Objectives
We sought to assess the feasibility of prospective electrocardiogram triggering for achieving low-dose computed tomography coronary angiography (CTCA) in a large population.

Background
Prospective electrocardiogram triggering dramatically reduces radiation exposure for CTCA but requires heart rate (HR) control to obtain diagnostic image quality. Its feasibility in daily clinical routine has therefore remained to be elucidated.

Methods
We evaluated 612 patients consecutively referred for CTCA by 64-slice computed tomography. Intravenous metoprolol (2 to 30 mg) was administered if necessary to achieve a target HR below 65 beats/min. Image quality was assessed on a semiquantitative 4-point scale for each coronary segment.

Results
Forty-six (7.5%) patients were deemed ineligible due to irregular heart rhythm (n = 19), insufficient response to metoprolol (n = 21), renal insufficiency (n = 3), or inability to follow breath-hold commands (n = 3). Mean effective radiation dose was 1.8 ± 0.6 mSv with a diagnostic image quality in 96.2% of segments. Finally, low-dose CTCA allowed a firm diagnosis with regard to the presence or absence of coronary artery disease in 527 (86.1%) patients. Intravenous metoprolol to achieve an HR below 65 beats/min was used in 64.4% of patients. Incidence of nondiagnostic segments was inversely related to HR (r = -0.809, p < 0.001). Below an HR cutoff of 62 beats/min, only 1.2% of coronary segments were nondiagnostic.

Conclusions
Low-dose CTCA by electrocardiogram triggering is feasible in the vast majority of an every-day population. However, HR control is crucial, as an HR below 62 beats/min favors diagnostic image quality. (J Am Coll Cardiol 2011;57:332–6) © 2011 by the American College of Cardiology Foundation
the feasibility of prospectively ECG-triggered low-dose CTCA in a large, consecutive population.

Methods

Study population. A total of 612 consecutive outpatients referred for CTCA were prospectively enrolled using the common exclusion criteria for spiral CTCA (8): irregular heartbeat, allergy to iodinated contrast agent, contraindications for beta-blocking drugs, renal insufficiency, or inability to follow breath-hold commands.

The study protocol was approved by the institutional review board, and written informed consent was obtained.

Protocol. Intravenous metoprolol (Beloc, AstraZeneca, Zug, Switzerland) up to a maximum dose of 30 mg was administered if necessary in order to achieve an HR below 65 beats/min. All patients received 2.5 mg of sublingual isosorbide dinitrate (Isoket, Schwarz Pharma, Monheim, Germany) 1 to 3 min prior to scanning. All patients were scanned on a LightSpeed VCT XT scanner (GE Healthcare) with prospective ECG triggering as previously reported (3,9). Average scan length was 118 ± 22 mm, and 75 ± 12 ml of contrast agent (Visipaque 320, GE Healthcare) was applied. The smallest possible window at only 1 distinct end-diastolic phase of the RR cycle (i.e., setting the ECG trigger at 75%) was chosen (Fig. 1).

Analysis. Coronary arteries were subdivided into 16 segments (10). Segments with a diameter of at least 1.5 mm at origin were included. Image quality was semiquantitatively assessed on a 4-step scale: 1, excellent (clear segment delineation); 2, good (minor artifacts, mild blurring); 3, adequate (moderate artifacts/blurring); and 4, nonevaluative (doubling or discontinuity). As 2 readers yielded excellent interobserver agreement (κ = 0.90) in the first 100 scans (discrepancies resolved by consensus), a single reader assessed the remaining scans. Coronary artery calcium scores (CACS) were available from nonenhanced computed tomography (CT) in 313 patients.

The relationship among HR, HR variability, body mass index (BMI), CACS, and image quality was analyzed using Spearman rank correlation coefficients. A chi-square test was applied to assess the distributions of nondiagnostic segments above and below an HR cutoff.

Effective radiation dose for contrast-enhanced CTCA was estimated as the dose-length product multiplied by a conversion coefficient for the chest (k = 0.014 mSv/mGy·cm).

Results

Patient population. Baseline characteristics are given in Table 1. The reason for referral was suspected (n = 547, 89.4%) or clinical deterioration of known (n = 65, 10.6%) CAD.

We excluded 46 patients from scanning due to renal insufficiency (n = 3, 0.5%), inability to follow breath-hold commands (n = 3, 0.5%), or irregular heart rhythm (n = 19, 3.1%). Twenty-one patients (n = 3.4%) failed to reach a target HR below or equal to 65 beats/min before scanning despite administration of metoprolol (n = 21, 3.4%). Thus, 566 patients (92.5%) underwent CTCA. Additional intravenous metoprolol (mean dose: 13 ± 7 mg, range 2 to 30 mg) was administered for HR control in 394 patients (64.4%), yielding a mean HR of 56.9 ± 6.6 beats/min (range 36 to 82 beats/min) during

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Baseline Clinical Characteristics (n = 612)</th>
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<tbody>
<tr>
<td>Male, %</td>
<td>65</td>
</tr>
<tr>
<td>Age, yrs</td>
<td>Mean ± SD 59 ± 12 Range 13–85</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>Mean ± SD 26 ± 5 Range 18–49</td>
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<tr>
<td>Framingham risk score, %</td>
<td>Low 73  Intermediate 18 High 9</td>
</tr>
<tr>
<td>Cardiovascular risk factors, %</td>
<td>Obesity (BMI &gt;30 kg/m²) 15 Smoking 34 Diabetes 9 Hypertension 49 Dyslipidemia 42</td>
</tr>
<tr>
<td>Positive family history of early onset coronary heart disease</td>
<td>37</td>
</tr>
<tr>
<td>Clinical symptoms, %</td>
<td>Typical angina pectoris 15 Atypical angina pectoris 46 Dyspnea 14 Asymptomatic 29</td>
</tr>
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BMI = body mass index.
image acquisition and a mean heart rate variability of 1.9 ± 2.3 beats/min (range 0.0 to 20.1 beats/min). Mean CACS was 348 ± 670 Agatston units (range 0 to 5,477 Agatston units).

Effective radiation dose. Mean dose-length product was 130.0 ± 45.4 mGy · cm, resulting in a mean effective radiation dose exposure of 1.8 ± 0.6 mSv (range 0.8 to 4.0 mSv).

Image quality. In 566 patients, a total of 2,264 vessels and 7,814 coronary artery segments were evaluated. A total of 918 segments were missing for reasons not related to the technique. Sixteen segments were occluded, and 268 had a diameter of less than 1.5 mm at their origin. Forty additional segments had been stented and were therefore not evaluated. Thus, a total of 7,814 segments were evaluated, of which 7,516 (96.2%) were of diagnostic image quality (score 1 to 3), i.e., 4,182 (53.5%) segments with excellent image quality (score 1), 2,392 (30.6%) with good quality (score 2), and 942 (12.1%) with adequate image quality (score 3).

In 504 patients (89.0%), each individual segment was of diagnostic image quality. In the remaining 62 patients, a single, nondiagnostic segment was found in 32%, 2 nondiagnostic segments in 18%, and 3 or more nondiagnostic segments were found in the remaining patients. However, in a substantial fraction of patients (n = 23, 37%) with a nondiagnostic segment, there was at least 1 other diagnostic segment with an obstructive lesion (Fig. 2), allowing us to reach nevertheless a firm conclusion. Thus, in 93.1% of patients who underwent CTCA, a final diagnosis with regard to presence or absence of CAD could be obtained. On an intention-to-diagnose approach, low-dose CTCA turned out to be feasible in 527 patients (86.1%) (Fig. 3).

Determinants of image quality. CACS (r = −0.21, p < 0.001, SEE = 0.802) as well as BMI (r = −0.142, p < 0.001, SEE = 0.799) showed a modest inverse correlation to image quality. By contrast, there was a strong correlation between rising HR and the incidence of nondiagnostic segments (r = 0.809, p < 0.001, SEE = 0.161).

Cutoff values for HR as related to more frequent nondiagnostic segments were illustrated with receiver-operator curve analysis (Fig. 4). Nondiagnostic segments were significantly less common with an HR below 62 beats/min (1.2%) compared with an HR above or equal to 62 beats/min (8.4%; p < 0.001).
Discussion

The present study is the first to our knowledge to provide evidence that low-dose CTCA with prospective ECG triggering is feasible in a large, real-world, clinical patient population. These results confirm that an HR below 62 beats/min is a requirement to obtain adequate image quality, which explains the frequent beta-blocker administration in this study. The present findings illustrate that this HR can be successfully reached in a vast majority of a daily clinical routine population. On an intention-to-diagnose basis including all enrolled patients, a diagnostic scan resulted in 86.1% of patients, comparing well with previously published reports (11). Of note, in 93.1% of those patients who underwent CTCA, the scan allowed a firm final diagnosis, indicating that only a minor fraction of patients was exposed to radiation without the benefit of firm diagnosis. The mean effective radiation dose exposure of 1.8 mSv is in line with the preliminary data of our previously published pilot feasibility (3) and accuracy (4) studies and compares favorably with the 12 mSv recently reported in a real-world survey of spiral CTCA (12).

Thus, our data establish prospective ECG triggering as a robust technique to perform low-dose CT for routine noninvasive coronary angiography with less radiation than an invasive angiography as recently reported in a head-to-head comparison (13). This shifts the benefit-to-harm ratio of this noninvasive technique to the favorable side of clinical benefit. Potentially, even CAD treatment monitoring may no longer be considered prohibitive for radiation concerns. New CTCA scan protocols using the conventional spiral mode but with a very fast table motion (“flash spiral” mode), covering the whole heart in 1 heart beat, may represent an alternative to prospective ECG triggering for low-dose CTCA (14). However, such a scan protocol requires a very high temporal resolution, which at present can only be achieved on dual-source devices. Such techniques suffer from limited availability as most CT scanners are single-source systems on which flash spiral mode is not feasible. By contrast, the convincing advantage of prospective ECG triggering lies in its striking potential to be universally applicable on a large variety of scanners regardless of vendor or device-specific characteristics. It may therefore also be implementable in the latest and future scanner generations; as for example demonstrated in a preliminary report using a 320-slice scanner that allows full heart coverage in 1 rotation (15). This illustrates that prospective ECG triggering is not only feasible with present state-of-the-art technology but may also be endorsed by future technical developments.

Study limitations. The growing awareness of contraindications to CTCA among the referring physicians may potentially have introduced a referral bias favoring the feasibility of low-dose CTCA in our study. This, however, reflects a positive aspect of daily routine (i.e., appropriate patient selection for the most suitable test). Another limitation is the lack of accuracy data for CTCA versus invasive coronary angiography as standard of reference. However, although the accuracy of low-dose CTCA has been reported previously (4), the aim of the present observational study was to establish feasibility of this technique in a real-world clinical setting consisting of an unselected, consecutive population.

Conclusions

Achieving low-dose CTCA by ECG triggering is feasible in an everyday population but requires careful patient preparation, whereby HR control is crucial. If an HR of 62 beats/min or below can be achieved, diagnostic image quality can be obtained at a very low radiation dose (1.8 ± 0.6 mSv).

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REFERENCES


Key Words: CT coronary angiography • feasibility • low radiation dose • prospective ECG triggering.