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#### Research paper

# Estimation of cardiovascular risk on routine chest CT: Ordinal coronary artery calcium scoring as an accurate predictor of Agatston score ranges

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#### ABSTRACT

*Background:* Coronary artery calcium (CAC) is often identified on routine chest computed tomography (CT). The purpose of our study was to evaluate whether ordinal scoring of CAC on non-gated, routine chest CT is an accurate predictor of Agatston score ranges in a community-based population, and in particular to determine the accuracy of an ordinal score of zero on routine chest CT.

Methods: Two thoracic radiologists reviewed consecutive same-day ECG-gated and routine non-gated chest CT scans of 222 individuals. CAC was quantified using the Agatston scoring on the ECG-gated scans, and using an ordinal method on routine scans, with a score from 0 to 12. The pattern and distribution of CAC was assessed. The correlation between routine exam ordinal scores and Agatston scores in ECG-gated exams, as well as the accuracy of assigning a zero calcium score on routine chest CT was determined.

Results: CAC was most prevalent in the left anterior descending coronary artery in both single and multivessel coronary artery disease. There was a strong correlation between the non-gated ordinal and ECG-gated Agatston scores ( $r=0.811,\ p<0.01$ ). Excellent inter-reader agreement (k=0.95) was shown for the presence (total ordinal score  $\ge 1$ ) or absence (total ordinal score =0) of CAC on routine chest CT. The negative predictive value for a total ordinal score of zero on routine CT was 91.6% (95% CI, 85.1–95.9). Total ordinal scores of 0, 1–3, 4–5, and  $\ge 6$  corresponded to average Agatston scores of 0.52 (0.3–0.8), 98.7 (78.2–117.1), 350.6 (264.9–436.3) and 1925.4 (1526.9–2323.9).

Conclusion: Visual assessment of CAC on non-gated routine chest CT accurately predicts Agatston score ranges, including the zero score, in ECG-gated CT. Inclusion of this information in radiology reports may be useful to convey important information on cardiovascular risk, particularly premature atherosclerosis in younger patients.

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#### 1. Introduction

Coronary heart disease is the leading cause of mortality in the US.<sup>1</sup> Traditionally, heart disease has been assessed qualitatively

Abbreviations: CAC, coronary artery calcium; CT, computed tomography; LM, left main; LCx, left circumflex; LAD, left anterior descending; RCA, right coronary artery; MIP, maximum intensity projection.

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with risk factor models incorporating demographics and/or biomarkers, such as the Framingham Risk Score, the European Society of Cardiology Score, and the AHA/ACC Pooled Cohort Equations.

In contrast to the binary nature of risk factors, imaging allows for the noninvasive quantification of atherosclerosis, specifically the quantification of coronary artery calcium through ECG-gated CT.<sup>5</sup> The most frequently used method for calcium quantification on CT, the Agatston score, relies on software to multiply the volume of coronary artery calcium deposits by a coefficient that corresponds to their peak density.<sup>5</sup>

Coronary artery calcium (CAC) scoring has been shown to be more predictive of cardiovascular events than traditional risk

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factors across various ethnicities, 6–11 with a net reclassification index as high as 66% in patients categorized as intermediate risk by the Framingham score. 12–14 Additional studies have demonstrated the prognostic value of CAC scoring for death, non-fatal myocardial infarction, and future revascularization. 8,15–20

When applied to routine non-ECG gated chest CT, the modified Agatston score has proven concordant with the ECG-gated scan derived Agatston score in lung cancer screening patients.<sup>21–23</sup> as well as in community-based populations.<sup>24</sup> Evaluating CAC on routine non-contrast chest CTs is a cost- and radiation-free method of quantifying coronary calcium, and it is increasingly utilized in clinical practice, particularly in the low dose lung cancer screening population.<sup>25,26</sup> While lung cancer is the leading cause of cancer mortality in the United States, heart disease remains the foremost cause of mortality even within the National Lung Cancer Screening Trial (NLST) cohort, 27 adding clinical relevance to "incidental" coronary calcium. CAC measurement is considered a reasonable tool (class IIa and/or IIb) for cardiovascular risk assessment, particularly for intermediate-risk asymptomatic adults.<sup>3,28,29</sup> Patient knowledge of their calcium score has also been shown to correlate with improved adherence to medical therapy and more effective lifestyle modification. 30,31

Qualitative visual assessment methods have been developed to quantify CAC.<sup>32–35</sup> One of the most widely used methods, ordinal scoring, relies on the visual assessment of the left main, left anterior descending, left circumflex, and right coronary arteries. Ordinal scoring has been shown to be independently predictive of cardiovascular death, with a quantitative relationship between the ordinal score and odds of cardiovascular death.<sup>36–38</sup>

In the United States in 2007, more than 600,000 dedicated CAC scoring exams were performed. In contrast, over 9 million routine chest CT exams were performed for a variety of indications, with the number only projected to rise. <sup>39</sup> Despite the routine visualization of coronary artery calcium on these exams, CAC is neither systematically nor routinely reported by radiologists. <sup>40,41</sup> In a study of 207 patients with CAC, radiologists reported the presence of CAC in only 44% of patients, with only 1% of the involved coronary vessels reported by name. <sup>41</sup>

As most CT chest exams are performed among community-living individuals, we sought to assess ordinal scoring on routine chest CT scans as an accurate predictor of Agatston score ranges. Additionally, since the community-based population includes individuals younger than those included in the lung cancer screening population, we suggest a radiology-reporting method for coronary calcium burden relative to age and gender matched peers.

#### 2. Methods

#### 2.1. Study design

This retrospective HIPPA-compliant study protocol was approved by the institutional review board. The requirement for informed consent was waived.

#### 2.2. Subjects

Between 2008 and 2013, 3602 community-living individuals underwent ECG-gated cardiac CT examinations, 226 of whom who were self-or physician-referred for a "whole-body" CT scan in addition to the cardiac CT examination, with both exams performed consecutively on the same day. One patient with a previously implanted coronary artery stent was excluded from the study. Three individuals underwent same-day scanning twice during the study interval, with exclusion of the older scan set. This yielded 222 unique patients.

#### 2.3. Agatston and routine chest CT protocol

All patients underwent two consecutive CT examinations in one session using a 64-slice GE Lightspeed VCT scanner (GE Healthcare, Milwaukee, USA).

For ECG-gated calcium scoring CT, the scanning protocol was as follows: prospective ECG-triggering set at 75% of the RR interval; scan range, carina to cardiac apex; peak voltage, 120 kVp; tube current modulation 210–500 mA; rotation time, 0.35 s; detector collimation,  $64 \times 0.5$  mm; section thickness/increment, 2.5 mm/ 2.5 mm; reconstruction kernel, standard; field of view, 250 mm; matrix,  $512 \times 512$ .

For routine non-contrast chest CT, the protocol was as follows: scan range, thoracic inlet to adrenal glands; peak voltage, 120 kVp; tube current modulation  $80{-}500$  mA; rotation time, 0.4 s; pitch, 0.984; detector collimation,  $64\times0.5$  mm; section thickness/increment,  $2.5{-}5$  mm/ $2.5{-}5$  mm; reconstruction kernel, standard; field of view, 360 mm; matrix,  $512\times512$ . 199 (89.6%) non-gated scans were acquired at 5 mm slice thickness, with 23 (10.4%) acquired at 2.5 mm slice thickness.

#### 2.4. CAC assessment by Agatston scoring

CAC scoring on the ECG-gated studies was performed utilizing commercially available calcium scoring software (PHILIPS), which was used to identify and score any calcium in the four main coronary arteries, the left main (LM), left anterior descending (LAD), left circumflex (LCx), and right coronary artery (RCA), based on established minimum attenuation values. The Agatston score was generated by summing the scores of all lesions, which were derived by multiplying the lesion area by density in Hounsfield units. All identified plaque was manually evaluated by an investigator to exclude non-coronary artery calcium.

#### 2.5. CAC assessment by ordinal scoring

Two readers, thoracic radiologists with 20 and 4 years of experience, independently reviewed the ECG-gated and non-gated scans. Readers were blinded to the Agatston scores. The gated and the non-gated studies were scored at a one-week interval in random order.

Visual assessment of CAC was performed via ordinal scoring. Each of the four main coronary arteries was identified. Calcium was scored by the thoracic radiologists as 0, 1, 2, or 3 to correspond to absent, mild, moderate, or severe CAC in each vessel. Mild CAC was defined as involvement of less than one third of the vessel length (Fig. 1), moderate as involvement of one to two thirds of the vessel length (Fig. 2), with severe coronary artery calcium defined as involvement of greater than two thirds of the vessel length (Fig. 3). The scores were summed to yield ordinal scores of 0–12 for each scan.  $^{34,36}$  The total ordinal scores were then categorized as 0, 1–3,  $^{4-5}$ , and  $\geq 6$ .

#### 2.6. Statistical analysis

A binary scale was used to classify the ECG-gated exams as to the presence or absence of CAC (Agatston score of 0 versus Agatston score > 0). The sensitivity, specificity, positive predictive value, and negative predictive values were determined for the total ordinal score of zero. The inter-reader agreement for the detection of CAC by ordinal scoring was determined with Cohen's kappa coefficient.

The correlation between the ordinal and Agatston scores was determined with Pearson's correlation coefficient. The exams were then grouped by ordinal score ranges of 0, 1–3, 4–5, and  $\geq$ 6. The median, mean, absolute minimum, and absolute maximum

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