Ischemic Heart Disease Diagnosed by 64 Slice Computed Tomography Coronary Angiography.

V Mendoza – Rodríguez, L Llerena, L Llerena, L Rodríguez, E Olivares, R Linares, L López, J Hernández, J Linares, R Álvarez

Abstract

Background Invasive coronary angiography is considered the gold standard to study the coronary tree. The noninvasive multislice computed tomography coronary angiography is an almost established coronary imaging technique improving day by day. Objectives The aim of this study was to investigate the accuracy of 64 slices computed tomography coronary angiography for assessing significant coronary stenoses in comparison with invasive coronary angiography in our center. Methods One hundred and thirty patients in whom the coronary tree was first studied by 64 slice computed tomography angiography and afterwards, by invasive coronary angiography. One hundred and eleven (86 male; mean age 57± 11 years) were enrolled. The sensitivity, specificity, predictive positive value and negative predictive value were determined in order to validate the diagnostic accuracy of multislice computed tomography for detection of significant lesions (50% or higher luminal diameter reduction) compared with invasive coronary angiography. Results The sensitivity, specificity, positive predictive value, and negative predictive value were 98%, 92%, 90%, and 98% respectively per patients and 92%, 97%, 85% and 98% respectively per artery. The diagnostic accuracy in patients with heart rate ≤ 65 beats per minute calcium scoring ≤ 400 Agatston Units and body mass index lower than 30 kg/m² were very high. Conclusions Sixty four slice computed tomography coronary angiography has a very good diagnostic accuracy in our center overall in patients with heart rate ≤ 65 beat per minutes, calcium scoring ≤ 400 Agatston Units and body mass index lower than 30 kg/m².

ABBREVIATIONS

AU: Agatston units
CS: calcium scoring
HR: heart rate
CAD: coronary artery disease
ICA: invasive coronary angiography
MSCT – CA: multislice computed tomography coronary angiography
NPV: negative predictive value
PP: predictive precision
PPV: positive predictive value
bpm: beats per minute
BMI: body mass index
LR+: positive likelihood ratios
LR-: negative likelihood ratios
DOR: diagnostic odds ratio

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death in Western nations. In 2003, CAD accounted for 37, 3% of all 2,440,000 deaths in the United States. In Cuba, 72% of heart deaths were by CAD in 2006. Early diagnostic is very important for the promotion, prevention, treatment and finally has lower mortality. The clinical and noninvasive methods (Effort ECG, ECHO, nuclear medicine) have showed little precision. The sensitivity and specificity of these methods is lower than 87 % and 77% respectively. Invasive coronary angiography (ICA) is currently the gold standard diagnostic criterion for clinical evaluation of known or suspected CAD. Approximately, only 50% of all coronary angiographies in the world are performed in conjunction with an interventional procedure, whereas the remaining procedures only for diagnostic purposes.

The risks and complications are small, but serious and potentially life – threatening or sequelae may occur,
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including arrhythmia, stroke, coronary artery dissection, and access site bleeding, thrombosis or infection (total complication rate, 1.8%; mortality rate, 0.1%).

Furthermore, catheterization induces some discomfort and mandates routine follow-up care. Therefore, ICA should be restricted to stringent clinical indications.

Because of their small size, tortuous 3-dimensional anatomy, and fast continuous motion no cut plane modality has quite achieved this task yet. Good diagnostic accuracy has been reported with the use of alternative coronary imaging modalities such as electron-beam computed tomography and magnetic resonance.

However, in comparison with magnetic resonance, contrast enhanced computed tomography coronary angiography offers a singular combination of unprecedented temporal resolution and spatial resolution required for noninvasive morphologic assessment of the coronary arteries.

One recently developed modality that may potentially complement ICA is Multislice computed tomography (MSCT), which may achieve high level of reliability and accuracy in the visualization of the coronary tree.

This technology provides promising results in the assessment of CAD, although some coronary segments are not evaluable because of motion artifacts or severe vessel wall calcification.

The 64 slice computed tomography scanner generation provides 0.4 nearly isotropic voxels in a rotation time of 0.33 s, thus increasing temporal and spatial resolution when compared with previous CT scanner types.

Recent studies with this technology have tested the sensitivity and specificity of MSCT vs ICA based on patients, vessels and segments analysis, and they have suggested that MSCT of 64 slices is highly accurate.

The aim of our study was at investigating the accuracy of 64 slice CT for assessing significant coronary stenoses in comparison with ICA in our center.

METHODS

STUDY POPULATION

One hundred thirty patients in whom their coronary tree was first studied by MSCT and afterwards by ICA, were analyzed (Figure 1). One hundred eleven (86 male; mean age 57± 11 years) were included. Nineteen were excluded.

Exclusion criteria:

Irregular rhythm (atrial fibrillation, premature ectopic complexes).

Prior surgical revascularization or stent implantation.

Image with many artifacts by body movements or inability to hold breath.

PATIENT PREPARATION

Patients not previously on beta-blocking drugs received 100 mg of atenolol for heart rates over 65 bpm one hour before the MSCT imaging. Heart rate, electrocardiogram (ECG), and blood pressure were monitored, and additional intravenous metoprolol (5 to 30 mg) was administered to achieve a target rate lower than 65 bpm. However, no patient was excluded because of a heart rate above this target.

Sublingual nitroglycerin 0.4 mg was given 5 to 7 minutes before image acquisition and all were given thorough hold breath instruction.

MSCT SCANNING PROTOCOL AND IMAGING RECONSTRUCTION

MSCT was performed using a new - generation 64 SCT system (Somatom Sensation Cardiac 64, Siemens Medical Solution, Forchheim, Germany) which has a gantry rotation time of 330 msec, a temporal resolution of 165 msec, and a spatial resolution of 0.4 mm. First calcium scoring (CS) was performed using standardized scan parameters; 64-x 1.2 mm collimation; 330 ms rotation time; table feed 3.8 mm/rotation; tube voltage 120 mV; and prospective X ray tube modulation.

The MSCT coronary angiography parameters were: 32 x 0.6 mm collimation with dual focal spots per detector row; rotation time 330 ms; table feed 3.8 mm/rotation; tube voltage 120 Mv; effective Ma 900. Estimated effective radiation dose was 13mSv for men and 18 mSv for women.

A contrast enhanced scan was obtained using 80 to 100 ml of Iopromide (Ultravist 370 mg/dl, Schering) injected through a 18 gauge needle in an antecubital vein at 5 ml/s followed by 50 to 80 ml saline chaser. A bolus tracking technique was used to synchronize the arrival of contrast in the coronary arteries, and the scan was started once the contrast attenuation in a pre-selected region of interest in the descending aorta had reached a predefined threshold of 100 to 120 Hounsfield Units.

Electrocardiographically gated datasets were reconstructed automatically at 60%, 65%, and 70% of R-R cycle length if heart rate was lower than 65 bpm and 35% to 40% R-R
length to approximate end systole if heart rate was higher than 65 bpm. Additional reconstruction windows were acquired after examination of datasets if motions artifacts were present and ectopic beats disabled.

**NONINVASIVE MSCT ANGIOGRAPHIC ANALYSIS**

Calcium scores in Agatston Units were analyzed using SYNGO software (Siemens Medical Systems; Forcheim, Germany); MSCT angiograms were analyzed on three-dimensional workstation (Aquarius, TeraRecon, San Mateo, California). Scans were analyzed by consensus of two observers with more than two year experience (VM and LRLL).

The 15 – segment American Heart Association model of the coronary tree was employed. (Figure 1).

**Figure 1**

Figure 1. Volume rendering images. American Heart Association Segmentation.

Coronary segmentation: Figure 1

Right coronary artery (RCA) proximal. RCA middle. RCA distal. Postelateral branches. Left main. Left anterior descending artery(LDA) proximal. LDA middle. LDA distal. 1st diagonal. 2nd diagonal. Left circumflex artery(LCA) proximal. LCA distal. 1st marginal branch. 2nd marginal branch. Posterior descending artery.

We considered proximal, middle and distal segments:

Proximal: 1,5,6 and 11
Middle: 2,7
Distal: 3, 8, 12 and Branches: 4, 9,10,13,14 and 15

Each lesion identified was examined using maximum intensity projection and multiplanar reconstruction techniques along multiple longitudinal axes and transversely. Patients were classified as positive for the presence of significant coronary artery disease if there was a 50% or higher stenosis in any artery visually detected by consensus.

**INVASIVE ANGIOGRAPHIC ANALYSIS**

Invasive coronary angiograms were evaluated by two observers blinded to the MSCT results(LDLL and LL). Segmental disease was analyzed in each vessel using the same 15 – segment model employed for MSCT analysis. Stenosis severity, in each segment, was classified according to the maximal luminal diameter stenosis visually detected by consensus. Lesions were examined at least in two orthogonal views.

**ANALYSIS DESIGN**

A qualitative evaluation was performed to assess the accuracy of MSCT to detect significant lumen narrowing (defined as >= 50% diameter stenosis)

The accuracy of MSCT to detect significant disease was compared to invasive quantitative coronary angiography according to the following analyses:

1. Per - patients analysis, evaluating the presence of any significant lesion in a given patient.
2. Per- artery analysis, examining the presence of significant lesion in each of the major coronary vessels (left main coronary artery, right coronary artery, left circumflex, left anterior descending artery including their main branches (diagonal, marginal obtuse, posterior descending or intermedium).
3. Per – segment analysis, examining the presence of significant lesion in proximal, middle or distal segment of major coronary vessels.

**STATISTICAL ANALYSIS**

The diagnostic performance of MSCT for detecting significant stenoses in the coronary arteries (using qualitative coronary angiography as the standard of reference) is presented as sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and precision predictive (PP). Positive likelihood ratios \( LR+ = \frac{\text{Sensitivity}}{1- \text{Specificity}} \) and negative likelihood ratios \( LR- = \frac{1- \text{Sensitivity}}{\text{Specificity}} \) were calculated. The
likelihood ratio for a positive result (LR+) is a measure of how much the odds of the disease increase when a test is positive, while the likelihood ratio for a negative result (LR-) tells how much the odds of the disease decrease when a test is negative. Thus, the combined likelihood ratios provided the diagnostic odds ratio (=Sensitivity/(1-Specificity) /((1-Specificity)/Sensitivity = true positive x true negative/false positive x false negative. The result is a ratio of the odds of a positive test result among diseased to the odds of a positive test result among non-diseased. Diagnostic odds ratio is considered as a more precise parameter for accuracy tests independent of prevalence. Moreover, prevalence in each data category (patient, artery and segment) were calculated as well.

Categorical variable are expressed by numbers and percentages and quantitative variables by mean ± standard deviation. Statistical software SPSS 13.0 for Windows was employed.

RESULTS

One hundred thirty patients were evaluated for enrollment. Nineteen were excluded: patients with post surgical revascularization status (n = 8), premature ectopic complexes (n = 5) and inability breath hold (n = 6).

A high number of enrolled patients (n = 111) had hypertension (69 %), hypercholesterolemia (53 %), and family history of CAD (58 %) (Table 1).

Table 1. Patient demographic and clinical characteristics (n=111)

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Males</th>
<th>Hypertension</th>
<th>Hypercholesterolemia</th>
<th>Diabetes melitus</th>
<th>Smoking habitus</th>
<th>Family history of CAD</th>
<th>BMI (Kgm^2/CS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>57 ± 11</td>
<td>86</td>
<td>73</td>
<td>59</td>
<td>31</td>
<td>54</td>
<td>64</td>
<td>64</td>
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<tr>
<td>0 – 10</td>
<td>38</td>
<td>37</td>
<td>37</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
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<tr>
<td>11 – 400</td>
<td>50</td>
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<td>≥ 401</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
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<td>23</td>
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<tr>
<td>≤ 65 bpm</td>
<td>82</td>
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<td>82</td>
<td>82</td>
</tr>
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</table>

CAD: coronary artery disease; bpm: beats per minute; CS: corporal surface.

Using ICA, a total of 47 patients were diagnosed as positive because significant coronary stenosis. Nonsignificant coronary stenosis (was absent) in 64 patients (Figure 2). The prevalence of significant CAD was 42,3% per patients, 16% per arteries and 5,3 % per segments.

Figure 2

Figure 2. Significant coronary stenosis diagnosed by both methods

Eighty (89/111) percent of patients were taking oral beta-
blockers as treatment. Additional beta – blocker were administered in 30% (33/111) of patients and the mean heart rate during the scan was 60 ± 9 bpm in these patients. In figure 3 is showed a patient with heart rate lower than 65 bpm who resulted a true negative by artery.

**Figure 4**
Figure 3. Computed tomography, coronary angiography and ICA in a patient with heart rate lower than 65 beats per minute

Ninety- seven percent of the arteries had nonsignificant stenosis and 92 % with significant stenosis were diagnosed as true negative and true positive respectively.

**Figure 5**
Figure 4 showed a patient who was a true positive case

Almost twenty (22/111) patients presented with one vessel disease, 12.6%, with two vessel diseases (14/111), and 9.9% with three vessel diseases (11/111).

On a per – patient analysis, MSCT had a sensitivity of 97.8% (46/47) in detecting significant coronary stenosis and a specificity of 92% (59/64). The PPV was 90% (46/51), and the NPV was 98% (59/60). One hundred percent of arteries could be analyzed. On a per – arteries basis, MSCT had a sensitivity of 92% (69/75), specificity of 97% (357/369), PPV of 85% (69/81), and NPV of 98% (357/363). On a per – segment analysis the diagnostic accuracy was very high too in this group of patients, nevertheless, the diagnostic precision in the branches was low (Table2).

**Figure 6**
Table 2. Diagnostic accuracy of coronary angiography by MSCT compared to invasive technique for detection of significant stenoses in patients, arteries and segments

<table>
<thead>
<tr>
<th>N</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>PP</th>
<th>NP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients: 111</td>
<td>46/47</td>
<td>59/64</td>
<td>46/51</td>
<td>59/60</td>
<td>195/213</td>
<td>95</td>
</tr>
<tr>
<td>Arteries:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LM</td>
<td>111</td>
<td>46/59</td>
<td>106/110</td>
<td>99/102</td>
<td>119/121</td>
<td>97</td>
</tr>
<tr>
<td>LDA</td>
<td>111</td>
<td>25/26</td>
<td>77/81</td>
<td>79/82</td>
<td>120/122</td>
<td>98</td>
</tr>
<tr>
<td>RCA</td>
<td>111</td>
<td>28/30</td>
<td>81/82</td>
<td>81/82</td>
<td>130/131</td>
<td>99</td>
</tr>
<tr>
<td>LCX</td>
<td>111</td>
<td>12/15</td>
<td>93/96</td>
<td>97/98</td>
<td>137/139</td>
<td>98</td>
</tr>
<tr>
<td>Total</td>
<td>444</td>
<td>69/75</td>
<td>357/369</td>
<td>357/363</td>
<td>426/444</td>
<td>95</td>
</tr>
</tbody>
</table>

MSCT: multislice computed tomography; LM: left main; LDA: left anterior descending artery; RCA: right coronary artery; LCX: left circumflex artery; PPV: positive predictive value; NPV: negative predictive value; P: proximal; M: medium; D: distal; B: branches; I: right; L: left; R: positive likelihood ratios; L: negative likelihood ratios; D: diagnostic odds ratio.
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Figure 7
Figures 5A and 5B show a patient with significant stenosis in left circumflex who resulted a true positive by artery.

Figure 5. A. Invasive coronary angiography. Two stenoses in left circumflex artery (arrows). B. Computed tomography coronary angiography. Maximum intensity projection (MIP) curved of left coronary artery. Two stenoses in left circumflex artery (arrows).

The diagnoses accuracy of patients with heart rate lower than 65 bpm were much better than when higher (Table 3).

Table 3. Diagnostic accuracy of coronary angiography by MSCT compared to invasive technique for detection of significant stenoses in patients and arteries according to calcium score.

<table>
<thead>
<tr>
<th>Heart rate (bpm)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>PP</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>82</td>
<td>3973 (97)</td>
<td>7/388</td>
<td>39/33 (96)</td>
<td>37/386 (97)</td>
</tr>
<tr>
<td>&gt; 65</td>
<td>29</td>
<td>1917 (94)</td>
<td>10/194 (55)</td>
<td>3/4 (75)</td>
<td>1923 (93)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 25</td>
<td>27</td>
<td>1017 (98)</td>
<td>3/4 (75)</td>
<td>1923 (93)</td>
<td></td>
</tr>
<tr>
<td>25 – 29</td>
<td>20</td>
<td>1217 (95)</td>
<td>3/4 (75)</td>
<td>1923 (93)</td>
<td></td>
</tr>
<tr>
<td>29 – 39</td>
<td>25</td>
<td>1617 (93)</td>
<td>3/4 (75)</td>
<td>1923 (93)</td>
<td></td>
</tr>
<tr>
<td>&gt; 39</td>
<td>30</td>
<td>1917 (94)</td>
<td>10/194 (55)</td>
<td>3/4 (75)</td>
<td>1923 (93)</td>
</tr>
</tbody>
</table>

MSCT: multislice computed tomography; PPV: positive predictive value; NPV: negative predictive value; PP: predictive precision; BMI: body mass index; CS: coronary score.

The sensitivity, specificity, PPV, and NPV were 94%, 50%, 84%, and 75% respectively in patients with calcium scoring higher than 401 Agatston Units (Table 3). Figure 6C and 6D show a patient who resulted a false positive case with high CS.

Figure 10
Figure 6. C. Computed tomography coronary angiography. Maximum intensity projection (MIP) curved of left coronary artery. Proximal calcified segment (arrow). D. Invasive coronary angiography of patient in figure 6C. Left coronary artery without significant stenosis (False positive).

DISCUSSION
The prevalence of CAD is very high in developed countries, that is why, early diagnostic is necessary to start the treatment and apply prophylactic measures in order to reduce morbidity and mortality. Clinical and noninvasive methods have showed little precision. In the last century, several companies have been working in developing new techniques to improve the study of the coronary arteries.

To become a clinically accepted tool for the examination of patients with suspected CAD, the main requisite for CT
coronary angiography includes the complete visualization of all epicardial coronary arteries without excluding their segments.  

Four row and 16 row MSCT Scanner have poor temporal resolution and spatial resolution that is why some segments could not be evaluated because motion artifacts, several vessels calcifications and small diameter. Nevertheless, the data reported with 64 slice CT scanner suggest a certain improvement regarding diagnostic accuracy.  

In comparison to 4 and 16 slice MSCT scanners, the 64 – slice scanner has increased slices per gantry rotation (64 vs 16) and faster gantry speed (330 ms/rotation vs 375), which are translated into superior spacial resolution (0.4 vs 0.75 mm) and temporal resolution (165 vs 188 ms). This developed scanner allows the study of coronary arteries with very high quality images, overall in patients who have been well prepared with beta blocker therapy.

The high NPV of 98% per patients and 98% per arteries in this study suggests an important role of CT coronary angiography for reliably excluding coronary artery disease. The NPV was not affected by the prevalence in this study. if MSCT - CA clearly demonstrates normal coronary arteries, invasive angiography is not necessary.

According to previous results and to ours, the diagnostic accuracy is significantly better in patients with heart rate ≤ 65 bpm, calcium scoring ≤ 400 AU and body mass index lower than 30 kg/m² SC. The number of false positive increased in patients with higher than 400 AU. The calcium appearance, secondary to atherosclerosis, generally is located at the wall of the vessels and in excess may cause blooming artifact, that is why, we may overestimate or underestimate the severity of lesions. After this results we considered that patients with CS higher than 400 AU and typical angina as high risk and very high probability of significant CAD, that is why, these patients must be sent directly to catheterism.

In our study we used beta blocker treatment, that is why, 73.9% of patients had heart rate ≤ 65 bpm, resulting in a good image quality without movement artifacts and a little group with heart rate > 65 bpm where the diagnostic precision was a little lower. Studies with a higher number of patients and with 64 slices scanner reported similar results.

When heart rate was higher than 65 beats per minute, generally appeared motion artifacts and this impaired the image quality. The right coronary artery is the most affected by the movement of the heart, secondary to higher heart rate than 65 beats per minute. The image quality improved when we made the reconstruction, immediately after systolic phase, generally, at 40% of the cardiac cycle, but it is necessary to have regular rhythm during the image captation.

As Gilbert Raff in his first experience with 70 patients, we saw too very low diagnostic precision in patients with body mass index higher than 30 kg/m² /CS. The high level of image noise in these patients degrades both spatial and contrast resolution such as the evaluation of small vessels, and noncalcified atherosclerotic changes can be dramatically impaired. In a little percent of patients with this BMI but with regular rhythm and coronary calcium scoring lower than 400 AU, we obtained better image quality increasing the contrast media volume.

The coronary branches usually have small diameter, that is why, the majority of authors had reported worse precision in the diagnostic of significant stenosis in these segments and sensitivity and PPV in this study is very low and we think that the main cause is the limited spacial resolution of this technology and may also explain the low prevalence of stenosis in these vessels.

Clearly, 64 slice CTA has limitations and should not be expected to widely completely replace invasive, catheter-based diagnostic cardiac catheterization in the foreseeable future. Spatial resolution limits the ability of CTA to provide exact, quantitative measures of severity stenosis. In addition to limitations caused by calcium and rapid coronary motion, patients at atrial fibrillation or with other arrhythmias as well as patients with contraindications to iodinated contrast agents can not be studied. Coronary CTA is furthermore a purely diagnostic tool. As opposed to invasive coronary angiography, there is no option to immediate intervention.

Dual source computed tomography with better temporal resolution allows the study of coronary tree without the use of beta blocker treatment to control heart rate. Patients with calcium scoring higher than 400 AU and obesity can be studied too without any problems. This system has a very good tool to measure the grade of stenosis and plaque characterization. Several studies had reported good results, without movement artifacts, the majority of segments could be evaluated with very high image quality and diagnostic accuracy.
LIMITATIONS OF THE STUDY

Our casuistic is not a consecutive study. Patients were selected by nonprobabilistic model. We performed invasive coronary angiography despite negative finding at MSCT because this group of patients had either persistent clinical symptoms or positive stress tests results. We think that is not ethic to study patients first with MSCT – CA and afterwards with ICA if the first result is quite normal. Both techniques have risks for patients related with radiations exposure, contrast media agents and other complications, especially with ICA.

Due to the spatial resolution, MSCT is limited for discriminating between the internal lumen and vessel wall, the analysis of stenosis was not performed in a quantitative fashion. There is a little number of significant stenosis in coronary branches and left main artery, it may to have an influence on the results.

CONCLUSIONS

Our initial results suggests that 64 MSCT has a good diagnostic accuracy in detecting significant coronary stenosis overall in patients with heart rate, calcium scoring and body mass index lower than 65 beat per minute, 400 Agatston units and 30 kg/m² /SC respectively. Due to the very high NPV of this technic, the most important application is to ruleout the presence of significant stenoses in patients with suspected coronary artery disease but high probability of negative test.

References

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