Prognostic Value of Coronary Artery Calcium Score in Acute Chest Pain Patients Without Known Coronary Artery Disease: Systematic Review and Meta-analysis

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**INTRODUCTION**

The coronary artery calcium score (CACS) is a well-established test for risk stratifying asymptomatic patients, is an independent predictor of long-term prognosis,1 and performs better than many other risk-stratifying tools.2 According to the most recent American Heart Association and American College of Cardiology Foundation guidelines, CACS has class IIA and IIB recommendations for assessing risk in intermediate- and low- to intermediate-risk asymptomatic patients, respectively,3 and in guiding management of hyperlipidemia.4 Recent studies also indicate that CACS may accurately risk stratify both low-risk stable patients with new-onset chest pain5,6 and those presenting to the emergency department (ED) with acute chest pain symptoms.7 Most studies in the latter group were limited by relatively small numbers of patients.

Hence, the objective of this systematic review and meta-analysis was to evaluate the prognostic value and accuracy of a zero (normal) CACS for identifying patients at acceptable low risk for future cardiovascular events who might be safely discharged home from the ED.

**MATERIALS AND METHODS**

Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines8 were followed for the conduct of the current systematic review and meta-analysis. We searched MEDLINE, EMBASE, and the Cochrane Library database...
Editor’s Capsule Summary

What is already known on this topic
Although coronary artery calcium score (CACS) is used to risk stratify asymptomatic patients for cardiac events, studies examining this test in the emergency department (ED) are underpowered.

What question this study addressed
It described the prognostic value and accuracy of CACS to predict major adverse cardiac events in ED patients.

What this study adds to our knowledge
In this systematic review of 8 studies that included patients with nonischemic ECG results and normal troponin levels, the risk of major adverse cardiac events was considerably lower in the 60% of patients with a CACS of 0 (relative risk 0.06; 95% confidence interval 0.04 to 0.22).

How this is relevant to clinical practice
The absence of calcium on coronary computed tomography is associated with a far lower risk of major adverse cardiac events, but it remains unclear whether this reduction in risk warrants the cost and radiation burden of this procedure.

for studies assessing prognostic value of CACS by computed tomography (CT). We used the text words and related Medical Subject Headings for “cardiac,” “calcification,” “computed tomography,” “prognosis,” “mortality,” “event,” “death,” “survival,” and “myocardial infarction.” Our search query was coronary OR “cardiac” AND (“calcification” OR “calcified” OR “calcium”) AND (“computed” AND “tomography” OR “CT”) AND (“prognosis” OR “mortality” OR “event” OR “death” OR “survival” OR “[myocardial” AND “infarction”]). We chose not to limit the search by whether the population was symptomatic or asymptomatic from the initial search strategy to include as many potential studies as possible. The initial search results were further investigated manually, as described below. The last search was performed on September 5, 2015.

We initially reviewed the title and abstracts of retrieved citations. Then full texts of those citations considered relevant were assessed for eligibility for inclusion. Inclusion criteria were the following:
1. Prospective cohort studies that involved patients without known coronary artery disease or history of coronary revascularization (percutaneous coronary intervention and coronary artery bypass graft surgery) who presented with acute chest pain to the ED and were evaluated with CACS testing. Studies with mixed populations (acute chest pain, chronic chest pain, asymptomatic or established coronary artery disease, and suspected coronary artery disease) could be included in our meta-analysis if the studies explicitly mentioned CACS and cardiovascular events in the subgroup of acute chest pain patients without known coronary artery disease. Studies with cross-sectional design were not included.
2. CACS that was performed by CT, either multidetector CT or electron-beam CT, and quantified with the Agatston method. CACS testing could be either isolated CACS assessment or CACS assessment performed before contrast-enhanced coronary CT angiography studies.
3. Studies that reported major adverse cardiovascular events (MACEs) at greater than or equal to 1 month after the index ED visit. MACEs could be all-cause death, cardiac death, acute coronary syndrome, nonfatal myocardial infarction, coronary revascularization, ischemic stroke, or cardiac hospitalization.

We did not include case reports, non-English studies, review articles without systematic approach and meta-analysis data, or conference abstracts. Two physician-investigators (K.C. and H.Y.J.) independently assessed studies for eligibility. Discrepancy was resolved by consensus determined by an additional investigator (physician-investigator G.P.S.S).

Data Collection and Processing

Two coauthors (physician-investigators K.C. and H.Y.J.) independently extracted data from the included full-text citations. The following information was abstracted: the last name of the first author; publication year; country where the study was performed; total participants in the study; number of male participants; percentage with white, black, and Asian races, and Hispanic ethnicity; baseline cardiovascular risk profile (mean age, mean body mass index, and percentage with diabetes mellitus, hypertension, dyslipidemia, smoking [ever smoked], or family history of coronary artery disease); type of CT scanner; CACS results; and cardiovascular events with median follow-up duration. Cardiovascular events included the combined incidence of MACEs and the independent outcomes of all-cause death and nonfatal myocardial infarction. For studies that reported adjusted measures of association with MACEs (CACS = 0 compared with >0), the variables that were adjusted in these analyses were abstracted. We assessed quality of included studies with the Newcastle-Ottawa Quality Assessment Scale for cohort studies.
with greater than or equal to 5 stars were considered to be high quality.

**Primary Data Analysis**

We performed 4 analyses: unadjusted risk ratios for MACEs, unadjusted risk ratios for hard events (death or nonfatal myocardial infarction), prognostic accuracy of CACS for MACEs, and pooled event rates between the CACS=0 and greater than 0 groups. For the prognostic performance analyses, we focused on sensitivity and negative likelihood ratio because CACS is more suitable to be a rule-out test in this setting.

We combined data by using the Der Simonian and Laird random-effects model with inverse variance weighting, considering the clinical and statistical heterogeneity between studies. Estimates were reported as relative risk (RR) comparing CACS=0 versus CACS greater than 0, with 95% confidence intervals (CIs). Differences were considered statistically significant according to 2-tailed analysis with \( P < 0.05 \). Heterogeneity across studies was assessed with the Cochran \( Q \) statistic \((\chi^2)\) and with the \( I^2 \) test. We considered \( Q \) statistic \( P < 0.10 \) and an \( I^2 \) greater than 50% suggestive of statistically significant interstudy heterogeneity. If heterogeneity was present, meta-regression was performed to investigate the sources of heterogeneity in the included studies. Furthermore, we performed subgroup analysis of studies stratified by type of CT scanner (electron beam versus multidetector CT), duration of follow-up (<1 or >1 year), race (predominantly white versus nonwhite), whether it was a single versus multicenter study, and type of cardiac events (all events and hard events). Also, we performed 2 sensitivity analyses: (1) restricted to studies with a Newcastle-Ottawa Quality Assessment Scale score of 6 points or more; and (2) using a 1-study-removed analysis (meta-influence analysis), in which 1 study at a time was removed from the pool analysis to assess whether 1 or more studies had greater influence on the strength of association. We then evaluated the effect of removal of such studies on the pooled estimate. Subgroup and sensitivity analyses were planned a priori. For prognostic accuracy of CACS for MACEs, we used absolute counts to analyze pooled sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, and summary receiver operator characteristic curves. For the meta-analytic method to pool event rates between groups, we used the incidence rate method, which has been shown to give more clinical interpretability. Publication bias was assessed with the Egger linear regression test and visual inspection of funnel plots. The trim-and-fill method was used to adjust for publication bias, if present. All the analyses were performed with

**Figure 1.** Flowchart diagram of study inclusion.
<table>
<thead>
<tr>
<th>Source</th>
<th>Region</th>
<th>Design</th>
<th>Follow-up, months</th>
<th>Cardiovascular Events</th>
<th>CT System</th>
<th>N</th>
<th>Timing of Patient Enrollment</th>
<th>Control Group</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pursnani, 2015&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Multicenter, US</td>
<td>Prospective</td>
<td>1</td>
<td>ACS, death, revascularization</td>
<td>MDCT</td>
<td>473</td>
<td>After initial negative ECG result and initial normal cardiac enzyme levels</td>
<td>Standard ED evaluation per local providers</td>
<td>4/0/3/7</td>
</tr>
<tr>
<td>Chang, 2011&lt;sup&gt;11&lt;/sup&gt;</td>
<td>PA, US</td>
<td>Prospective</td>
<td>1</td>
<td>Death, MI, revascularization</td>
<td>MDCT</td>
<td>990</td>
<td>After initial (or serial) negative ECG result and initial (or serial) normal cardiac enzyme levels</td>
<td>No</td>
<td>4/0/3/7</td>
</tr>
<tr>
<td>Laudon, 2010&lt;sup&gt;13&lt;/sup&gt;</td>
<td>MN, US</td>
<td>Prospective</td>
<td>60</td>
<td>Death, ACS, revascularization</td>
<td>EBCT</td>
<td>263</td>
<td>After initial negative ECG result and initial normal cardiac enzyme levels</td>
<td>No</td>
<td>4/0/2/6</td>
</tr>
<tr>
<td>Nabi, 2010&lt;sup&gt;7&lt;/sup&gt;</td>
<td>TX, US</td>
<td>Prospective</td>
<td>7.4</td>
<td>Cardiac death, ACS</td>
<td>MDCT</td>
<td>1,031</td>
<td>After serial negative ECG result and serial normal cardiac enzyme levels</td>
<td>No</td>
<td>4/0/3/7</td>
</tr>
<tr>
<td>Hoffman, 2009&lt;sup&gt;14&lt;/sup&gt;</td>
<td>MA, US</td>
<td>Prospective</td>
<td>6</td>
<td>ACS, death, revascularization</td>
<td>MDCT</td>
<td>368</td>
<td>After initial negative ECG result and initial normal cardiac enzyme levels</td>
<td>No</td>
<td>4/0/3/7</td>
</tr>
<tr>
<td>Georgiou, 2001&lt;sup&gt;15&lt;/sup&gt;</td>
<td>CA, US</td>
<td>Prospective</td>
<td>50</td>
<td>Cardiac death, MI, revascularization, ischemic stroke, angina, hospitalization</td>
<td>EBCT</td>
<td>192</td>
<td>After initial negative ECG result and initial normal cardiac enzyme levels</td>
<td>No</td>
<td>4/0/3/7</td>
</tr>
<tr>
<td>Laudon, 1999&lt;sup&gt;16&lt;/sup&gt;</td>
<td>MN, US</td>
<td>Prospective</td>
<td>4</td>
<td>ACS</td>
<td>EBCT</td>
<td>105</td>
<td>After initial negative ECG result and initial normal cardiac enzyme levels</td>
<td>No</td>
<td>4/0/2/6</td>
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<tr>
<td>McLaughlin, 1999&lt;sup&gt;17&lt;/sup&gt;</td>
<td>IL, US</td>
<td>Prospective</td>
<td>1</td>
<td>MI, revascularization</td>
<td>EBCT</td>
<td>134</td>
<td>After initial negative ECG result and initial normal cardiac enzyme levels</td>
<td>No</td>
<td>4/0/2/6</td>
</tr>
</tbody>
</table>

Sel/Com/Out/Tot, Selection/comparison/outcome/total; ACS, acute coronary syndrome; MDCT, Multi-detector computed tomography; MI, myocardial infarction; EBCT, Electron beam computed tomography.
Table 2. Characteristics of study participants from included studies.

<table>
<thead>
<tr>
<th>Source</th>
<th>Age, Year</th>
<th>Men, %</th>
<th>BMI, kg/m²</th>
<th>White</th>
<th>Black</th>
<th>Asian</th>
<th>Hispanic</th>
<th>HTN, %</th>
<th>DM, %</th>
<th>DLP, %</th>
<th>Cig, %</th>
<th>FH CAD, %</th>
<th>Prevalence, n</th>
<th>Events, n</th>
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<td></td>
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<td>CACS = 0</td>
<td>CACS &gt;0</td>
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<td></td>
<td>MACEs Death</td>
<td>MI</td>
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<td></td>
<td>MACEs Death</td>
<td>MI</td>
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<td></td>
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<td></td>
<td>All</td>
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<tr>
<td>Pursnani, 2015¹²</td>
<td>54</td>
<td>53</td>
<td>29.4</td>
<td>67</td>
<td>27</td>
<td>3</td>
<td>13</td>
<td>53</td>
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<td>46</td>
<td>50</td>
<td>28</td>
<td>253</td>
<td>220</td>
</tr>
<tr>
<td>Chang, 2011¹¹</td>
<td>48</td>
<td>43</td>
<td>NR</td>
<td>31</td>
<td>62</td>
<td>NR</td>
<td>NR</td>
<td>46</td>
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<td>22</td>
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<td>19</td>
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<td>Laudon, 2010¹³</td>
<td>45</td>
<td>60</td>
<td>28.7</td>
<td>95</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>84</td>
<td>16</td>
<td>NR</td>
<td>53</td>
<td>42</td>
<td>133</td>
<td>130</td>
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<tr>
<td>Nabi, 2010⁷</td>
<td>54</td>
<td>40</td>
<td>30.6</td>
<td>68</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>57</td>
<td>15</td>
<td>34</td>
<td>19</td>
<td>5</td>
<td>625</td>
<td>406</td>
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<tr>
<td>Hoffman, 2009¹⁴</td>
<td>53</td>
<td>61</td>
<td>29.0</td>
<td>85</td>
<td>8</td>
<td>1</td>
<td>12</td>
<td>39</td>
<td>11</td>
<td>37</td>
<td>49</td>
<td>NR</td>
<td>197</td>
<td>171</td>
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<td>Georgiou, 2001¹⁵</td>
<td>53</td>
<td>54</td>
<td>NR</td>
<td>36</td>
<td>25</td>
<td>14</td>
<td>26</td>
<td>61</td>
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<td>37</td>
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<td>116</td>
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<tr>
<td>Laudon, 1999¹⁶</td>
<td>48</td>
<td>54</td>
<td>NR</td>
<td>95</td>
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<td>1</td>
<td>1</td>
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<td>46</td>
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<tr>
<td>McLaughlin, 1999¹⁷</td>
<td>53</td>
<td>37</td>
<td>NR</td>
<td>28</td>
<td>71</td>
<td>1</td>
<td>19</td>
<td>64</td>
<td>27</td>
<td>25</td>
<td>4</td>
<td>35</td>
<td>48</td>
<td>86</td>
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</tbody>
</table>

B, Results based on CACS findings.

<table>
<thead>
<tr>
<th>CACS</th>
<th>Race, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Years</td>
<td>Men, %</td>
</tr>
<tr>
<td></td>
<td>White</td>
</tr>
<tr>
<td>Pursnani, 2015¹²</td>
<td>0 &gt;0</td>
</tr>
<tr>
<td>Chang, 2011¹¹</td>
<td>NR</td>
</tr>
<tr>
<td>Laudon, 2010¹³</td>
<td>NR</td>
</tr>
<tr>
<td>Nabi, 2010⁷</td>
<td>NR</td>
</tr>
<tr>
<td>Hoffman, 2009¹⁴</td>
<td>NR</td>
</tr>
<tr>
<td>Georgiou, 2001¹⁵</td>
<td>NR</td>
</tr>
<tr>
<td>Laudon, 1999¹⁶</td>
<td>NR</td>
</tr>
<tr>
<td>McLaughlin, 1999¹⁷</td>
<td>45</td>
</tr>
</tbody>
</table>

BMI, Body mass index; HTN, hypertension; DM, diabetes mellitus; DLP, dyslipidemia; Cig, cigarette smoking; FH, family history; CAD, coronary artery disease; NR, not reported.

*Statistical significance level (p<.05).
RESULTS

From a total of 2,372 unique citations identified, 42 full-text articles were assessed for eligibility and 34 were excluded (Figure 1). Out of 2,372 unique studies, 2,366 (2,358 excluded and 8 included) were in agreement for inclusion or exclusion between both investigators. There were 6 studies (eventually not included in the meta-analysis) for which we involved the third investigator for consensus. The interrater reliability was good (weight $k = 0.73$; 95% CI 0.52 to 0.98). Eight studies were finally included for qualitative synthesis.7-11 All 8 studies were also included in the meta-analysis for defining RRs of MACEs, death or nonfatal myocardial infarction, and prognostic accuracy parameters.

All studies were conducted in the United States from 1999 to 2015 and were of good quality (Table 1). One was a multicenter study. Of these 8 studies, 4 used electron beam CT13,15-17 to assess CACS and the remainder multidetector CT.7,11,12,14 Although it is well established that there are some differences between electron beam CT and multidetector CT,18 both CT scanner types have been shown to have equivalent reproducibility for measuring coronary artery calcium.19 The CACS scanning, postprocessing, and interpretation protocols are the same as originally described by Agatston et al.20

A total of 3,556 patients with acute chest pain were evaluated with CACS (pooled mean age 51 years, 95% CI 48 to 54 years; 50% men, 95% CI 43 to 58 years). Most studies were performed on predominantly white patients, but 2 had predominantly black participants.11,17 Other relevant baseline patient characteristics are shown in Table 2A. Pooled prevalence of CACS=0 was 60.2% (2,141/3,556) (95% CI 40% to 76%). Studies that provided comparisons between baseline patient characteristics and CACS results reported overall lower markers of comorbidity in patients with CACS=0 versus those with CACS greater than 0 (Table 2B).12,13,17

During a median follow-up of 10.5 months (interquartile range 1 to 29 months; range 1 to 60 months; 37,234 patient-months), the overall pooled MACEs rate was 7.6%/year (0.64 MACEs per 100 patient-months, or 237 events in 37,234 patient-months). Patients with CACS=0 had a significantly lower risk of MACEs compared with patients with CACS greater than 0 (RR 0.06; 95% CI 0.04 to 0.11; $P < 0.001$). The heterogeneity among studies was low, with an $I^2 = 0%$ (Figure 2A). The risk difference was 0.19 (95% CI 0.11 to 0.27). Subgroup and meta-regression analyses demonstrated that the effect size was not dependent on type of CT scanner, duration of follow-up, race, or type of study (single-center versus

![Figure 2. A, Forest plot of all included studies (n=8) evaluating risk ratio of CACS=0 for MACEs compared with CACS greater than 0. B, Forest plot of all included studies (n=5) evaluating risk ratio of CACS=0 for all-cause death or nonfatal myocardial infarction compared with CACS greater than 0.](image)
multicenter). The pooled event rate of MACEs for CACS=0 (0.8%/year [0.07 MACEs per 100 patient-months, or 13 events in 18,874 patient-months]) was significantly lower than for CACS greater than 0 (14.6%/year [1.22 MACEs per 100 patient-months, or 224 events in 18,360 patient-months]).

Subgroup analyses in the 5 studies evaluating death or nonfatal myocardial infarction showed an overall pooled death or myocardial infarction rate of 1.9%/year (0.16 death/myocardial infarction per 100 patient-months, or 39 deaths/myocardial infarction in 25,006 patient-months) during a median follow-up of 8.6 months (interquartile range 1 to 29 months; range 1 to 60 months; 25,006 patient-months). Patients with CACS=0 had a significantly lower risk of death or nonfatal myocardial infarction compared with patients with CACS greater than 0 (RR 0.19; 95% CI 0.08 to 0.47) (Figure 2B). The heterogeneity among studies was low, with an $I^2$ of 0%. The risk difference was 0.03 (95% CI 0 to 0.05). The pooled event rate for death or nonfatal myocardial infarction with a CACS=0 (0.5%/year [0.04 death/myocardial infarction per 100 patient-months, or 6 deaths/myocardial infarction in 13,656 patient-months]) was significantly less than with a CACS greater than 0 (3.5%/year [0.29 death/myocardial infarction per 100 patient-months, or 33 deaths/myocardial infarction in 11,350 patient-months]).

**Sensitivity Analyses**

All included studies were classified as good quality, with Newcastle-Ottawa Quality Assessment Scale scores of 6 to 7. Meta-influence analysis (Figure 3A and B) showed possibly a higher influence on the effect estimate attributable to the study by Chang et al in regard to RR for MACEs. Removal of this study improved the strength of association of lower RR of MACEs in the CACS=0 group (RR 0.043; 95% CI 0.022 to 0.083).

Summary receiver operator characteristic analysis of all included studies (Figure 4) demonstrated a summary area under the receiver operator characteristic curve of 0.81.
(95% CI 0.71 to 0.91) for prediction of MACEs. Two outliers were noted in studies with predominantly black patients. Pooled testing parameters of all studies showed significant interstudy heterogeneity, with $I^2$ greater than 50% for all parameters. Subgroup analysis including only studies with predominantly white patients (n=6) showed interstudy homogeneity ($I^2$ 0% to 15%). Analysis of pooled testing parameters from these studies showed a sensitivity of 96% (95% CI 93% to 98%), specificity of 60% (95% CI 58% to 62%), positive likelihood ratio of 2.36 (95% CI 2.22 to 2.51), and negative likelihood ratio of 0.07 (95% CI 0.04 to 0.14) (Figure 5). In studies with predominantly black patients, all pooled testing parameters showed significant heterogeneity. Assessment of testing parameters for death and nonfatal myocardial infarction was limited because of significant interstudy heterogeneity. Further exploratory subgroup analysis was limited by a low number of available studies.

Visual inspection of funnel plots for MACEs showed evidence for some missing studies, with possible weaker strengths of association ranging between log risk ratio −1 and −2, although this was not statistically significant by the Egger’s regression test ($P$=.14). The results of trim-and-fill analysis showed that 2 studies may have been missing, and the addition of these 2 studies to the pooled analysis for MACEs difference would have made the RR 0.07 (95% CI 0.04 to 0.11) (Figure 6).

**LIMITATIONS**

Our meta-analysis results have several limitations. All studies included in this meta-analysis enrolled hemodynamically stable acute chest pain patients after the absence of ischemic ECG changes and increased cardiac marker results. This does not represent all acute chest pain patients presenting to the ED. The context of included studies, and therefore this meta-analysis, did not integrate the emerging concept of accelerated diagnostic testing pathways for acute chest pain patients (eg, the HEART [History, Electrocardiogram, Age, Risk factors, Troponin] Pathway) to CACS testing. Patient eligibility and prognostic performance of CACS testing under these accelerated diagnostic testing pathways should not be assumed from this meta-analysis. Lack of adjusted risk models with higher event rates in the positive-CACS group could possibly be due to a confounding effect or moderated by other clinical covariates. Racial differences were also one of the limitations because most of the included studies enrolled predominantly white patients, who may differ in their prevalence of coronary atherosclerosis from other ethnic groups. A limited number of studies reported CACS severity, resulting in inadequate power to analyze the prognostic implications of CACS over the spectrum of abnormal results.

**DISCUSSION**

Our meta-analysis found that acute chest pain patients without a history of coronary artery disease, ischemic ECG changes, or increased cardiac enzyme levels who had a CACS of 0 had a significantly lower risk of future cardiovascular events compared with those with a positive CACS and with an acceptable low (<1%/year) rate of both MACEs and hard cardiac events. CACS assessment as an initial test in properly selected patients can effectively identify 60% with a score of 0 who are at very low risk and unlikely to benefit from hospital admission or further diagnostic testing.

Many studies during the past decade have established the value of CACS for risk stratifying asymptomatic patients, which is now reflected in all major cardiology guidelines. Conversely, the use of CACS in symptomatic patients is more controversial, although several studies have shown that CACS has good sensitivity to detect obstructive coronary artery disease (95% to 98%) and a comparably high negative predictive value (>99%). CACS also predicts prognosis independent of stress myocardial perfusion imaging results and may have diagnostic superiority to stress perfusion imaging in evaluating low-risk patients with new-onset stable chest pain. Likewise, in acute chest pain patients, available prognostic evidence with CACS is limited because of relatively small studies of...
Prognostic accuracy indices of CACS (0, >0) for cardiovascular events among included studies with predominantly white patients (6 studies, 2,432 patients).

**Figure 5.** Prognostic accuracy indices of CACS (0, >0) for cardiovascular events among included studies with predominantly white patients (6 studies, 2,432 patients).
various sample size (n = 105 to 1,031), as summarized in our analysis. This has led to inconsistencies across clinical practice guidelines for recommending the use of CACS in an acute chest pain population (not endorsed by the American College of Cardiology/American Heart Association but endorsed by the National Institute for Health and Care Excellence).

To our knowledge, our study is the first meta-analysis to address the prognostic value and accuracy of CACS in acute chest pain patients. All studies enrolled acute chest pain patients with suspected angina and without known coronary artery disease after the absence of ischemic ECG changes and increased cardiac marker levels. This patient population is akin to the low- to intermediate-risk acute chest pain patients enrolled in studies evaluating the use of CT coronary angiography, in which the overall MACEs rate is reported to be even lower than ours, at 4.9%. We demonstrate that a CACS of zero predicts a very-low-risk population for total MACEs (0.8%/year) and death or myocardial infarction (0.5%/year). Thus, there was an 18-fold difference in MACEs between patients dichotomized at a CACS of 0 and greater than 0 (0.8% versus 17.6%), with a 10-fold reduction in MACEs among the CACS=0 group compared with the overall population (7.6%/year). The very low (<1%/year) incidence of MACEs we report for CACS=0 is comparable to that reported for a normal stress echocardiogram (0.80% to 1.20%/year), stress myocardial perfusion studies (0.35% to 1.95%/year), and computed tomography angiography (CTA) (Coronary Computed Tomographic Angiography for Systematic Triage of Acute Chest Pain Patients to Treatment [CT-STAT] trial 0.8%). Furthermore, the sensitivity of CACS for detecting MACEs in acute chest pain patients (96%) is comparable to, if not better than, that reported for coronary computed tomographic angiography (CCTA) (95%), stress echocardiography (84%), or stress myocardial perfusion imaging (85%).

On the other hand, the specificity and positive likelihood ratio of CACS are relatively low. Therefore, for patients with positive CACS (40% of the patients included in this meta-analysis), the result could lead physicians to pursue further downstream testing, which also has risk (eg, additional radiation exposure, risk from complications of invasive procedures).

CACS may have several advantages over conventional imaging with either CTA or stress single-photon emission computed tomography. Compared with CTA, CACS is a more rapid, simple test that has no contraindications; requires no patient preparation, pulse rate optimization, or intravenous contrast; is performed on conventional CT systems; incurs little radiation exposure (1.1 to 1.5 mSv for CACS versus 5 to 13 mSv for CCTA), is easily interpretable; and is relatively inexpensive ($50 to $350 per scan for CACS versus $500 to $1,000 per scan for CCTA). Unlike CACS, single-photon emission computed tomography requires patient preparation; must be performed in conjunction with exercise or pharmacologic stress through coordination of medical and technical staff; depends on radiotracer availability; has various radiation exposures, depending on acquisition protocol used; and may require considerable expertise for accurate interpretation. CACS as an initial test may optimize patient triage, particularly because 60% of patients are anticipated to have a CACS of 0, which would indicate low risk for ischemia or subsequent cardiac events. Nevertheless, CACS is not without risk. Performing CACS testing is associated with a relatively small amount of radiation exposure, which nevertheless presents a risk. However, newer models of CT machines or newer scanning techniques have already been shown to be associated with lower radiation exposure than the current scanning protocol.

Acute chest pain patients without a history of coronary artery disease, ischemic ECG changes, or increased cardiac enzyme levels commonly have a CACS of zero (60%), with a very low subsequent annual MACE (0.8%) or risk of death or myocardial infarction (0.5%). This meta-analysis proffers the potential role of initial CACS testing for avoiding unnecessary hospitalization and further cardiac testing in acute chest pain patients with a CACS of zero.
REFERENCES


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