breath for 15 s, renal dysfunction (creatinine clearance ≤60 mL/min), and known contrast allergy. The institutional Ethical Review Board approved the study protocol, which complied with the declaration of Helsinki. All patients gave written informed consent.

Multislice computed tomography protocol, radiation dose calculation, and image reconstruction
Patients with a resting heart rate above 65 b.p.m. received oral beta-blockers (metoprolol 50–100 mg) or a non-dihydropyridine calcium-antagonist (diltiazem 60–120 mg) together with 0.5–1 mg lorazepam 1 h before the scan. An
additional IV bolus of metoprolol (5–10 mg) was occasionally administered where the heart rate remained above 65 b.p.m. The examination was performed using previously reported methodology. In brief, CTCA data were acquired using a 64-slice CT scanner (Sensation 64, Siemens, Germany). A non-enhanced calcium scoring scan was only obtained in patients without previous PCI or CABG using the following parameters: collimation 64 × 0.6 mm, tube rotation time 330 ms, table feed 3.8 mm per rotation, tube current 150 mA s at 120 kV, and prospective X-ray tube modulation. Angiographic scan parameters were identical aside from a tube current that ranged between 850 and 960 mA s without the use of dose pulsing. The effective radiation dose was calculated separately for patients with and without previous CABG using dedicated software (iMPACT CT Patient Dosimetry Calculator, version 0.99x), as described in the European Guidelines on Quality Criteria for Computed Tomography (available at: http://www.drs.dk/guidelines/ct/quality/index.html).

A bolus of 100 mL of contrast (iomeprol, 400 mg iodine/mL, Iomeron50, Bracco, Milan, Italy) was administered in all patients. The standard injection rate was 5 mL/s, but was decreased to 4 mL/s in patients who had previous CABG. We did not use a saline chaser after contrast administration. A bolus tracking technique was used to monitor the appearance of contrast material in the aortic root cranial to the origin of the left coronary artery. Once the signal in the ascending aorta reached a predefined threshold of 100 HU, CT data were acquired during an inspiratory breath-hold.

All scans were analysed off-line using a Leonardo workstation (Siemens Medical Solutions) by two independent observers who were blinded to the results of ICA. Images were reconstructed using ECG-gating to obtain optimal, motion-free image quality. Data sets were routinely obtained during the mid-to-end diastolic phase (−300, −350, −400, −450 ms before the next R-wave or at 60–70% of the R-R interval). Additional reconstruction windows in systole (in general at 25–35% of the R–R interval) were explored when image quality was suboptimal on the standard reconstructions. In 31% of the cases, the end-systolic data set was used for image analysis.

Image quality was evaluated on a per-segment basis and classified as good (defined as the absence of any image-degrading artefacts related to motion, calcification, or insufficient contrast enhancement), adequate (presence of image-degrading artefacts, but evaluations possible with moderate confidence), or poor (presence of image-degrading artefacts and evaluation only possible with low confidence). Coronary artery segments with poor image quality were judged to be ‘unevaluable’.

Computed tomography coronary angiography analysis

All evaluable coronary segments were visually scored for the presence of significant BLs (diameter reduction of ≥50%) by careful axial scrolling and using (curved) multiplanar reconstructions. A BL was defined as a stenosis that involved the origin of a side branch (SB), ≥2.0 mm in diameter.7 The presence or absence of SB pathology was determined by evaluating the first 10 mm of the SB for the presence of significant lumen narrowing. Disagreement between observers was resolved by a third observer, and the consensus reading was subsequently compared with the ICA.

High-resolution thin slab multiplanar reconstructions (reconstructed slice thickness of 0.75 mm) were used for assessment of bifurcation angles. The three orthogonal planes as provided when opening a CT data set were carefully oriented according to the geometrical orientation of the main vessel (MV) and SB at the bifurcation point (Figure 1A). To determine the angle of bifurcation, we depicted two lines (in the centre of each vessel lumen) along the initial course of the distal part of the main branch (MB) and SB using the MPR view in which the angulation between the proximal parts of these two vessels was maximal (Figure 1B). We only used diastolic data sets to measure bifurcation angles. Subsequently, BL with significant lumen narrowing were categorized using a recently introduced classification scheme, known as the Medina bifurcation classification (Figure 2).5 The Medina classification is a simple binary system whereby significant lumen narrowing is classified as present (1) or absent (0) in the proximal MB, distal MB, and SB. Modification and scrolling of MPR images originating from the bifurcation site was used to confirm the exact spatial relation of the lumen obstruction in relation to the branching point.

Quantitative coronary angiography

Coronary angiograms were obtained in multiple projections after intracoronary nitrate administration with standard techniques. Two experienced cardiologists blinded to CTCA results identified all available coronary segments using a 17-segment modified American Heart Association (AHA) classification and classified all coronary segments as ≤2 and ≥2 mm in diameter using validated, automated, edge-detection software (CAAS II, Pie Medical, Maastricht, The Netherlands).8 Only segments classified as ≥2 mm in reference diameter were considered for comparison with CTCA. In the presence of an occluded coronary artery, we only assessed the segments that were located proximal to the occlusion. Standard measurements were made for the MB analysis; the proximal border of the SB was depicted manually by extending the reference point into the MV, as previously reported.9 Significant lumen narrowing was defined as a lumen diameter reduction of ≥50% in the MB and/or SB. Identified BLs were subsequently classified according to the Medina classification system.6 All measurements, including bifurcation angles, were determined using end-diastolic frames.

Statistical analysis

Continuous variables are presented as mean ± standard deviation and compared by Student’s t-test. A two-sided P < 0.05 was considered to be significant. Categorical variables are presented as counts and percentages. The diagnostic performance of CTCA for the detection of significant BL, when compared with quantitative coronary angiography (QCA), is presented as sensitivity, specificity, and positive and negative predictive value and reported with associated 95% confidence intervals based on binomial probabilities. Diagnostic performance indices are presented separately for all ‘evaluable’ segments and for the overall population,
Figure 1 (A) Visualization of the circumflex-obtuse marginal bifurcation by invasive coronary angiography (a) and volume-rendered computed tomography coronary angiography (b). The three-dimensional representation of the heart, as shown in (b), can be obtained by summation of the ‘raw’ axial computed tomography images that have a defined $x$–$y$–$z$ dimension. The conventional planes that are used for visualization of this volume data set are the axial plane (axial), the coronal plane (coronal), and the sagittal plane (sagittal). CX, circumflex coronary artery; LAD, left anterior descending coronary artery; OM, obtuse marginal branch. (B) Scrolling of axial images provides a quick view of the data set to assess crudely the main features of the coronary anatomy. To obtain a precise view of the structure of interest, in this example, the circumflex-obtuse marginal bifurcation, the planes of visualization need to be orientated to the geometrical orientation of the coronary structures. As a first step, the three conventional image planes are centred at the level of the branching point (a–c). The three-dimensional nature of the computed tomography data allows to subsequently tilt these image planes in any orientation. The resulting multiplanar reconstruction (d) precisely shows the relationship of the main vessel with the side branch and is used to assess the angle between the initial course of distal portion of the main vessel and the side branch (in this example, 31°). Also shown is a maximum intensity projection computed tomography image (e) to demonstrate the anatomical correlation with the angiographic view. We did not use this maximum intensity projection reconstruction to determine bifurcation angles. CX, circumflex coronary artery; LAD, left anterior descending coronary artery; OM, obtuse marginal branch.
including coronary segments with poor image quality. These unevaleuable segments were classified as having a stenosis on CTCA. Because of potentially interdependent observations, i.e. multiple bifurcations in the same patient, an additional measurement of diagnostic accuracy was performed for a random selection of single observations per patient. Statistical analysis was performed with SPSS, version 11.5 (SPSS Inc., Chicago, USA).

**Results**

All 323 patients tolerated the CTCA procedure well and no complications occurred. The average time required for the cardiac CT examination, including patient preparation for scanning, image acquisition, and reconstruction of the appropriate data sets was 20–25 min. Evaluation of the CT coronary angiogram took on average about 5–10 min; the extra time needed to specifically assess the bifurcations was about 5 min.

Patient characteristics are summarized in Table 1. Mean periscan heart rate was 58 ± 7.2 b.p.m. Of the theoretically available 5491 segments, 582 were excluded because the diameter was <2 mm and 161 because they were distal to an occluded segment. In addition, 470 segments were absent on CCA. After exclusion of 189 stented segments and 74 grafted vessels (267 segments), 3822 segments (1218 bifurcations) were available for further analysis. Poor image quality was present in 5% (211/3822; 88 bifurcations) of coronary segments and was related to a technically inadequate scan (breathing artefacts or fast or irregular heart rate, \( n = 53 \)), severe calcification (\( n = 62 \)), cardiac motion artefacts (\( n = 58 \)), or insufficient contrast enhancement (\( n = 38 \)). The effective radiation dose was calculated as 19 mSv (1.6 mSv for the calcium score scan and 17.4 mSv for the contrast-enhanced scan) in patients without previous CABG and 22 mSv in patients with previous CABG.

Table 2 summarizes the diagnostic accuracy of 64-slice CT compared with QCA for the evaluation of coronary bifurcations. A total of 1130 evaluable bifurcations were available for analysis. Fifty-four BL in 49 patients were identified on CTCA. QCA identified 48 BL in 43 patients. Thus, CTCA incorrectly classified the severity of BL in 10 patients. In eight patients, a significant BL on CTCA was not confirmed on ICA; in six of these eight patients, this misclassification was related to the presence of calcification. In two patients, the severity of the lesion was underestimated: one patient had a calcified lesion of the left main/left anterior descending bifurcation; the second had a short lesion of the distal right coronary artery-posterolateral branch bifurcation. When the 88 bifurcations with poor image quality were arbitrarily scored as having significant lumen narrowing on CTCA, the sensitivity and specificity for detection of significant BL were 95% (41/43; 95% CI 85–99) and 95% (266/280; 95% CI 92–97) on a ‘patient level’ and 96% (46/48; 95% CI 86–99) and 92% (1074/1170; 95% CI 90–93) on a lesion level (1218 bifurcations).
The angiographic and CTCA characteristics of the patients with identified BL are shown in Table 3. Lesions were predominantly located in the left main or at the left anterior descending/first or second diagonal bifurcation. The angle between MV and SB differed significantly when assessed by CTCA when compared with ICA (60 ± 19 vs. 51 ± 18 °, respectively, P < 0.0001).

Table 4 describes in detail the lesion distribution in coronary bifurcations, as assessed by CTCA and ICA. In all but two patients, the bifurcation classification on CTCA was concordant with that on ICA (agreement between CTCA and ICA in 44/46 BLs). In one patient, ICA underestimated the severity of stenosis in the left main bifurcation and the patient was referred for CABG, based on the CTCA assessment (Figure 3). In the second patient, significant involvement of the ostium of the first diagonal branch was not detected on CTCA and the lesion was classified as Medina type 1.1.0 instead of type 1.1.1.

Discussion
BLs provide a challenge in terms of both assessment and management. Vessel overlap, foreshortening, beam attenuation (particularly in obese patients), and

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### Table 1 Patient characteristics (n = 323)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>61.3 ± 10.4</td>
</tr>
<tr>
<td>Male (%)</td>
<td>72</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.2 ± 4.3</td>
</tr>
<tr>
<td>Clinical presentation</td>
<td></td>
</tr>
<tr>
<td>Stable angina (%)</td>
<td>60</td>
</tr>
<tr>
<td>ACS (%)</td>
<td>14</td>
</tr>
<tr>
<td>Other (%)</td>
<td>26</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>27</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>53</td>
</tr>
<tr>
<td>Dyslipidaemia (%)</td>
<td>81</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>16</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.97 ± 0.2</td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>33</td>
</tr>
<tr>
<td>Prior PCI (%)</td>
<td>32</td>
</tr>
<tr>
<td>Prior CABG (%)</td>
<td>10</td>
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</table>

#### Vessel disease (%)
- Non-significant disease: 28
- One-vessel disease: 38
- Two-vessel disease: 18
- Three-vessel disease: 8
- Left main disease: 5
- Graft disease: 3

Basal heart rate: 68.5 ± 10.2

Heart rate during CTCA: 58 ± 7.2

CTDVol no previous CABG (Gy): 70.5

CTDVol previous CABG (Gy): 61

Dose estimate (no previous CABG) (mSV)²: 19

Dose estimate (previous CABG) (mSV)²: 22

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Categorical data are presented as numbers (%) and continuous data as mean values ± SD. ACS, acute coronary syndrome; CABG, coronary artery bypass graft surgery; CAD, coronary artery disease; CTCA, computed tomography coronary angiography; CTDVol, volume computed tomography dose index; MI, myocardial infarction; PCI, percutaneous coronary intervention.

²The estimated radiation dose is higher in bypass patients because of the longer scan length.
underopacification may hinder accurate assessment of the anatomy, particularly with respect to the assessment of ostial SB involvement. Errors in diagnosis may have significant consequences for patient management. 10 When CABG is the treatment strategy, underestimation of an SB lesion may inadvertently result in the SB not being grafted. Where PCI is the preferred option, accurate anatomic information is crucial in planning the treatment strategy, to anticipate plaque shift with resulting lumen compromise. 11,12 In this study, we demonstrated that in selected patients the use of 64-slice CTCA accurately detected angiographically significant BL when compared with ICA, which is in keeping with the diagnostic accuracy of 64-CTCA to detect significant non-bifurcation coronary lesions with reported sensitivity values in the 90–95% range. 4,13-16

Table 3  Angiographic and computed tomography characteristics of patients (n = 41) with bifurcation lesions (n = 46)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Bifurcation lesions (n)</th>
<th>Location of bifurcation lesion</th>
<th>Angiographic variables, main branch</th>
<th>Angiographic variables, side branch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion length (mm)</td>
<td>11.8 ± 6.6</td>
<td>Reference diameter (mm)</td>
<td>2.82 ± 0.53</td>
<td>Lesion length (mm)</td>
</tr>
<tr>
<td>% diameter stenosis</td>
<td>59 ± 19</td>
<td>MLD (mm)</td>
<td>1.14 ± 0.49</td>
<td>Reference diameter (mm)</td>
</tr>
<tr>
<td>Angiographic variables, side branch</td>
<td></td>
<td>% diameter stenosis</td>
<td>41 ± 24</td>
<td>MLD (mm)</td>
</tr>
<tr>
<td>Previous heart rate lowering medication (%)</td>
<td>82</td>
<td>Additional heart rate lowering drugs (%)</td>
<td>58</td>
<td>Reference diameter (mm)</td>
</tr>
<tr>
<td>Angulation by CTCA (degrees)</td>
<td>60 ± 19</td>
<td>Calcium score (mean ± SD)a</td>
<td>704 ± 955</td>
<td>Reference diameter (mm)</td>
</tr>
</tbody>
</table>

CABG, coronary artery bypass graft surgery; CTCA, computed tomography coronary angiography; CX, circumflex coronary artery; ICA, invasive coronary angiography; MLD, minimal lumen diameter; OM, obtuse marginal branch; PCI, percutaneous coronary intervention; PD, posterior descending coronary artery; PL, posterolateral branch; RCA, right coronary artery; SB, side branch.
aAgatston score.

The general consensus with regard to the treatment of BLs is that, ideally, the MV only should be stented, with provisional stenting of the SB where the ostium is severely compromised. 19 In situations where both branches need to be stented, the interventional approach (i.e. selection of stenting technique) is determined by the angle between the MV and SB. In our study, assessment of the bifurcation angle on CTCA was relatively straightforward. The angle determined by the three-dimensional assessment on CTCA differed significantly from that measured on ICA. These findings are consistent with the results of a recent study demonstrating that bifurcation angles measured by CTCA were more accurate when compared with invasive angiography. 16

Current 64-slice CT scanners are sufficiently reliable to exclude the presence of significant coronary artery stenoses. CTCA therefore seems most useful for the assessment of symptomatic patients who have a low-to-intermediate probability of significant coronary artery stenosis. A recent meta-analysis of all major published studies on 16- and 64-slice CT technology showed that in patients with high prevalence of CAD the specificity of CT is still insufficient to allow its implementation as an alternative to ICA. 20 ICA should continue to be the preferred option in patients with typical angina and/or previously known CAD because it allows ad hoc PCI to be performed, where appropriate, and because the high prevalence of calcification in this population would hamper accurate assessment by CTCA. In the current study, the prevalence of pre-existing CAD was relatively high (50%) and severe calcifications were the main reason for uninterpretable coronary artery segments (39%, 62/158 segments) after exclusion of the six patients (53 segments) who had a technically inadequate CT scan. Our preliminary study provides proof of concept for the potential of CTCA to accurately detect coronary artery lesions, even in the presence of complex anatomy such as BLs.

Limitations

Although our report concerns a large consecutive series of patients who were scanned prior to ICA during a 9-month period, the retrospective nature of the study is a limitation. However, even with a prospectively conducted study it would be difficult to prove the clinical benefit of a ´pre-interventional´ CT evaluation since the optimal approach to PCI for a BL is currently unknown.

General limitations of CTCA are the additional contrast load and the considerably higher radiation exposure compared with ICA. However, these drawbacks should be balanced against the additional costs and risks of a prolonged angiographic procedure with, in general, the use of more contrast, catheters and additional invasive tools such as IVUS for assessment of difficult lesion subsets such as bifurcations.

In this study, we demonstrated the feasibility of CTCA to accurately assess coronary bifurcations for the presence or absence of significant disease and we found CTCA to be more accurate than ICA for the measurement of bifurcation angles. Whether the information provided by a CT exam would influence the therapeutic strategy when attempting PCI for a BL remains unproven and needs further study.
The results of this study are only applicable to a selected patient population (patients in sinus rhythm, who are relatively young, with coronary arteries that do not contain severe calcifications) and were obtained in a centre with experienced investigators.

Observations (bifurcations) within the same patient are not statistically independent. We recalculated the diagnostic accuracy parameters after random selection of a single bifurcation per patient. Sensitivity and specificity for detection of significant BLs was respectively 100% (10/10; 95% CI 72–100) and 95% (296/313; 95% CI 91–97). Fewer observations resulted in wider confidence intervals.

Finally, current studies reporting on the diagnostic accuracy of 64-slice CTCA in general included vessels with a reference size up to 1.5 mm. This is a reasonable threshold since smaller-sized vessels usually do not constitute targets for revascularization. In this study, we limited the assessment of BL to branches with a reference diameter >2 mm for two reasons: (i) this cut-off value is a generally accepted criterion to define clinically relevant SBs and (ii) current spatial resolution is not sufficient for accurate plaque imaging in vessels with a reference size <2 mm.\textsuperscript{17,21–24}

**Conclusions**

Sixty-four-slice CTCA provides an accurate and comprehensive assessment of coronary bifurcation pathology in a selected patient population. These preliminary data support the potential of CTCA to replace coronary angiography as the preferred diagnostic tool for coronary imaging in this setting.
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References


