

# Reporting Coronary Artery Calcium on Low-Dose Computed Tomography Impacts Statin Management in a Lung Cancer Screening Population

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**Background:** Cigarette smoking is an independent risk factor for atherosclerotic cardiovascular disease (ASCVD). Concomitant use of low-dose computed tomography (LDCT) for coronary artery calcium (CAC) scoring with lung cancer screening (LCS) has been proposed to further determine ASCVD risk and mortality. We aimed to determine the validity of LDCT in identifying CAC and its impact on statin management.

**Methods:** We conducted a retrospective review from November 2020 to May 2021 of Military Health System (MHS) beneficiaries who received LCS with LDCT and were referred for CAC scoring with electrocardiogram-gated CT. Of the 190 participants initially identified, 170 met study eligibility. The Agatston method was used to score CAC on both scan types.

**Results:** Participants had a mean (SD) age of 62.1 (4.6) years and were 70.6% male. CAC was seen more on ECG-

gated CT compared with LDCT (88% vs 74%,  $P < .001$ ). The Spearman correlation and Kendall  $W$  coefficient of concordance of CAC scores between the 2 scan types was 0.945 ( $P < .001$ ) and 0.643, respectively. The  $\kappa$  statistic between CAC scores on the 2 different scans was 0.49 ( $SE_{\kappa} = 0.048$ ; 95% CI, -0.726-1.706), and the weighted  $\kappa$  statistic was 0.711. Bland-Altman analysis demonstrated a mean bias of 111.45 Agatston units, with limits of agreement between -268.64 and 491.54, suggesting CAC scores on electrocardiogram-gated CT were on average about 111 units higher than those on LDCT. There was a statistically significant proportion of nonstatin participants who met statin criteria based on additional CAC reporting ( $P < .001$ ).

**Conclusions:** CAC scores are highly correlated and concordant between LDCT and electrocardiogram-gated CT. Smokers undergoing annual LDCT may benefit from concomitant CAC scoring to help stratify ASCVD risk.

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Cigarette smoking is an independent risk factor for lung cancer and atherosclerotic cardiovascular disease (ASCVD).<sup>1-3</sup> The National Lung Screening Trial (NLST) demonstrated both lung cancer mortality reduction with the use of surveillance low-dose computed tomography (LDCT) and ASCVD as the most common cause of death among smokers.<sup>4,5</sup> ASCVD remains the leading cause of death in the lung cancer screening (LCS) population.<sup>2,3</sup> After publication of the NLST results, the US Preventive Services Task Force (USPSTF) established LCS eligibility among smokers and the Center for Medicare and Medicaid Services approved payment for annual LDCT in this group.<sup>1,6,7</sup>

Recently LDCT has been proposed as an adjunct diagnostic tool for detecting coronary artery calcium (CAC), which is independently associated with ASCVD and mortality.<sup>8-13</sup> CAC scores have been recommended by the 2019 American College

of Cardiology/American Heart Association cholesterol treatment guidelines and shown to be cost-effective in guiding statin therapy for patients with borderline to intermediate ASCVD risk.<sup>14-16</sup> While CAC is conventionally quantified using electrocardiogram (ECG)-gated CT, these scans are not routinely performed in clinical practice because preventive CAC screening is neither recommended by the USPSTF nor covered by most insurance providers.<sup>17,18</sup> LDCT, conversely, is reimbursable and a well-validated ASCVD risk predictor.<sup>18,19</sup>

In this study, we aimed to determine the validity of LDCT in identifying CAC among the military LCS population and whether it would impact statin recommendations based on 10-year ASCVD risk.

## METHODS

Participants were recruited from a retrospective cohort of 563 Military Health System (MHS) beneficiaries who received

LCS with LDCT at Naval Medical Center Portsmouth (NMCP) in Virginia between January 1, 2019, and December 31, 2020. The 2013 USPSTF LCS guidelines were followed as the 2021 guidelines had not been published before the start of the study; thus, eligible participants included adults aged 55 to 80 years with at least a 30-pack-year smoking history and currently smoked or had quit within 15 years from the date of study consent.<sup>6,7</sup>

Between November 2020 and May 2021, study investigators screened 287 patient records and recruited 190 participants by telephone, starting with individuals who had the most recent LDCT and working backward until reaching the predetermined 170 subjects who had undergone in-office consents before ECG-gated CT scans. Since LDCT was not obtained simultaneously with the ECG-gated CT, participants were required to complete their gated CT within 24 months of their last LDCT. Of the 190 subjects initially recruited, those who were ineligible for LCS (n = 4), had a history of angioplasty, stent, or bypass revascularization procedure (n = 4), did not complete their ECG-gated CT within the specified time frame (n = 8), or withdrew from the study (n = 4) were excluded. While gated CT scans were scored for CAC in the present time, LDCT (previously only read for general lung pathology) was not scored until after participant consent. Patients were peripherally followed, via health record reviews, for 3 months after their gated CT to document any additional imaging ordered by their primary care practitioners. The study was approved by the NMCP Institutional Review Board.

### Coronary Artery Calcification Scoring

We performed CT scans using Siemens SOMATOM Flash, a second-generation dual-source scanner; and GE LightSpeed VCT, a single-source, 64-slice scanner. A step-and-shoot prospective trigger technique was used, and contiguous axial images were reconstructed at 2.5-mm or 3-mm intervals for CAC quantification using the Agatston method.<sup>20</sup> ECG-gated CT scans were electrocardiographically triggered at mid-diastole (70% of the R-R interval). Radiation dose reduction tech-

**TABLE 1** Participant Demographics

Characteristics	Results
Mean age, (SD), y	62.1 (4.6)
Sex, No. (%)	
Male	120 (70.6)
Female	50 (29.4)
Statin use, No. (%)	117 (68.8)
Hyperlipidemia, No. (%)	132 (77.7)
Hypertension, No. (%)	109 (64.1)
Diabetes mellitus, No. (%)	46 (27.1)
LDL, mean (SD), mg/dL <sup>a</sup>	100.7 (33.7)
10-year ASCVD risk, mean (SD) <sup>b</sup>	16.1 (9.8)
Pack-year history, mean (SD)	44.7 (19.2)
Median LDCT RADS category <sup>c</sup>	2
Follow-up cardiac imaging, No.	5
Lung cancer developed, No.	1
Ischemic ASCVD developed, No.	0
CAC evidence, No. (%)	
LDCT	126 (74.1)
ECG-gated CT	150 (88.2)

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; CAC, coronary artery calcium; CT, computed tomography; ECG, electrocardiogram; LDCT, low-dose CT; LDL, low-density lipoprotein; RADS, Reporting and Data System. <sup>a</sup>12 participants had no reported LDL value; 11 participants had an LDL value > 24 months from ECG-gated CT. <sup>b</sup>32 participants had no calculable 10-y ASCVD risk score. <sup>c</sup>RADS categories: 0, incomplete; 1, negative; 2, benign appearance; 3, probably benign; 4A, suspicious; 4B/4X, very suspicious; S, other significant findings.

niques involved adjustments of the mA according to body mass index and iterative reconstruction. LDCT scans were performed without ECG gating. We reconstructed contiguous axial images at 1-mm intervals for evaluation of the lung parenchyma. Similar dose-reduction techniques were used, to limit radiation exposure for each LDCT scan to < 1.5 mSv, per established guidelines.<sup>21</sup> CAC on LDCT was also scored using the Agatston method. CAC was scored on the 2 scan types by different blinded reviewers.

**TABLE 2** Computed Tomography CAC Characteristics

Computed tomography modality	Agatston score range					Vessels with CAC, median (SD)	CAC score, median (IQR)
	0	1-10	11-100	101-400	> 400		
Low-dose, No.	44	16	48	30	32	1 (1.3)	48.1 (0-295.5)
Electrocardiogram-gated, No.	21	18	47	40	44	2 (1.3)	107.5 (18-419.8)

Abbreviation: CAC, coronary artery calcium.

### Covariates

We reviewed outpatient health records to obtain participants' age, sex, medical history, statin use, smoking status (current or former), and pack-years. *International Classification of Diseases, Tenth Revision* codes within medical encounters were used to document prevalent hypertension, hyperlipidemia, and diabetes mellitus. Participants' most recent low-density lipoprotein value (within 24 months of ECG-gated CT) was recorded and 10-year ASCVD risk scores were calculated using the pooled cohorts equation.

### Statistical Analysis

A power analysis performed before study initiation determined that a prospective sample size of 170 would be sufficient to provide strength of correlation between CAC scores calculated from ECG-gated CT and LDCT and achieve a statistical power of at least 80%. The Wilcoxon rank sum and Fisher exact tests were used to evaluate differences in continuous and categorical CAC scores, respectively. Given skewed distributions, Spearman rank correlations and Kendall W coefficient of concordance were respectively used to evaluate correlation and concordance of CAC scores between the 2 scan types.  $\kappa$  statistics were used to rate agreement between categorical CAC scores. Bland-Altman analysis was performed to determine the bias and limits of agreement between ECG-gated CT and LDCT.<sup>22</sup> For categorical CAC score analysis, participants were categorized into 5 groups according to standard Agatston score cutoff points. We defined the 5 categories of CAC for both scan types based on previous analysis from Rumberger and colleagues: CAC = 0 (absent), CAC = 1-10 (minimal), CAC = 11-100 (mild), CAC = 101-400 (moderate), CAC > 400 (severe).<sup>23</sup> Of note,

LDCT reports at NMCP include a visual CAC score using these qualitative descriptors that were available to LDCT reviewers. Analyses were conducted using SAS version 9.4 and Microsoft Excel; *P* values < .05 were considered statistically significant.

### RESULTS

The 170 participants had a mean (SD) age of 62.1 (4.6) years and were 70.6% male (Table 1). Hyperlipidemia was the most prevalent cardiac risk factor with almost 70% of participants on a statin. There was no incidence of ischemic ASCVD during follow-up, although 1 participant was later diagnosed with lung cancer after evaluation of suspicious pulmonary findings on ECG-gated CT. CAC was identified on both scan types in 126 participants; however, LDCT was discordant with gated CT in identifying CAC in 24 subjects (*P* < .001).

The correlation between CAC scores on ECG-gated CT and LDCT was 0.945 (*P* < .001) and the concordance was 0.643, indicating moderate agreement between CAC scores on the 2 different scans (Figure 1). Median CAC scores were significantly higher on ECG-gated CT when compared with LDCT (107.5 vs 48.1 Agatston units, respectively; *P* < .05). Table 2 shows the CAC score characteristics for both scan types. The  $\kappa$  statistic for agreement between categorical CAC scores on ECG-gated CT compared with LDCT was 0.49 ( $SE_{\kappa}$  = 0.05; 95% CI, -0.73-1.71), and the weighted  $\kappa$  statistic was 0.71, indicating moderate to substantial agreement between the 2 scans using the specified cutoff points. The Bland-Altman analysis presented a mean bias of 111.45 Agatston units, with limits of agreement between -268.64 and 491.54, as shown in Figure 2, suggesting that CAC scores on

ECG-gated CT were, on average, about 111 units higher than those on LDCT. Finally, there were 24 participants with CAC seen on ECG-gated CT but none identified on LDCT ( $P < .001$ ); of this cohort 20 were already on a statin, and of the remaining 4 individuals, 1 met statin criteria based on a  $> 20\%$  ASCVD risk score alone (regardless of CAC score), 1 with an intermediate risk score met statin criteria based on CAC score reporting, 1 did not meet criteria due to a low-risk score, and the last had no reportable ASCVD risk score.

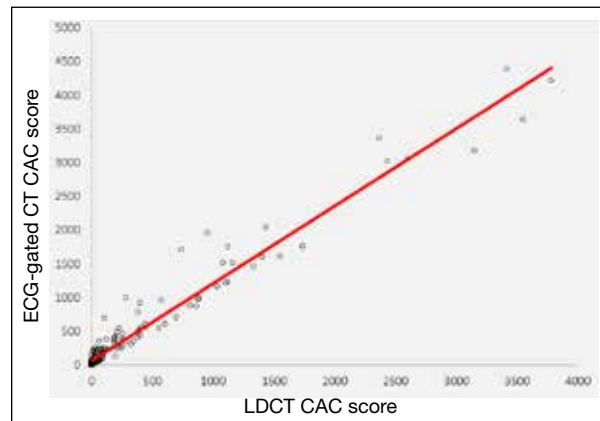
In the study, there were 80 participants with reportable borderline to intermediate 10-year ASCVD risk scores ( $5\% \leq 10\text{-year ASCVD risk} < 20\%$ ), 49 of which were taking a statin. Of the remaining 31 participants not on a statin, 19 met statin criteria after CAC was identified on ECG-gated CT (of these 18 also had CAC identified on LDCT). Subsequently, the number of participants who met statin criteria after additional CAC reporting (on ECG-gated CT and LDCT) was statistically significant ( $P < .001$  and  $P < .05$ , respectively). Of the 49 participants on a statin, only 1 individual no longer met statin criteria due to a CAC score  $< 1$  on gated CT.

## DISCUSSION

In this study population of recruited MHS beneficiaries, there was a strong correlation and moderate to substantial agreement between CAC scores calculated from LDCT and conventional ECG-gated CT. The number of nonstatin participants who met statin criteria and would have benefited from additional CAC score reporting was statistically significant as compared to their statin counterparts who no longer met the criteria.

CAC screening using nongated CT has become an increasingly available and consistently reproducible means for stratifying ASCVD risk and guiding statin therapy in individuals with equivocal ASCVD risk scores.<sup>24-26</sup> As has been demonstrated in previous studies, our study additionally highlights the effective use of LDCT in not only identifying CAC, but also in beneficially impacting statin decisions in the high-risk smoking population.<sup>24-26</sup> Our results also showed LDCT missed CAC in

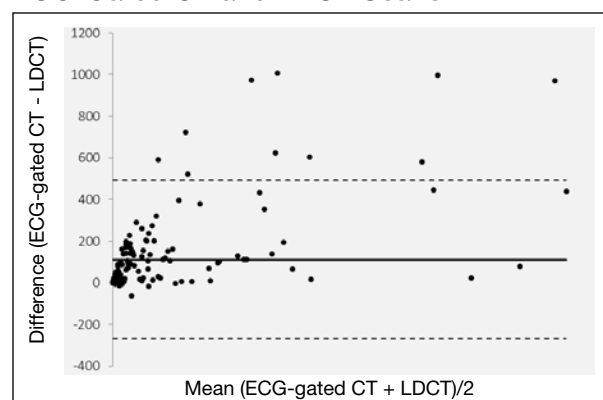
**FIGURE 1** Scatter Plot Agatston CAC Score on LDCT and ECG-Gated CT Scans<sup>a</sup>



Abbreviations: CAC, coronary artery calcium; CT, computed tomography; ECG, electrocardiogram; LDCT, low-dose CT.

<sup>a</sup>Spearman rank correlation  $r = 0.945$ ,  $P < .001$ .

**FIGURE 2** Bland-Altman Plot of ECG-Gated CT and LDCT Scans<sup>a</sup>



Abbreviations: CAC, coronary artery calcium; CT, computed tomography; ECG, electrocardiogram; LDCT, low-dose CT.

<sup>a</sup>Mean bias (center line) was 111.45 Agatston units, with limits of agreement between  $-268.64$  and  $491.54$  (bottom and top dashed lines, respectively).

participants, the majority of which were already on a statin, and only 1 nonstatin individual benefited from additional CAC reporting. CAC scoring on LDCT should be an adjunct, not a substitute, for ASCVD risk stratification to help guide statin management.<sup>25,27</sup>

Our results may provide cost considerate implications for preventive CAC screening. While TRICARE covers the cost of ECG-gated CT for MHS beneficiaries, the same is not true of most nonmilitary insurance providers. Concerns about cancer risk from radiation exposure may also lead to hesitation about receiving

additional CTs in the smoking population. Since the LCS population already receives annual LDCT, these scans can also be used for CAC scoring to help primary care professionals risk stratify their patients, as has been previously shown.<sup>28-31</sup> Clinicians should consider implementing CAC scoring with annual LDCT scans, which would curtail further risks and expenses from CAC-specified scans.

Although CAC is scored visually and routinely reported in the body of LDCT reports at our facility, this is not a universal practice and was performed in only 44% of subjects with known CAC by a previous study.<sup>32</sup> In 2007, there were 600,000 CAC scoring scans and > 9 million routine chest CTs performed in the United States.<sup>33</sup> Based on our results and the growing consensus in the existing literature, CAC scoring on nongated CT is not only valid and reliable, but also can estimate ASCVD risk and subsequent mortality.<sup>34-36</sup> Routine chest CTs remain an available resource for providing additional ASCVD risk stratification.

As we demonstrated, median CAC scores on LDCT were on average significantly lower than those from gated CT. This could be due to slice thickness variability between the GE and Siemens scanners or CAC progression between the time of the retrospective LDCT and prospective ECG-gated CT. Aside from this potential limitation, LDCT has been shown to have a high level of agreement with gated CT in predicting CAC, both visually and by the Agatston technique.<sup>37-39</sup> Our results further support previous recommendations of utilizing CAC score categories when determining ASCVD risk from LDCT and that establishing scoring cutoff points warrants further development for potential standardization.<sup>37-39</sup> Readers should be mindful that LDCT may still be less sensitive and underestimate low CAC levels and that ECG-gated CT may occasionally be more optimal in determining ASCVD risk when considering the negative predictive value of CAC.<sup>40</sup>

### Limitations

Our study cohort was composed of MHS beneficiaries. Compared with the general

population, these individuals may have greater access to care and be more likely to receive statins after preventive screenings. Additional studies may be required to assess CAC-associated statin eligibility among the general population. As discussed previously LDCT was not performed concomitantly with the ECG-gated CT. Although there was moderate to substantial CAC agreement between the 2 scan types, the timing difference could have led to absolute differences in CAC scores across both scan types and impacted the ability to detect low-level CAC on LDCT. CAC values should be interpreted based on the respective scan type.

### CONCLUSIONS

LDCT is a reliable diagnostic alternative to ECG-gated CT in predicting CAC. CAC scores from LDCT are highly correlated and concordant with those from gated CT and can help guide statin management in individuals with intermediate ASCVD risk. The proposed duality of LDCT to assess ASCVD risk in addition to lung cancer can reduce the need for unnecessary scans while optimizing preventive clinical care. While coronary calcium and elevated CAC scores can facilitate clinical decision making to initiate statin therapy for intermediate-risk patients, physicians must still determine whether additional cardiac testing is warranted to avoid unnecessary procedures and health care costs. Smokers undergoing annual LDCT may benefit from standardized CAC scoring to help further stratify ASCVD risk while limiting the expense and radiation of additional scans.

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### Disclaimer

The opinions expressed herein are those of the authors and do not necessarily reflect those of *Federal Practitioner*, Frontline Medical Communications Inc., the US Government, or any of its agencies.

### Ethics and consent

Research data were derived from an approved Naval Medical Center Portsmouth Institutional Review Board protocol.



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