Does Nonenhanced CT-based Quantification of Abdominal Aortic Calcification Outperform the Framingham Risk Score in Predicting Cardiovascular Events in Asymptomatic Adults?

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Conflicts of interest are listed at the end of this article.

Purpose: To determine if abdominal aortic calcification (AAC) at CT predicts cardiovascular events independent of Framingham risk score (FRS).

Materials and Methods: For this retrospective study, electronic health records for 829 asymptomatic patients (mean age, 57.9 years; 451 women, 378 men) who underwent nonenhanced CT colonography screening between April 2004 and March 2005 were reviewed for subsequent cardiovascular events; mean follow-up interval was 11.2 years ± 2.8 (standard deviation). Institutional review board approval was obtained. CT-based AAC was retrospectively quantified as a modified Agatston score by using a semiautomated tool. Kaplan-Meier curves and Cox proportional hazards models were used for time-to-event analysis; receiver operating characteristic curves and net reclassification improvement compared predictive abilities of AAC and FRS.

Results: An index cardiovascular event occurred after CT in 156 (19%) of 829 patients (6.7 years ± 3.5, including heart attack in 39 [5%] and death in 79 [10%]). AAC was higher in the cardiovascular event cohort (mean AAC, 3478 vs 664; \( P < .001 \)). AAC was a strong predictor of cardiovascular events at both univariable and multivariable Cox modeling, independent of FRS (\( P < .001 \)). Kaplan-Meier plots showed better separation with AAC over FRS. The area under the receiver operating characteristic curve (AUC) was higher for AAC than FRS at all evaluated time points (eg, AUC of 0.82 vs 0.64 at 2 years; \( P = .014 \)). By using a cutoff point of 200, AAC improved FRS risk categorization with net reclassification improvement of 35.4%.

Conclusion: CT-based abdominal aortic calcification was a strong predictor of future cardiovascular events, outperforming the Framingham risk score. This finding suggests a potential opportunistic role in abdominal nonenhanced CT scans performed for other clinical indications.

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Cardiovascular disease is widespread. Heart disease, the most common manifestation of cardiovascular disease, is the leading cause of mortality and morbidity in the United States, affecting 28.4 million adults and resulting in 633,842 deaths in 2015 alone (1). Stroke, another leading manifestation of cardiovascular disease, affects 2.7% of the U.S. population and led to an additional 140,323 deaths in 2015 (1). Globally, cardiovascular diseases are the number one cause of mortality, causing 17.7 million deaths in 2015, including 37% of all premature deaths (2). Accurate assessment of risk for future cardiovascular events can help to guide patient management, aggressively treating those at highest risk while protecting those at low risk from the costs, potential adverse effects, and other risks related to unnecessary interventions. The American College of Cardiology and the American Heart Association recommend that adults aged 20–79 years undergo cardiovascular disease risk assessment and be reassessed every 4 to 6 years (3). The Framingham risk score (FRS) is a well-known and well-validated prediction model for cardiovascular disease based on traditional risk factors, including age, sex, cholesterol level, and blood pressure (4,5). However, many patients evaluated by this or other clinical prediction models fall into an indeterminate risk category, prompting the use of additional noninvasive measures for refining risk assessment (5,6,7). This includes measures of subclinical atherosclerosis, such as CT-based coronary artery calcification, an established independent risk predictor for cardiovascular disease (8,9).

Abdominal aortic calcification (AAC) correlates with coronary artery calcification (10–12) and, when only considering the presence or absence of calcification, the two measures have similar performance in predicting cardiovascular events (13). AAC is associated with risk factors of cardiovascular disease (14–16) and correlates with asymptomatic coronary artery disease (17), prompting assessment of its value for prediction of cardiovascular disease. Several studies have measured AAC and confirmed its association with cardiovascular disease (18,19). However, these studies were imprecise, estimating AAC burden from radiographs or dual x-ray absorptiometry scans (18,19). A few studies have quantified AAC by using CT, but only evaluated association with risk factors (14) or had limited follow-up (20). Finally, others have evaluated abdominal
Nonenhanced CT-based quantification of abdominal aortic calcification predicts future cardiovascular events in asymptomatic adults. Aortic calcium scores outperform the clinically based Framingham risk score.

Implications for Patient Care
- Nonenhanced CT-based abdominal aortic calcification outperformed the Framingham risk score for estimating risk of future cardiovascular events in asymptomatic adults.
- Noncontrast abdominal CT scans obtained for other indications may provide an opportunity to quantify abdominal aortic calcification.

Aortic atherosclerosis at MRI, demonstrating that mean aortic wall thickness conferred an increased risk for a combination of hard and soft cardiovascular end points (including heart attack, stroke, transient ischemic attacks, revascularization, hospitalization for atrial fibrillation) and requiring a dedicated examination (21). We hypothesized that nonenhanced CT-based AAC predicts future cardiovascular events in generally healthy asymptomatic adults and improves prediction beyond the FRS in a cohort with more than a decade in average follow-up time.

Materials and Methods

Study Site and Cohort
Our retrospective study was Health Insurance Portability and Accountability Act–compliant and institutional review board approval for chart review was obtained. The requirement for informed consent was waived. Nonenhanced CT of the abdomen and pelvis was performed on all consecutively registered asymptomatic outpatient adults undergoing CT colonography screening at one institution over the 12-month period from April 2004 to March 2005. This remote period was selected to allow for the potential of more than a decade of follow-up for subsequent cardiovascular events. Patients were excluded if AAC could not be measured due to orthopedic hardware or quantum mottle, if missing data prevented calculation of FRS, or (for patients who did not have cardiovascular events) if there was less than 2 years of clinical follow-up.

CT Protocol
Supine CT scans of the abdomen and pelvis were obtained without intravenous contrast material with an eight-section or 16-section multidetector CT scanner (LightSpeed Series; GE Healthcare, Waukesha, Wis), calibrated daily for attenuation. The voltage was 120 kVp with modulated tube current ranging from 30 mA to 300 mA, and a noise index of 50. Images were reconstructed with a 1.25-mm section thickness at 1-mm intervals, as per standard protocol for CT colonography. Details regarding CT colonography–specific technique for colonic preparation and distention have been previously described (22). In brief, the bowel was prepared by using a cathartic agent and oral contrast tagging, then distended by using carbon dioxide delivered through a rectal tube under low pressure. Patients were then scanned in supine and prone positions. Only supine images were analyzed for AAC, as most CT examinations are performed in the supine position.

AAC Measurement
A semiautomated tool (V3D-Calcium Scoring; Viatronix, Stony Brook, NY) was used to retrospectively quantify the AAC at noncontrast multidetector CT by one author (S.D.O, with 3 years of radiology research experience) who was blinded to patient outcomes. This tool was initially developed for quantifying coronary artery calcification and was subsequently applied to the abdominal aorta. The user drew regions of interest around the vessel of interest on the supine axial images and the tool used a threshold of 130 HU and region growing algorithms to report calcium load in terms of modified Agatston score, volume, and mass scores. The threshold of 130 HU is a standard across multiple studies of vascular calcification, including the original coronary artery calcification study by Agatston (23) as well as studies of coronary artery calcification (24,25), thoracic aortic calcification (12,15), and AAC (14,15). The tool colored the areas of calcification for the user on the axial, sagittal, and coronal views for review by the user, and the user could redraw the regions of interest until satisfied with the result (Fig 1). For our study, we used the modified Agatston score for the abdominal aorta. AAC was measured from the diaphragm to the aortic bifurcation. Iliac calcification was also segmented and scored, but these results were not included due to concerns over reproducibility of regions of interest drawn in the axial plane on these commonly tortuous vessels and for simplicity.

Follow-up Methodology, FRS Scoring, and Cardiovascular Event Determination
Electronic health records were extensively manually reviewed in several rounds over a period of years to identify values required to calculate FRS (discussed next) (4) and to assess for cardiovascular events. Initial chart review, including gathering of data necessary to calculate FRS, was performed by one author (S.D.O) who was blinded to AAC. Subsequent chart reviews, for the purpose of recording additional cardiovascular events, were performed by S.D.O and P.M.G (with 3 years of radiology research experience), who were blinded to FRS and AAC scores at the time of review. A minimum of 2 years of adequate clinical follow-up was required for inclusion of patients without a defined event; potential patients who did not meet this requirement were excluded from the final cohort. Patients without events were censored at the date of their last note in the electronic health record. The last electronic health record follow-up was performed in October 2017, allowing for an interval of more than 12–13 years from the CT scan.

The FRS (4) requires age, sex, total cholesterol level, high-density lipoprotein cholesterol level, blood pressure, diabetes status, and smoking status to estimate the 10-year risk of coronary heart disease. These values were obtained from the electronic health records if they were recorded within the 2 years before or after a patient’s CT examination. If multiple values were...
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For survival-type time-to-event analysis, Kaplan-Meier curves were created for AAC and FRS, splitting the curves by using quartiles of the predictor variables. P values were derived by using two-sided alternative and DeLong method. To assess the statistical significance of the variables, Cox proportional hazards models were fit to the data, using AAC and FRS alone and combined. Because of the heavy right skew in AAC scores, the natural log of the value became the predictor. The proportionality of the Cox model was then tested. To evaluate the impact of prior events, age, and sex in addition to AAC and FRS, a separate Cox proportional hazard model was fit to the data by using AAC, FRS, prior events, age, and sex. A Type III analysis of variance table was then built with all five variables to test for significance of each variable after correcting for the other four.

For ROC curve analysis, restricted data sets are necessary because time to event is not considered. Three arbitrary cutoffs were used: 2-year, 5-year, and 10-year survival (ie, time to defined cardiovascular event). To create these data sets, all patients having an event within those time frames were included. Only patients having at least 2-year, 5-year, and 10-year follow-up, respectively, were included in each analysis if they did not experience an event. ROC AUCs and 95% confidence intervals were calculated.

For net reclassification improvement analysis, which measures the improvement in reclassification of biomarkers while balancing the sensitivity and specificity (27), FRS was used to categorize patients into categories of low risk (<5%), intermediate risk (5% to <7.5%), and high risk (≥7.5%) for cardiovascular events for 5-year risk. These cutoffs were chosen to match American College of Cardiology and American Heart Association treatment categories (7). In addition, net reclassification improvement analysis was also performed for 10-year risk by using risk categories of less than 10%, 10%–15%, and greater than 20%. These cutoffs were chosen to create equal and comparable groups within the data. AAC was categorized into low, intermediate, and high values and used to adjust patients’ categorizations by recalculating their 5- and 10-year risks by using a model with both FRS and the categorized AAC. The low classification was always considered as an AAC value of zero, whereas the second cutoff point was allowed to vary. The AAC threshold value producing the best balance between correctly upgrading and downgrading patient classification was determined.

Figure 1: Images from CT colonography show segmented abdominal aortic calcification measured with semiautomated CT tool on (a) coronal and (b) sagittal images. Within region of interest over aorta selected by user, tool automatically segments and quantifies aortic calcification (shown in blue).
Results

Study Cohort
A total of 1030 asymptomatic adults underwent nonenhanced CT colonography over a 12-month period; because of artifact from orthopedic hardware and quantum mottle, AAC could not be measured in 80 patients who were excluded (Fig 2). A total of 121 patients were excluded because data necessary to calculate the FRS were missing or the patient did not have either a cardiovascular event or at least 2 years of clinical follow-up. After these exclusions, 829 patients remained within the cohort.

Cardiovascular Events Subsequent to CT
The mean follow-up interval for the final cohort of 829 patients was 11.2 years ± 2.8 (standard deviation) (range, 0.2–13.5 years; median, 12.5 years; interquartile range, 11.2–12.8 years). Electronic health record review identified 156 patients (19%) with at least one defined event occurring in the follow-up interval after CT. The mean time interval from CT to the initial cardiovascular event was 6.9 years ± 3.8 (range, 0.05–12.8 years; median, 7.0 years; interquartile range, 3.5–10.1 years). Event types included myocardial infarction (39 of 829, 5%), stroke (26 of 829, 3%), congestive heart failure (63 of 829, 8%), and death (79 of 829, 10%); 42 patients had two or more events subsequent to CT, and eight patients had three or more events. A total of 45 patients (45 of 829, 5%) had a documented event prior to CT; including 26 of the patients with an event after CT (26 of 156, 17%).

AAC and FRS in the Study Cohort
The median CT-based AAC for the entire cohort of 829 patients in our final study cohort was 108 (interquartile range, 10–867). The values were heavily skewed to the right, with a mean of 1193 and a standard deviation of 2911. The FRS was more normally distributed, with a median of 6.0 (interquartile range, 4.0–9.0) and a mean of 7.5 ± 5.3 (Table 1). Mean AAC values for patients with and patients without a subsequent cardiovascular event after CT were 3478 and 664 (median, 1145 vs 71; P < .001), respectively (Table 1). For FRS, mean values for patients with and patients without a subsequent event were 10.1 and 6.9, respectively (median, 8.0 vs 6.0). The AAC score was not significantly different between patients in the final cohort and those excluded due to lack of clinical follow-up or data necessary to calculate FRS (median AAC, 108 vs 162; P = .31).

Time-to-Event Analysis
Patients were grouped into quartiles for both AAC and FRS values, and Kaplan-Meier curves were created (Fig 3). The rate of cardiovascular events was greater with each quartile of AAC, from 4% (eight of 209) for adults in the first quartile, 12% (25 of 206) for the second quartile, 18% (38 of 207) for the third quartile, and 41% (85 of 207) for the fourth quartile. To a lesser degree, the rate of cardiovascular events was greater with each quartile of FRS, from 12% (32 of 276) for adults in the first quartile, 15% (24 of 156) for the second quartile, 17% (38 of 219) for the third quartile, and 34% (62 of 180) for the fourth quartile. Clustering of FRS data prevented even quartering of the cohort. Table 2 compares patients with cardiovascular events according to both AAC and FRS quartiles. AAC classification by quartile is substantially improved over FRS.

Cox proportional hazards models were created for AAC alone, FRS alone, and AAC combined with FRS. Both AAC and FRS are predictors of cardiovascular events when modeled separately (P < .001 for both). Concordance, a measure similar to AUC for ROC curves, measuring the percentage of cardiovascular events the model correctly predicts, was higher in the univariable AAC model when compared with the FRS model (0.736 vs 0.657). In a multivariable model including AAC and FRS, both variables were significant, although FRS much less so (P < .001 for AAC and P = .007 for FRS). The concordance of the multivariable model, 0.744, was slightly higher compared with the univariable AAC model. The proportionality assumption was not violated in any model (AAC alone, P = .54; FRS alone, P = .95; AAC combined with FRS, P = .81). When a Cox proportional hazard model including AAC, FRS, prior event, age, and sex was fit to the data, and these variables were then evaluated by using a Type III analysis of variance table, all variables except FRS were statistically significant: age (P < .001), prior event (P = .001), AAC (P = .001), sex (P = .03), and FRS (P = .72).

Findings were also statistically significant in a model including both AAC and FRS while correcting for patients who had cardiovascular events prior to CT (P < .001 for AAC and P = .001 for FRS). However, because subsequent cardiovascular events are clinically significant in all patients, irrespective of cardiovascular event history, we have chosen not to expand on these results.
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ROC Curves
The value of AAC and FRS for predicting future cardiovascular events was analyzed by using ROC curves for 2-year, 5-year, and 10-year time intervals. The AUC values for the ROC curves for univariable and multivariable models are shown in Table 3. ROC AUC values for AAC were greater than FRS at all three calculated time intervals. For the 2-year analysis, the addition of FRS to AAC did not improve on the performance of AAC alone in terms of AUC values (Fig 4; \( P = .57 \)). For the 5-year and 10-year time intervals, only minimal additive gain to AAC alone was seen by combining FRS with AAC (\( P = .08 \)).

Net Reclassification Improvement
Although AAC score thresholds of 500 and 700 had the highest total net reclassification improvement for both 5-year (37.2%) and 10-year (35.8%) risk, respectively, the gain was purely due to downgrading cardiovascular nonevents, because there was a negative impact on cardiovascular events (−1.3% and −10.3%, respectively). In comparison, an AAC threshold of 200 provided the best overall balance for both 5-year and 10-year risk. For 5-year and 10-year risk using an AAC cutoff of 200, the total net reclassification improvement was 36.8% and 35.4%, respectively. Event reclassification improvement of 17.9% and nonevent reclassification improvement of 18.9% were found for the 5-year risk. For the 10-year risk, there was an event reclassification improvement of 12.2% and nonevent reclassification improvement of 23.2%.

Discussion
AAC derived from abdominal CT scans has the potential to provide valuable cardiovascular disease risk information beyond existing clinical risk estimates, such as the FRS, and may increase the overall accuracy of patient risk stratification. We showed a strong association between AAC and definable future cardiovascular events. Prior studies focusing on conventional radiography and dual x-ray absorptiometry (18,19) or CT (15) have found greater hazard ratios across ordinal categories of higher AAC, but scoring is more subjective. Other studies that measured AAC at CT found a significant association between AAC and cardiovascular risk factors without evaluating cardiovascular events (14) or similarly found larger hazard ratios for cardiovascular events with higher AAC, but follow-up was shorter than in our study (20).

By using semiautomated CT quantification, we found clear separation of risk for cardiovascular events by using AAC quartiles, whereas substantial overlap was seen between FRS quartiles and with less separation. When AAC is considered as a continuous variable, we found it to be a statistically significant predictor of cardiovascular events based on Cox proportional hazards, maintaining its predictive power in a multivariable model.

The ability of AAC to predict cardiovascular events, which persisted after controlling for FRS, prompted review of ROC curves to evaluate the usefulness of this measure for improving risk prediction. Because ROC curves cannot account for time to an event, ROC curves were analyzed at the 2-year, 5-year, and 10-year time points. At all time points assessed, AAC was a better predictor of cardiovascular events than was FRS, as evidenced by greater AUC values. Furthermore, when the predictive model combined AAC and FRS, the additive value of FRS was largely negligible relative to AAC alone, particularly at the 2-year interval. When using conventional radiography for less precise scoring of AAC, others have shown its benefit in multivariable models for cardiovascular disease (28,29).

Patients may be assigned to preventive treatment regimens based on their cardiovascular risk categories, with patients at higher risk undergoing more aggressive approaches. By finding a net reclassification improvement of greater than 35% over FRS by using an AAC threshold of 200, including both appropriate upgrades and downgrades in risk stratification, our data suggest that AAC not only improves cardiovascular disease risk prediction, but also potentially impacts patient care. For example, more aggressive treatment may be indicated in patients with a high AAC score but lower risk based on the FRS. Additionally, because coronary artery calcification scoring has been shown to improve adherence to risk modification regimens assigned by their physicians (30,31), CT-based AAC scoring may have a similar positive effect.

Although the results of our study demonstrate the utility of CT-derived AAC in predicting future cardiovascular events, this should not be considered an endorsement for
obtaining an abdominal CT for the sole purpose of cardiovascular disease risk screening. However, reporting AAC scores from abdominal CT scans obtained for other indications (such as CT colonography) represents another example of opportunistic screening that adds potential value to the examination, without the need for additional patient time or radiation dose. Bone mineral density assessment for osteoporosis is another key emerging opportunistic screening add-on using abdominal CT (32–34); other examples include screening for abdominal aortic aneurysms, hepatic steatosis and iron overload, sarcopenia, and visceral fat (35–38). Although these secondary or incidental screening opportunities have received the most attention in CT colonography (39,40), much greater impact and benefit could be derived from applying this to other clinical indications for abdominal CT, given the much larger volume of routine studies being performed (41). Furthermore, many or all of these CT tools have the potential to be fully automated, which could further increase their utility (42–44). For future investigations, we plan to combine fully automated opportunistic screening measures of AAC, bone mineral density assessment, muscle, and fat for predicting important cardiometabolic outcomes at abdominal CT, whether nonenhanced or contrast material–enhanced, in even larger patient cohorts. Ultimately, it is our hope that these opportunistic measures can be applied and reported prospectively as part of routine clinical practice for patients undergoing abdominal CT, regardless of the imaging indication.

Our study had several limitations. By necessity, we used a retrospective design, which allowed us to derive long-term patient follow-up of greater than 11 years on average. A prospective trial of this magnitude would be costly and challenging, and the final results would not be available for more than a decade. We recognize that imaging technology is constantly evolving and that technical factors could introduce unexpected

### Table 1: Relationships between Patient Demographics, AAC, FRS, and Cardiovascular Events

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Total Cohort ( (n = 829) )</th>
<th>Cardiovascular Event ( (n = 156) )</th>
<th>No Cardiovascular Event ( (n = 673) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>57.8 ± 7.8</td>
<td>64.1 ± 9.7</td>
<td>56.3 ± 6.4</td>
</tr>
<tr>
<td>Median*</td>
<td>56 (52–62)</td>
<td>60 (54–70)</td>
<td>55 (51–60)</td>
</tr>
<tr>
<td>Range</td>
<td>37–91</td>
<td>50–81</td>
<td>37–87</td>
</tr>
<tr>
<td>Sex†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>451 (54)</td>
<td>61 (39)</td>
<td>390 (58)</td>
</tr>
<tr>
<td>Male</td>
<td>378 (46)</td>
<td>95 (61)</td>
<td>283 (42)</td>
</tr>
<tr>
<td>Measured variables</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AAC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>1193 ± 2911</td>
<td>3478 ± 5042</td>
<td>664 ± 1758</td>
</tr>
<tr>
<td>Median*</td>
<td>108 (10–867)</td>
<td>1145 (159–4672)</td>
<td>71 (6–482)</td>
</tr>
<tr>
<td>Range</td>
<td>0–22 542</td>
<td>0–22 542</td>
<td>0–22 114</td>
</tr>
<tr>
<td>FRS</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>7.5 ± 5.3</td>
<td>10.1 ± 6.5</td>
<td>6.9 ± 4.7</td>
</tr>
<tr>
<td>Median*</td>
<td>6.0 (4.0–9.0)</td>
<td>8.0 (6.0–13.0)</td>
<td>6.0 (4.0–9.0)</td>
</tr>
<tr>
<td>Range</td>
<td>4–40</td>
<td>6–37</td>
<td>4–40</td>
</tr>
</tbody>
</table>

Note.—Cardiovascular events subsequent to CT included myocardial infarction, stroke, congestive heart failure, death, or a combination thereof (see article). Unless otherwise specified, data are means ± standard deviations. AAC = abdominal aortic calcification, FRS = Framingham risk score.

* Data in parentheses are interquartile ranges.
† Data are the number of patients, with percentages in parentheses.

### Table 2: Patients with Cardiovascular Events \( (n = 156) \) According to AAC and FRS Quartiles

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AAC Quartile 1</th>
<th>AAC Quartile 2</th>
<th>AAC Quartile 3</th>
<th>AAC Quartile 4</th>
<th>Total FRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRS Quartile 1</td>
<td>5</td>
<td>8</td>
<td>6</td>
<td>13</td>
<td>32 (21)</td>
</tr>
<tr>
<td>FRS Quartile 2</td>
<td>0</td>
<td>4</td>
<td>7</td>
<td>13</td>
<td>24 (15)</td>
</tr>
<tr>
<td>FRS Quartile 3</td>
<td>1</td>
<td>6</td>
<td>14</td>
<td>17</td>
<td>38 (24)</td>
</tr>
<tr>
<td>FRS Quartile 4</td>
<td>2</td>
<td>7</td>
<td>11</td>
<td>42</td>
<td>62 (40)</td>
</tr>
<tr>
<td>Total AAC</td>
<td>8 (5)</td>
<td>25 (16)</td>
<td>38 (24)</td>
<td>85 (54)</td>
<td>156</td>
</tr>
</tbody>
</table>

Note.—Data in parentheses are percentages. AAC = abdominal aortic calcification, FRS = Framingham risk score.

### Table 3: ROC AUC for Cardiovascular Event Prediction by Using FRS and AAC

<table>
<thead>
<tr>
<th>Parameter</th>
<th>FRS Alone</th>
<th>AAC Alone</th>
<th>( P ) Value*</th>
<th>Combined FRS and AAC</th>
<th>( P ) Value†</th>
<th>( P ) Value‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-year</td>
<td>0.64 (0.52, 0.77)</td>
<td>0.82 (0.71, 0.92)</td>
<td>.01</td>
<td>0.82 (0.71, 0.92)</td>
<td>.0144</td>
<td>.57</td>
</tr>
<tr>
<td>5-year</td>
<td>0.64 (0.52, 0.77)</td>
<td>0.75 (0.68, 0.82)</td>
<td>.08</td>
<td>0.76 (0.70, 0.83)</td>
<td>.0132</td>
<td>.15</td>
</tr>
<tr>
<td>10-year</td>
<td>0.67 (0.60, 0.75)</td>
<td>0.76 (0.72, 0.81)</td>
<td>.01</td>
<td>0.78 (0.73, 0.82)</td>
<td>.0005</td>
<td>.08</td>
</tr>
</tbody>
</table>

Note.—Data in parentheses are 95% confidence intervals. AAC = abdominal aortic calcification, AUC = area under the curve, FRS = Framingham risk score, ROC = receiver operating characteristic.

* Indicates FRS vs AAC.
† Indicates FRS vs combined.
‡ Indicates AAC vs combined.
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bias. When used clinically, measurement tools such as the one used in our study will need to be robust enough to produce constant scores with differing image acquisition technology. It is important to note that our current AAC findings strictly apply to nonenhanced CT scans in the supine position. Additional validation and testing is required for use in intravenous contrast-enhanced CT as well as nonenhanced CT scans performed with different image acquisition protocols and in differing positions. We are currently investigating a fully automated version for CT-based AAC scoring and plan to validate this tool for both nonenhanced and contrast-enhanced scans. Although iliac calcification was segmented and scored, it was not included in the final analysis because clear distal borders were often difficult to identify on the axial images used for segmentation. However, the additional information in the score from the iliacs could further improve the utility of AAC. When an automated tool for CT-based AAC scoring becomes available, scores without and scores with iliac calcification should be evaluated. Our study focused on evaluating the utility of AAC in predicting cardiovascular events—we did not measure the reproducibility of the scores our tool produced. Future studies focusing on tool development should address this issue, as well as validate automated and semiautomated tools. Finally, because the presence of a prior cardiovascular event (before the CT scan) did not substantively alter our overall results, we chose not to exclude these patients. Their inclusion could allow this tool to be applied to more patients given validation for cohorts with and cohorts without a prior cardiovascular event.

In summary, quantification of AAC at CT was a strong predictor of future cardiovascular events, clearly outperforming the FRS in our study. This suggests a potential opportunistic role for aortic calcium scoring at noncontrast abdominal CT performed for other indications. Anticipated validation for use in contrast-enhanced CT, as well as development of a fully automated version, could result in more widespread implementation in the near future.

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