Assessment of coronary artery stent restenosis by 64-slice multi-detector computed tomography

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KEYWORDS
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Aims We investigated the feasibility of assessing coronary artery stent restenosis using a new generation 64-slice multi-detector computed tomography-scanner (MDCT) in comparison to conventional quantitative angiography.

Methods and results MDCT was performed in 64 consecutive patients (mean age 58 ± 10 years) with previously implanted coronary artery stents (102 stented lesions: mean stent diameter 3.17 ± 0.38 mm). Each stent was classified as 'evaluable' or 'unevaluable', and in evaluable stents, the presence of in-stent restenosis (diameter reduction ≥50%) was determined visually. Results were verified against invasive, quantitative coronary angiography. Fifty-nine stented lesions (58%) were classified as evaluable in MDCT. The mean diameter of evaluable stents was 3.28 ± 0.40 mm, whereas the mean diameter of non-evaluable stents was 3.03 ± 0.31 mm (P = 0.0002). Overall, six of 12 in-stent restenoses were correctly detected by MDCT [50% sensitivity (confidence interval 22–77%)] and in 51 of 90 lesions, in-stent restenosis was correctly ruled out [57% specificity (confidence interval 46–67%)]. In evaluable stents, six of seven in-stent restenoses were correctly detected, and the absence of in-stent stenosis was correctly identified in 51 of 52 cases [sensitivity 86% (42–99%) and specificity 98% (88–100%)].

Conclusion Stent type and diameter influence evalubility concerning in-stent restenosis by MDCT. The rate of assessable stents is low, but in evaluable stents, accuracy for detection of in-stent restenosis can be high.

Introduction

The clinical incidence of restenosis after coronary stent implantation is ~20–35% for bare metal stents and 5–10% for drug-eluting stents,1–7 but it can be higher in certain subsets of lesions such as long stenoses, bifurcation lesions, or lesions in small coronary arteries.6–8 Given the high number of patients who receive coronary artery stents, a non-invasive tool for the reliable detection of in-stent restenosis would be clinically useful. Standard non-invasive techniques, such as stress testing, lack sufficient sensitivity and specificity.9 Thus, there has been growing interest in the use of multi-detector computed tomography (MDCT) for the assessment of coronary artery stents. Sixteen-slice and 64-slice MDCT have been shown to permit the detection of coronary artery stenoses in the native coronary arteries with sensitivities and specificities up to 99%,10–13 but did not show sufficient spatial and temporal resolution for the detection of in-stent restenosis. In five studies performed with 16- and 40-slice MDCT and including 42 to 232 stents, up to 77% of stents were considered 'unevaluable' and even in the evaluable stents, sensitivities and specificities for the detection of in-stent restenosis were as low as 54%.21–25 Two studies (29 and 75 patients) investigated the use of 16- and 64-slice CT for the assessment of stents in the left main coronary artery and found lower rates of unevaluable stents (7 and 5%).26,27 In both studies, all in-stent restenoses were detected by MDCT. The mean diameter of the stents was 3.9 mm in both studies, which indicated that the limited spatial resolution of 16-slice MDCT may be one of the reasons for the low number of evaluable stents in the other coronary arteries.

Sixty-four-slice MDCT has higher spatial and temporal resolution than previous scanner generations, but its accuracy for detection of in-stent restenosis has not been reported. We therefore investigated 64 consecutive patients with 102 stented lesions to systematically evaluate the method’s potential to assess coronary artery stents of various types and sizes concerning the presence of in-stent restenosis.

Methods

Sixty-four consecutive patients with previous stent implantation (102 stented lesions) who were scheduled for invasive coronary angiography were included in the study. If two stents were contiguously implanted in one lesion, they were considered as one single...
stent (in all lesions with two implanted stents, the stents were of equal type and diameter).

Forty-one patients were male and 23 were female, the mean age was 58 ± 10 years. Table 1 lists details of the implanted stents. The mean time interval from stent implantation to inclusion in the study was 13.5 ± 16.4 months (4–70 months).

Stent-in-stent implantation and renal failure, known allergy to contrast agent, possible pregnancy, and non-sinus rhythm were exclusion criteria for the study. All coronary artery stents in native or coronary bypass vessels were included, and stent type and nominal stent diameter were documented. All patients gave written informed consent to the study procedure and the study was approved by the institutional review board.

Patients with a heart rate greater than 60 b.p.m. received 100 mg of atenolol orally 45 min before MDCT. If the heart rate remained above 60 b.p.m. at the time of the MDCT scan, up to four doses of 5 mg metoprolol were given intravenously. Mean heart rate during the MDCT scan was 60 ± 5 b.p.m. (range: 49–64 b.p.m.). All patients received a total dose of 0.8 mg isosorbide dinitrate sublingually before the MDCT examination.

Images were acquired using a 64-slice MDCT scanner (Somatom Sensation 64, Siemens Medical Solutions, Forchheim, Germany), with 64 × 0.6 mm collimation, 330 ms rotation time, and a table feed of 3.8 mm per rotation. The contrast agent transit time was measured using a test bolus injection (10 mL contrast agent, followed by 50 mL saline solution, all at a flow rate of 5 mL/s) as reported previously. For visualization of the coronary arteries and stents, 55–75 mL of contrast agent (370 mg iodine/mL) was injected intravenously at 5 mL/s, followed by 50 mL of saline solution. Tube voltage was 120 kV and effective tube current was 850 mAs. Tube current modulation was used in 34 patients with a heart rate of >60 b.p.m. to reduce radiation exposure during systole. In patients with a heart rate of greater than 60 b.p.m., tube current modulation was deactivated to allow maximal flexibility in choosing image reconstruction intervals.

Reconstructions were obtained at 70% of the R–R interval using a sharp reconstruction kernel (B46f), with a slice thickness of 0.6 mm and increment of 0.3 mm. If the data set showed motion artefact, additional reconstructions were performed in 5% decrements (65%, 60%, 55%, …) until a data set free of motion artefact was obtained. This included data sets reconstructed in systole, if diastolic data sets showed motion artefact. If no data set was entirely free of motion artefact, the data set with best image quality in the sets showed motion artefact. If no data set was entirely free of artefact, the data set with best image quality in the sets showed motion artefact. If no data set was entirely free of artefact, the data set with best image quality in the sets showed motion artefact. If no data set was entirely free of artefact, the data set with best image quality in the sets showed motion artefact. If no data set was entirely free of artefact, the data set with best image quality in the sets showed motion artefact. If no data set was entirely free of artefact, the data set with best image quality in the sets showed motion artefact.

MDCT data sets were analysed on dedicated workstations (Leonardo®, Siemens Medical Solutions). Review of the original transaxial images, oblique multi-planar reconstructions (MPRs), and curved MPR were used to evaluate the implanted coronary stents concerning the presence of in-stent restenosis (Figure 1). Two readers experienced in cardiac MDCT and blinded to the patients’ clinical history as well as the stent type and dimensions jointly analysed all implanted coronary artery stents in consensus. In a first step, each stent was classified as ‘evaluable’ or unevaluable. A stent was classified as unevaluable if blurring of the stent contours or image noise prevented clear separation of the metal stent structure and the in-stent lumen. In a second step, evaluable stents were visually classified as to the presence or absence of in-stent restenosis (diameter reduction >50%).

Invasive coronary angiography was performed 1–20 days after MDCT scanning. After intracoronary injection of 0.2 mg of isosorbide dinitrate, standardized projections showing the stented segment in at least two projections were obtained. Invasive angiograms were evaluated off-line using quantitative coronary angiography (QCA) software (QuantCor®, Siemens Medical Solutions) by an experienced observer unaware of MDCT results. A significant in-stent restenosis was classified if a diameter reduction of 50% or more when compared with the original stent diameter was present.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for evaluable stents, for stents with a diameter >3.0 mm, equal to 3.0 mm, and <3.0 mm as well as per patient (detection of at least one in-stent stenosis per patient, with unevaluable stents classified as having in-stent stenosis). Confidence intervals were calculated using the efficient-score method (corrected for continuity). As no patient had more than one lesion with in-stent stenosis, correction for in-patient correlation was not performed.

χ² test was used to compare the rate of unevaluable stents depending on heart rate and stent type. Mean diameters of evaluable and unevaluable stents were compared using the Mann–Whitney U test. All tests were two-tailed and a P-value less than 0.05 was considered significant.

A sample size of 100 stented lesions was determined under the assumption of a restenosis rate of 20% in order to be able to prove a sensitivity of at least 75% of MDCT for detection of in-stent stenosis with a power of 75%.

### Results

Eighty-four patients were initially screened for inclusion in the study. Twenty could not be included because of elevated serum creatinine level (>1.5 mg/dL, n = 8), atrial fibrillation (n = 7), previous stent-in-stent implantation (n = 2), or because they refused participation (n = 3), so that 64 patients underwent 64-slice MDCT.

Fifty-nine of all 102 stented lesions (58%) were classified as evaluable in MDCT. The mean diameter of stents classified as unaevaluable was 3.03 ± 0.31 mm (range: 2.5–4.0 mm), whereas the mean diameter of evaluable stents was 3.28 ± 0.40 mm (range: 2.75–5.0 mm, P = 0.0002). Of all 13 stents with a diameter of <3.0 mm, only one stent (2.75 mm diameter) was classified as evaluable (and correctly determined to be free of restenosis). Thirty-three of all 57 stents with a diameter of 3.0 mm and 25 of 32 stents with a diameter >3.0 mm were classified as evaluable. Motion artefacts were visually detectable in 15 stents, which were classified as unaevaluable (Figure 2). Nineteen of 46 stents in patients with a heart rate ≤60 b.p.m. and 24 of 36 stents in patients with a heart rate >60 b.p.m. were classified as unaevaluable (P = 0.08).

Stent type had an influence on evaluable. Of all 31 stents with a diameter ≥3.0 mm that were classified as unaevaluable, 30 were of the BxSonic® (n = 20), or Cypher® type (n = 10), both share the same strut width with a strut thickness of 0.14 mm. In comparison, only one of nine Taxus® stents, which have strut thickness of 0.13 mm, was classified as unaevaluable (P = 0.001 for Cypher in comparison with Taxus and 0.03 for BxSonic in comparison with Taxus).

Overall, 12 out of 102 stented lesions showed significant in-stent stenosis in QCA. Six of these were correctly detected by MDCT (overall sensitivity 50%, confidence

### Table 1

<table>
<thead>
<tr>
<th>Type of stent</th>
<th>n</th>
<th>Mean diameter (mm)</th>
<th>Evaluable (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BX Sonic®</td>
<td>62</td>
<td>3.24</td>
<td>38 (61)</td>
</tr>
<tr>
<td>Cypher®</td>
<td>28</td>
<td>2.96</td>
<td>10 (36)</td>
</tr>
<tr>
<td>Taxus®</td>
<td>9</td>
<td>3.17</td>
<td>8 (89)</td>
</tr>
<tr>
<td>Othera</td>
<td>3</td>
<td>4.00</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>102</td>
<td>3.20</td>
<td>59 (58%)</td>
</tr>
</tbody>
</table>

*Other stents: 2 × Vision® (diameters 3.0 and 4.0 mm) and 1 × Lekton® (diameter 6.0 mm).
Figure 1 Patient with a BX Sonic stent (3.0/18 mm) in the left circumflex coronary artery. (A) MPR showing the stent in MDCT, without restenosis (arrows indicate proximal and distal ends of stent). (B) Curved MPR showing the LM (arrowhead) and left circumflex coronary artery. Severe atherosclerosis is seen, as well as the stent without in-stent restenosis (arrows indicate proximal and distal stent borders). (C) Invasive coronary angiogram. The stent (two arrows indicate stent position) does not display in-stent restenosis (arrowhead, left main coronary artery).

Figure 2 Stents classified as unevaluable. (A) Stent of type BxSonic (2.5/18 mm) implanted in the RCA (arrows indicate proximal and distal ends of stent) of a patient with previous bypass surgery. Owing to artefacts caused by the dense stent material, the assessment of the lumen within the small stent is not possible. (B) Corresponding invasive coronary angiogram. No restenosis is present. (C) Stent of type BxSonic (3.5/13 mm) in the proximal RCA (small arrows indicate proximal and distal stent borders). Owing to artefacts caused by motion, assessment of the coronary lumen within the stent was not considered possible. (D) Corresponding invasive coronary angiogram. No restenosis is present. Arrows indicate stent position.
interval 22–77%). Fifty-one of 90 stented lesions without restenosis were correctly classified by MDCT (overall specificity 57%, confidence interval 46–67%).

In the 59 evaluable stented lesions, MDCT correctly detected six of seven in-stent restenoses (sensitivity 86%, confidence interval 42–99%) and correctly ruled out the presence of in-stent restenosis in 51 of 52 cases (specificity 98%, confidence interval 88–99%). PPV was 86% (confidence interval 42–99%) and NPV was 98% (confidence interval 88–99%) (Table 2; Figures 3 and 4).

Table 2  Number of evaluable stented lesions in MDCT, and for evaluable stented lesions, accuracy for detection of restenosis in comparison with QCA

<table>
<thead>
<tr>
<th>Number</th>
<th>Evaluable (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive predictive value (%)</th>
<th>Negative predictive value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stents</td>
<td>102</td>
<td>59 (58)</td>
<td>86 (42–99)</td>
<td>98 (88–100)</td>
<td>86 (42–99)</td>
</tr>
<tr>
<td>≥3.5 mm</td>
<td>32</td>
<td>35 (78)</td>
<td>100 (5–100)</td>
<td>100 (83–100)</td>
<td>100 (5–100)</td>
</tr>
<tr>
<td>3.0 mm</td>
<td>57</td>
<td>33 (58)</td>
<td>83 (36–99)</td>
<td>96 (79–99)</td>
<td>83 (36–99)</td>
</tr>
<tr>
<td>&lt;3.0 mm</td>
<td>13</td>
<td>1 (8)</td>
<td>—</td>
<td>100 (5–100)</td>
<td>—</td>
</tr>
<tr>
<td>Per patient*</td>
<td>64</td>
<td>33 (52)</td>
<td>83 (36–99)</td>
<td>46 (33–60)</td>
<td>10 (5–30)</td>
</tr>
</tbody>
</table>

Confidence intervals are given in parentheses.

*In the per-patient analysis, unevaluable stents were regarded as having significant in-stent restenosis in MDCT.

Figure 3  Patient with a stent in the proximal left anterior descending and distal RCA. (A) Transaxial MDCT image of the stent (BxSonic 3.5/8 mm) implanted in the proximal left anterior descending coronary artery (arrows). No in-stent restenosis. (B) Corresponding invasive coronary angiogram (arrows indicate stent position). (C) Transaxial MDCT image of the stent implanted in the distal RCA (BxSonic 3.0/18 mm). A restenosis (arrowhead) was detected in the proximal section of the stent. Arrows indicate proximal and distal borders of stent. (D) Corresponding invasive coronary angiogram. A stenosis extending proximal to and into the stent can be seen (arrows indicate stent position).
Owing to artefacts caused by metal, the visualization of the lumen within coronary artery stents by MDCT is more challenging than the assessment of the native coronary arteries. Although accuracies reported for the assessment of coronary artery stenoses in non-stented arteries by 16- and 64-slice MDCT are high, only a small number of studies have evaluated the value of MDCT to detect in-stent restenosis. In those studies, most performed by 16-slice CT, the rate of evaluable stents was low and even in assessable stents—with the exception of large stents implanted in the left main coronary artery—sensitivity for the detection of in-stent restenosis was only between 54 and 83%. Next to the type of stent, as shown in phantom studies, also, there have been indications that stent diameter plays a significant role. In the study by Schuijf et al., which included only stents implanted in the left main coronary artery—with a large mean diameter of 3.9 mm—all stents were assessable and all four restenoses were detectable by CT. In another study by the same group—with 232 included stents, the largest such study to date—49% of stents with a diameter \( \leq 3.0 \) mm and 18% of stents with a diameter \( > 3.0 \) mm could be evaluated. Gaspar et al. found that with 40-slice CT (which has a similar spatial resolution to the 64-slice scanner), all of 111 stents were evaluable (with a mean stent diameter of 3.3 mm), but only 72% of in-stent restenoses were detected.

Our series confirms that even with improved scanner technology, evaluation of implanted coronary artery stents remains challenging. Similar to the earlier studies performed by 16- and 40-slice MDCT, we also found a significant influence of stent diameter on evaluability, with 3.5 mm being a threshold below which the rate of evaluable stents is very low. Stent type was associated with evaluability because Taxus stents (with a strut thickness of 0.13 mm) were evaluable at a substantially higher rate than those with a strut thickness of 0.14 mm (Cypher and BxSonic). After exclusion of all unevaluable stents, sensitivity for the detection of in-stent restenosis was 86% (with a specificity of 98%), which indicates that clinical applications might be possible if the problem of stent evaulability was solved. However, the high frequency of cases with un-interpretable image quality—an overall rate of 42% in our series and 32% even in patients with stents of \( > 3 \) mm diameter—precludes the application of MDCT for coronary angiography in unselected patients with implanted coronary artery stents.

Although we report on the first series of consecutive patients with implanted coronary artery stents evaluated by 64-slice CT to date, the study suffers several limitations. The overall rate of stents with a significant stenosis was low, with only 12 restenoses in 102 stented lesions and only seven restenoses in evaluable stents. The low rate of restenosis was below our assumptions for the power calculation and led to wide confidence intervals. The fact that 97% of included stents were of the type Taxus, Cypher, or BxSonic constitutes an advantage of our study, because it permits more systematic assessment of the influence of stent diameter, but also limits our results to only a small number of all coronary stents that are commercially available. Finally, we used a simple definition of in-stent restenosis (diameter reduction \( \geq 50\% \)), although many other potential definitions, such as per-segment restenosis and late lumen loss (absolute decrease of minimal stent lumen from post-intervention to follow-up), have also been proposed and there is no straightforward correlation between any definition of in-stent stenosis and its haemodynamic relevance.

In conclusion, our study helps to identify factors that influence the assessability of coronary artery stents by 64-slice CT, namely, stent type and diameter. It shows that under certain conditions, the detection of in-stent restenosis might be possible with an accuracy that could permit clinical applications, but that the relatively high rate of assessability of stents have been identified. They include the type of stent, as shown in phantom studies. Also, there have been indications that stent diameter plays a significant role. In the study by Schuijf et al., which included only stents implanted in the left main coronary artery—with a large mean diameter of 3.9 mm—all stents were assessable and all four restenoses were detectable by CT. In another study by the same group—with 232 included stents, the largest such study to date—49% of stents with a diameter \( \leq 3.0 \) mm and 18% of stents with a diameter \( > 3.0 \) mm could be evaluated. Gaspar et al. found that with 40-slice CT (which has a similar spatial resolution to the 64-slice scanner), all of 111 stents were evaluable (with a mean stent diameter of 3.3 mm), but only 72% of in-stent restenoses were detected.

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Figure 4 Patient with two contiguous stents (both BxSonic 3.5/13 mm) implanted into the proximal segment of a venous bypass graft to the right coronary artery. (A) Curved MPR in MDCT. An in-stent stenosis can be seen (arrowheads). Arrows indicate proximal and distal ends of stents. (B) Corresponding invasive coronary angiogram that confirms in-stent restenosis (arrows indicate stent position and arrowheads indicate stenosis).
unevaluable stents currently does not allow to use MDCT for coronary angiography in unselected patients with implanted stents in coronary arteries or bypass grafts.

Conflict of interest: S.A. and A.K. have received research grants from Siemens Medical Solutions.

References


