Noninvasive assessment of the prevalence and characteristics of coronary atherosclerotic plaques by multidetector computed tomography in asymptomatic type 2 diabetic patients at high risk of significant coronary artery disease: A preliminary study

Évaluation non invasive de la prévalence et des caractéristiques des plaques d’athérosclérose coronariennes par scanner multidétecteur chez des patients diabétiques de type 2 à haut risque de maladie coronarienne significative : une étude préliminaire

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Abbreviations: CAC, Coronary artery calcification; CAD, Coronary artery disease; CRP, C-reactive protein; CT, Computed tomography; cIMT, Carotid intima-media thickness; MDCT, Multidetector computed tomography.

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Background

Diabetic patients experience increased morbidity and cardiovascular complications compared with non-diabetic subjects [1–3], and coronary artery lesions have been proven angiographically to be more extensive and CAD has a worse prognosis [4,5]. Moreover, silent myocardial ischaemia occurs more frequently in diabetic patients than...

MOTS CLÉS

Diabète de type 2 ; Scanner multidétecteur ; Maladie coronarienne ; Plaque d’athérosclérose

Résumé

Contexte. — Il y a un intérêt à identifier les patients diabétiques à risque d’événements cardiovasculaires avant le début des symptômes.

Objectifs. — Évaluer la prévalence et les caractéristiques des plaques d’athérosclérose coronariennes chez des patients asymptomatiques diabétiques de type 2 à risque coronarien mais sans atteinte coronarienne connue par scanner multibarette.

Méthodes. — Un coroscanner 40 détecteurs a été réalisé de manière prospective chez 42 patients consécutifs diabétiques de type 2 (28 hommes ; âge moyen, 62 ans ; extrêmes, 50–77 ans) ayant au moins une plaque d’athérosclérose carotidienne et asymptomatiques sur un plan coronarien. Le score calcique et la présence de plaques coronariennes ont été évalués à partir des données scannographiques. Le type, la distribution le caractère extensif et la nature obstructive des plaques ont été déterminés par patient pour chaque segment.

Résultats. — Aucune plaque coronarienne n’a été détectée chez 11 (26,2 %) patients. La présence de plaques d’athérosclérose a été détectée chez 31 (73,8 %) patients. Un total de 147 segments coronaires avec des plaques ont été identifiés, parmi lesquels 11 (7,5 %) contenaient des plaques hypodenses, 28 (19 %) mixtes et 108 (73,5 %) calcifiées. La présence de plaques hypodenses était notée chez quatre (26,7 %) des 15 patients qui n’avaient pas de calcifications coronariennes. La majorité des plaques calcifiées et hypodenses étaient non obstructives alors que la majorité des plaques mixtes étaient obstructives. La présence d’une maladie obstructive a été notée chez neuf des 11 patients avec un score calcique élevé ( > 400).

Conclusion. — Cette étude préliminaire démontre qu’une proportion élevée de patients diabétiques de type 2 asymptomatiques ne présentent aucune plaque coronarienne détectable par scanner multidétecteur malgré la présence concomitante de lésions d’athérosclérose carotidiennes. Le scanner semble détecter une proportion importante de plaques coronariennes en comparaison à l’angiographie conventionnelle dans cette population particulière.

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in the general population and can lead to delayed diagnosis [6–8]. In addition, even after normal noninvasive stress testing, event rates are still higher in diabetic patients than in non-diabetic individuals [9,10], which is probably related to differences in coronary plaque burden and composition. Consequently, direct noninvasive imaging of coronary atherosclerotic plaques with MDCT has become a useful tool in the detection of both calcified and vulnerable non-calcified coronary lesions, in contrast to calcium scoring alone, and may allow improved cardiovascular risk stratification [11–14]. Recent reports have even demonstrated the ability of contrast-enhanced MDCT to detect differences in coronary plaque characteristics between patients with and without symptomatic diabetes [15]. However, the prevalence and characteristics of coronary plaques detected by MDCT in asymptomatic type 2 diabetic patients have not been evaluated systematically. The aim of our preliminary cross-sectional study was to assess prospectively the potential of MDCT to detect coronary artery plaques in asymptomatic type 2 diabetic patients without known CAD but considered to be at high risk of CAD because of the presence of carotid atherosclerotic lesions, and to study plaque prevalence, extent and characteristics.

**Methods**

**Study subjects**

The study population consisted of 42 consecutive type 2 diabetic patients (28 men; 14 women; mean age 62.1 years; range 50–77 years) in primary prevention without known symptoms suggestive of CAD, who were recruited prospectively from an endocrinology department between May 2006 and April 2007. All participants were required to have a carotid atherosclerotic plaque greater or equal to 1.5 mm thick at inclusion to increase the probability of finding coronary plaques. This threshold was set arbitrarily to ensure the selection of diabetic patients with a carotid atherosclerotic plaque that was sufficiently thick to be examined by high-resolution magnetic resonance imaging—a criterion that was part of another study that aimed to identify the different components of plaques with magnetic resonance imaging. Inclusion criteria were the presence of type 2 diabetes diagnosed according to the American Diabetes Association criteria (symptoms of diabetes and a casual plasma glucose level of greater than or equal to 11.1 mmol/L or a fasting plasma glucose level of greater than or equal to 7.0 mmol/L) [16], age at onset greater than or equal to 35 years, current age greater than or equal to 50 years, no personal history of CAD and normal electrocardiogram at rest. Exclusion criteria were age at onset of diabetes of less than 35 years, current age less than 50 years, pregnancy, known CAD, Cockroft and Gault creatinine clearance less than 50 mL/min and arrhythmia that did not allow electrocardiogram-triggering of the MDCT scan. All study-related data, including patient history, laboratory results and MDCT findings were analysed. The study protocol was approved by the local research ethics committee and all patients gave written informed consent before inclusion in the study.

**MDCT data acquisition**

All examinations were performed using a MDCT scan (Brilliance 40, Philips Medical Systems, Eindhoven, the Netherlands). First, a native prospective scan without contrast enhancement was performed to determine the total calcium burden of the coronary tree (sequential scan with 32 × 0.6 mm collimation, tube current 60 mA at 120 kV), followed by 40-slice contrast-enhanced CT coronary angiography performed with the use of a retrospective electrocardiogram-triggered spiral scan of the whole heart area with the following parameters: 40 × 0.625 mm collimation, 420 ms gantry rotation, pitch of 0.2, tube voltage at 120 kV, maximum current of 600–800 mAs depending on patient size, half-scan reconstruction mode and imaging craniocaudal direction. Tube current was modulated according to the electrocardiogram. The average radiation dose received for the study was approximately of 7 mSv. Contrast agent (80 mL iomeron [400 mg iodine/mL], Bracco Altana Pharma, Milan, Italy) was injected intravenously at a rate of 4–6 mL/s. Twenty-five (59.5%) of the 42 enrolled patients had a heart rate greater than or equal to 65 beats/min at the moment of the CT scan, and received metoprolol 5–20 mg intravenously before the examination. Transaxial image reconstruction was performed routinely using a window centred at 75% of the R-R interval to coincide with left ventricular diastole. For heart rates greater than or equal to 70 beats/min, an earlier reconstruction phase (40%) was used (coinciding with isovolumic relaxation). The position of the reconstruction window within the cardiac cycle was optimized individually to minimize motion artefacts. Image quality was good enough to allow analysis of MDCT data in all patients.

**MDCT image interpretation**

Cardiac MDCT image evaluation was performed independently on a separate workstation (Brilliance workstation, Philips Medical Systems, Eindhoven, the Netherlands) by two reviewers who were unaware of the clinical data. In cases where disagreement occurred, agreement was reached in a joint reading. A total Agatston calcium score was recorded for each patient. MDCT angiograms were analysed visually by assessment of the axial slices, the multiplanar reformations along the axis of the vessel of interest, the cross-sectional images perpendicular to the vessel centre line and the three thin-slab maximum intensity projections. The coronary artery tree was divided into 15 segments according to the American Heart Association classification [17]. In our analysis, segments were separated into proximal (1, 5, 6 and 11) and distal (2, 3, 4, 7, 8, 9, 10, 12, 13, 14 and 15) segments. Healthy segments were defined as those without any plaque and diseased segments as those containing non-calcified, mixed or calcified plaques. One coronary plaque was assigned per coronary segment. Plaques were classified as obstructive or non-obstructive using a 50% threshold of luminal narrowing. The presence of obstructive and non-obstructive CAD in one vessel (single-vessel disease) or in two or three vessels (multivessel disease) was also evaluated. The presence of non-calcified or hypodense plaques was defined as any discernible protrusive structure in the coronary artery wall with a CT density less than the contrast-
enhanced coronary lumen but greater than the surrounding connective tissue. Calcified atherosclerotic plaques were defined as plaques with high density exceeding the threshold of 130 Hounsfield units. In other words, any isolated coronary artery wall calcification was considered to be a calcified coronary plaque, whatever its protrusion in the lumen. Mixed plaques were defined as plaques with non-calcified and calcified components within the same plaque. Plaques were also classified as extensive and non-extensive using a 50% threshold of length spreading.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation and were compared using the two-tailed t test for independent samples. When not distributed normally, continuous variables are expressed as median (interquartile range) and were compared using the non-parametric Mann-Whitney test. Categorical variables are expressed as number (percentage) and compared between groups with the χ² or Fisher’s exact test. All statistical analyses were performed using Triomphe software [18] and Stata software (StataCorp, 2005; Stata statistical software: release 9.0. College Station, TX, USA). For all analyses, a p-value of less than 0.05 was considered to be the threshold of significance.

Results

A coronary MDCT investigation was performed in 42 type 2 diabetic patients and a total of 630 coronary segments were included in the analysis. The general characteristics of the study population are summarized in Table 1. Diabetes in our series was treated as in the overall diabetic population; all patients had oral antidiabetic medication or insulin therapy. No coronary calcifications were present in 15 of 42 (35.7%) patients, whereas calcified plaques were noted in 27 of 42 (64.3%) patients (Fig. 1). Subsequent contrast-enhanced coronary CT angiography revealed the presence of non-calcified plaques in four of 15 (26.7%) patients who had no coronary calcifications. In these patients, non-calcified plaques were the only manifestation of CAD. The overall prevalence of patients with non-calcified plaques as the only manifestation of CAD was 9.5% (4/42 patients). In patients with coronary calcifications, additional non-calcified plaques were detected in six of 27 (22.2%) patients.

In summary, CAD because of the presence of calcified or non-calcified plaques was detected in a total of 31 (73.8%) patients. In the remaining 11 (26.2%) patients, CAD was completely absent on MDCT. The proportion of men was significantly higher in patients with CAD (sex-ratio 3.4) and in patients with calcified plaques (sex-ratio 4.2) compared with in patients without CAD (sex-ratio 0.57) and without calcified plaques (sex-ratio 0.77), respectively. Patients with CAD, calcified plaques or non-calcified plaques were characterized by slightly higher total cholesterol and low-density lipoprotein concentrations. In addition, patients with CAD or calcified plaques were characterized by a trend of having a greater cIMT than patients with non-calcified plaques. Finally, the mean glycosylated haemoglobin level was significantly higher in patients with CAD than in those without CAD (mean 8.90 ± 1.29 g/L vs 7.86 ± 0.95 g/L; p < 0.05).

Table 1 summarizes the clinical and biological characteristics of diabetic patients with and without CAD in more detail. A total Agatston calcium score of zero or 1–10 was observed in 15 (35.7%) and no (0%) patients, respectively. A calcium score of 11–100 was observed in nine (21.4%) patients, while a score of 101–400 or greater than 400 was identified in seven (16.7%) and 11 (26.2%) patients, respectively. The presence of obstructive disease was noted

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Data</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>62.1 ± 7.9</td>
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<tr>
<td>Duration of diabetes (years)</td>
<td>14.2 ± 8.4</td>
</tr>
<tr>
<td>Smoking</td>
<td>5 (11.9)</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>32 (76.2)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>83.5 ± 13.4</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>101 ± 11.2</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.1 ± 4.7</td>
</tr>
<tr>
<td>Plasma triglycerides (g/L)</td>
<td>1.46 ± 0.95</td>
</tr>
<tr>
<td>Total cholesterol (g/L)</td>
<td>1.80 ± 0.38</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol (g/L)</td>
<td>0.54 ± 0.17</td>
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<tr>
<td>Low-density lipoprotein cholesterol (g/L)</td>
<td>0.98 ± 0.28</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>3.42 ± 3.24</td>
</tr>
<tr>
<td>Carotid intima-media thickness (mm)</td>
<td>0.843 ± 0.133</td>
</tr>
<tr>
<td>Glycosylated haemoglobin (g/L)</td>
<td>8.13 ± 1.57</td>
</tr>
<tr>
<td>Microalbuminuria</td>
<td>13 (30.9)</td>
</tr>
<tr>
<td>Creatinine clearancea (mL/min)</td>
<td>98.3 ± 23.9</td>
</tr>
</tbody>
</table>

Results are given as mean ± standard deviation or n (percentage).

a According to Cockroft and Gault formula.

Figure 1. Prevalence of calcified and non-calcified plaques in the study group. CAD: coronary artery disease; CT: computed tomography.
in nine of 11 patients with a high calcium score (> 400). The mean number of diseased segments and the mean number of segments containing calcified plaques were significantly higher in men than in women: 4.53 ± 1.8 versus 1.39 ± 1.78 (p < 0.05) and 3.46 ± 3.3 versus 0.78 ± 1.18 (p < 0.05), respectively. In the 31 (73.8%) patients with CAD, 147 (31.6%) coronary segments with plaques were observed among a total of 465 coronary segments. Of the segments containing plaques, 114 (77.5%) showed non-obstructive CAD and 33 (22.5%) showed obstructive CAD. Single-vessel disease was observed in 6/12 (50%) patients with obstructive CAD; the other six (50%) patients with obstructive CAD had multivessel disease. Most calcified (n = 96; 88.9%) and non-calcified (n = 10; 90.9%) plaques resulted in lumen narrowing of less than 50%, whereas most mixed plaques (n = 20; 71.4%) resulted in lumen narrowing in more than 50%. Of the segments containing non-obstructive plaques, 85 (74.6%) showed non-extensive and 29 (25.4%) showed extensive CAD, whereas six (18.2%) and 27 (81.8%) segments with obstructive plaques contained non-extensive and extensive plaques, respectively. In general, non-calcified plaques were observed in 11 (7.5%) segments, mixed plaques in 28 (19%) segments, and calcified plaques in 108 (73.5%) segments. Most segments with calcified (n = 64; 59.3%) or mixed (n = 16; 57.2%) plaques were distal segments, whereas most segments with non-calcified plaques (n = 7; 63.6%) were proximal segments. Table 3 summarizes the distribution of coronary plaques according to their characteristics.

### Discussion

As CAD is the major cause of the morbidity, mortality and medical cost of diabetes [19], early diagnosis of CAD to prevent progression and clinical events has intuitive appeal. Several studies have documented the ability of MDCT to visualize coronary atherosclerotic plaques in vivo [20—24]. Possible applications in the risk stratification of asymptomatic individuals have been discussed but require close scrutiny of the actual ability of MDCT to detect non-stenotic coronary plaques. Our study shows, firstly, that in asymptomatic subjects considered at high risk of CAD because of type 2 diabetes and the concomitant presence of a significant carotid atherosclerotic plaque, CAD is completely absent on MDCT in a high proportion (26.2%) of patients. These patients were characterized by a trend of having lower total cholesterol and low-density lipoprotein cholesterol concentrations and a smaller cIMT. This observation supports the fact that cIMT is a marker of atherosclerosis burden, as reported previously [25], and that increased cIMT in diabetes is associated with risk factors for atherosclerosis, and even with coronary and cerebral vascular events [26]. In addition, in the 31 (73.8%) patients with CAD, 147 (31.6%) coronary segments with plaques were observed among a total of 465 coronary segments, meaning that atheromatous burden per patient was slightly low and that our study population was at lower risk than was thought. However, the control of diabetes was statistically worse in patients with CAD than in patients without CAD (mean glycosylated haemoglobin level 8.90 ± 1.29 vs 7.86 ± 1.57, respectively; p < 0.05), which may represent a confounding factor in our study.

Sex was associated significantly with increased CAD and CAC in our study. Age and smoking were also associated with increased CAD and CAC, but the association did not reach statistical significance, probably because of the small number of patients. The volume of CAC is an excellent marker of overall atherosclerotic burden [27,28]. Calcium deposition occurs only when atherosclerosis is present and more severe plaques tend to have a greater amount of calcium [29]. Therefore, higher CAC scores are associated with a higher likelihood of significant coronary stenosis, whereas the absence of CAC is associated with a very low likelihood of obstructive CAD. In our population-based study, 16 of 42 (38.1%) asymptomatic subjects had some evidence of CAC, whereas 11 of 42 (26.2%) had a CAC score greater than 400.

### Table 2  Clinical and biological characteristics of diabetic patients with and without coronary artery disease.

<table>
<thead>
<tr>
<th></th>
<th>Patients with CAD (n = 31)</th>
<th>Patients without CAD (n = 11)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.6 ± 7.5</td>
<td>60.7 ± 8.7</td>
<td>0.55</td>
</tr>
<tr>
<td>Men</td>
<td>24 (77.4)</td>
<td>4 (36.4)</td>
<td>0.024</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>13.9 ± 8.4</td>
<td>15.1 ± 9.5</td>
<td>0.81</td>
</tr>
<tr>
<td>Smoking</td>
<td>4 (12.9)</td>
<td>1 (9.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>23 (74.2)</td>
<td>9 (81.8)</td>
<td>0.71</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>101.6 ± 11.5</td>
<td>99.4 ± 11.2</td>
<td>0.71</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28.6 ± 4.1</td>
<td>30.6 ± 6.2</td>
<td>0.56</td>
</tr>
<tr>
<td>Plasmatic triglycerides (g/L)</td>
<td>1.47 ± 0.99</td>
<td>1.40 ± 0.82</td>
<td>1.00</td>
</tr>
<tr>
<td>Total cholesterol (g/L)</td>
<td>1.84 ± 0.38</td>
<td>1.68 ± 0.19</td>
<td>0.20</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol (g/L)</td>
<td>0.54 ± 0.17</td>
<td>0.54 ± 0.15</td>
<td>0.62</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol (g/L)</td>
<td>1 ± 0.29</td>
<td>0.91 ± 0.26</td>
<td>0.30</td>
</tr>
<tr>
<td>C-reactive protein (mg/L)</td>
<td>3.32 ± 3.45</td>
<td>3.48 ± 2.67</td>
<td>0.50</td>
</tr>
<tr>
<td>Carotid intima-media thickness (mm)</td>
<td>0.855 ± 0.143</td>
<td>0.809 ± 0.096</td>
<td>0.39</td>
</tr>
<tr>
<td>Glycosylated haemoglobin (g/L)</td>
<td>8.90 ± 1.29</td>
<td>7.86 ± 1.57</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Results are given as mean ± standard deviation or n (percentage). p < 0.05 was statistically significant.

CAD: coronary artery disease
### Table 3

<table>
<thead>
<tr>
<th>Plaque Type</th>
<th>Proximal&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Distal&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcified plaques (&lt;n=108; 73.5%)</td>
<td>44 (40.7%)</td>
<td>64 (57.2%)</td>
</tr>
<tr>
<td>Mixed plaques (&lt;n=28; 19%)</td>
<td>3 (1.0%)</td>
<td>6 (5.1%)</td>
</tr>
<tr>
<td>Non-calcified plaques (&lt;n=11; 7.5%)</td>
<td>0 (0.0%)</td>
<td>1 (0.8%)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Segments 1, 5, 6 and 11.

<sup>b</sup> Segments 2, 3, 4, 7, 8, 9, 10, 12, 13, 14 and 15.

This proportion is higher than in non-diabetic patients, as reported by Schurgin et al. [30], who screened a cohort of 139 asymptomatic diabetic patients and matched control subjects. They concluded that extensive CAC (calcium score > 400) was more prevalent (25.9%) in diabetic patients than non-diabetic control subjects both without (7.2%) and with (14%) traditional risk factors. These findings are of interest, as a calcium score higher than 400 is associated with a high risk of myocardial perfusion impairment [31] and a high risk of any cardiovascular event in the short term [32]. In our study, the presence of obstructive disease was noted in nine of 11 patients with a high calcium score (> 400). In fact, 27 of 33 (81.8%) obstructive plaques were extensive.

Several studies have shown that the coronary artery calcium score is valuable in identifying patients with a high likelihood of inducible myocardial ischaemia [31,33]. These studies have observed consistently that the likelihood of ischaemia in patients with a calcium score less than 100 is negligible, whereas those with a score greater than or equal to 400 have a relatively high likelihood of inducible ischaemia. Anand et al. [34] studied asymptomatic patients with diabetes and confirmed the higher incidence of inducible ischaemia in patients with higher calcium scores. Nearly one third of those patients had a calcium score higher than 400, 28% of whom had large ischaemic defects. On the other hand, our prospective study indicated that mixed and non-calcified coronary plaques and their characteristics can be detected accurately with 40-slice CT angiography. In addition, our study showed that non-calcified coronary plaques, alone or in combination with calcifications, can also be detected in a high proportion of asymptomatic type 2 diabetic patients. Furthermore, our study demonstrated that non-calcified coronary plaques were the only manifestation of CAD in 9.5% of the study population (or in 26.7% of patients with a negative score for coronary calcifications). These findings demonstrate that calcium scoring with a prospective scan without contrast enhancement is not sufficient to determine the presence of coronary plaques. Patients with a high cardiovascular risk, as in our study, should have contrast-enhanced CT coronary angiography in cases of negative scan for calcium. Indeed, in a recent population study of 70 asymptomatic patients with type 2 diabetes, Scholte et al. [35] showed a relatively high proportion (41%) of non-calcified plaques detected by MDCT. Importantly, a calcium score less than 10 did not exclude CAD in these patients. The author concluded that MDCT might be a useful technique for identifying CAD in asymptomatic patients with type 2 diabetes with incremental value over calcium scoring.

The identification of patients at increased risk of an ischaemic and potentially fatal cardiac event is a difficult task in cardiovascular medicine. Despite extensive studies and the development of several risk-prediction models, traditional cardiovascular risk factors fail to predict the development of CAD in a large group of patients [36]. MDCT angiography has been introduced as a noninvasive technique for the reliable detection of coronary stenosis in addition to quantification of calcified plaque burden [37]. With the improved spatial resolution, CT angiography also allows for the detection of mixed and non-calcified coronary plaques. Sensitivity and specificity of 78% and 87–92%, respectively, have been reported by Leber et al. [13] and Achenbach et al. [11] for 16-slice CT for the detection of...
non-calcified plaques, alone or in combination with calcified plaques, compared with intravascular ultrasound. Of interest, patients with non-calcified plaques were characterized by a trend of having higher total cholesterol, low-density lipoprotein cholesterol and CRP levels. Although no association between CRP and the calcified plaque burden was found in the Study of Inherited Risk of Coronary Atherosclerosis [38], Hausleiter et al. [39] demonstrated that CRP values were significantly higher in patients with non-calcified plaques and that these elevated values correlated with earlier non-calcified stages of atherosclerotic plaque development, supporting the association of the inflammatory burden with increased cardiovascular risk [40].

Noninvasive atherosclerosis imaging techniques might further enhance the detection and management of patients at risk of coronary heart disease, but they are not perfect. It is recognized that a 'detection gap' exists, defined as the difference between coronary heart disease cases or events currently detected and the total burden of disease or events among the population [41]. This leaves room for the introduction of the noninvasive atherosclerosis CT imaging technique. Romeo et al. [42] used MDCT in 168 asymptomatic high-risk subjects (age 60 ± 7 years) and found that the prevalence of significant CAD (> 50% diameter stenosis) was 27%. Most of these subjects were diabetic (60%), 36% of whom had evidence of significant CAD. These subjects might benefit from coronary revascularization, although studies demonstrating that revascularization might improve prognosis in asymptomatic subjects are lacking. Well-designed studies need to be conducted to provide substantial evidence that CT coronary imaging has an independent predictive value in addition to common risk factors.

Of interest, a very high proportion of mixed plaques (71.4%) were obstructive in our study compared with calcified (11.1%) or non-calcified (9.1%) plaques. Accordingly, calcium scores may underestimate total coronary plaque burden to a higher extent in patients with diabetes. MDCT coronary angiography may therefore have substantial incremental value over coronary calcium scoring, although this concept needs further study. In our study, MDCT coronary angiography allowed the identification of two phenotypically different groups of diabetic patients with or without non-calcified plaques despite an identical cardiovascular risk (clinical and biological characteristics not statistically different). Nevertheless, Pundziute et al. [15] reported a significantly lower proportion of mixed coronary plaques in patients with diabetes (23%) than in patients without diabetes (38%), suggesting a more rapid development of atherosclerosis in the presence of diabetes, with faster progression from non-calcified lesions to completely calcified lesions. The proportion of mixed coronary plaques in patients with diabetes was quite similar in our study (19%). However, the most frequently obstructive character of mixed plaques was not obvious in this study. In addition, most segments with calcified (59.3%) or mixed (57.2%) plaques were distal segments, whereas most segments with non-calcified plaques (63.6%) were proximal segments. These findings could be attributed to better visualization of non-calcified plaques in proximal coronary vessels than in smaller distal segments on CT angiography.

Our study had some limitations. Firstly, this population-based study was biased, so the prevalence of coronary plaques can only be valid in this particular population and probably cannot be extended to the French standard diabetic population. Notably, all patients had at least one carotid atherosclerotic plaque at inclusion, considering arbitrarily and intuitively that it was an additional cardiovascular risk factor. Secondly, examinations were performed at a single time point and were not repeated over time. Also, MDCT angiograms were evaluated visually, as no reliable quantitative algorithms are currently available. Therefore, long-term follow-up data, not yet available in our study, are needed to determine whether the MDCT observations can provide prognostic information and be of potential use in the identification of diabetic patients at different levels of cardiovascular risk. Because of the relatively small number of patients, we could not draw definitive conclusions on the prevalence of coronary plaques by CT in our diabetic population and we could not evaluate significantly the effect of risk factors on coronary plaque characteristics. Further studies with larger populations should be conducted to clarify this important issue, as well as to confirm the predictive value of mild calcifications and non-calcified plaques for hard coronary events, particularly in type 2 diabetic patients without symptoms. On the other hand, the visualization of non-calcified plaques by MDCT is limited by plaque and vessel size; smaller plaques located predominantly in smaller coronary arteries may therefore be difficult to identify accurately with the current generation of CT scanners. Finally, the possible benefits of coronary plaque detection by MDCT need to be weighed against the potential hazards associated with the radiation dose delivered to the chest and the necessity for administration of intravenous contrast media.

Conclusions

Our study provides the first assessment of the accuracy of MDCT in detecting and quantifying coronary atherosclerotic plaques in a subgroup of particular asymptomatic type 2 diabetic patients at high risk of coronary disease. Notably, CT seems to detect a high proportion of coronary plaques compared with conventional angiography in these specific patients. However, the precise role of MDCT in the diagnostic work-up of patients with suspected CAD in relation to existing noninvasive functional tests is not yet established and, to date, the technique is not indicated clinically for coronary plaque detection in asymptomatic diabetic patients.

References


[40] Ridker PM, Cook N. Clinical usefulness of very high and very low levels of C-reactive protein across the full range of Framingham Risk Scores. Circulation 2004;109:1955–9.
