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Research paper

Self- vs provider-referral differences for coronary artery calcium testing

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ABSTRACT

Study objectives: The objectives of this study were to identify independent predictors for moderate/accentuated coronary artery calcium (CAC) score and compare patients who self-referred for CAC Computed Tomography (CT) testing to those who were provider-referred.
Design: Patients underwent CAC between January to July 2019. The analysis was divided into self-referred patients influenced by a CAC community campaign who identified themselves as having cardiovascular risk factors compared to provider-referred intermediate-risk patients who were asymptomatic. SAS version 9.4 (SAS Institute, Inc., Cary, NC) was used for all analyses.
Setting: Seven southwest Ohio hospitals from a single network.
Participants: 2124 adult patients who received CAC CT (163 self and 1961 provider-referred).
Interventions: CAC CT.
Main outcome measures: Demographics, risk factors, lab values, prescriptions, and referral status were used to compare CAC score differences between self- and provider-referred patients.
Results: For 2124 patients, three predictors for moderate/accentuated CAC score remained significant after multiple logistic regression: CKD (OR 0.24, CI 0.008–0.68, $p < 0.05$), COPD (OR 0.39, CI 0.19–0.80, $p < 0.05$), and CAD (OR 0.46, CI 0.22–0.98, $p < 0.05$). There were four differences between referred groups: history of PVD (OR 0.21, CI 0.05–0.86, $p < 0.05$), higher triglyceride (OR 1.004, CI 1.00–1.01, $p < 0.05$), higher LDL levels (OR 0.991, CI 0.98–1.00, $p < 0.05$), and beta blocker prescription (OR 4.38, CI 1.49–12.85, $p < 0.05$) in self-referred patients.
Conclusions: CAC CT testing is associated with independent risk predictors and can be used to clarify cardiovascular risk in self- and provider-referred patients with statistical similarity. Patients reliably self-refer for CAC CT when risk is present during a community initiative. Such initiatives may have a preventive benefit and lead to earlier pursuit and optimization of anti-lipid therapies.

1. Introduction

CAC CT is a noninvasive screening tool useful in risk decisions for patients with cardiovascular disease (CVD). If the decision to prescribe a statin is equivocal, the 2018 American College of Cardiology (ACC) and American Heart Association (AHA) Guideline recommend CAC testing for adults aged 40–75 years at 10-year atherosclerotic cardiovascular disease (ASCVD) intermediate risk (7.5–20%) without diabetes mellitus and with low-density lipoprotein (LDL) cholesterol 70–189 mg/dL [1–4]. Statin therapy should always be initiated for two groups: (1) baseline LDL ≥190 mg/dL and (2) diabetes where LDL ≥70 mg/dL [5].

When risk status is uncertain for individuals at intermediate ASCVD risk, CAC predicts who will and will not benefit from statin initiation. In such cases, if the absolute CAC = 0, treatment with statin therapy may be withheld or delayed in the absence of risk factors. In those ≥55 years of age, an absolute CAC score of 1–99 favors statin initiation. For any other patient, if the CAC score is ≥100 or ≥75th percentile, statin therapy is indicated unless otherwise deferred by the outcome of a clinician-patient risk discussion [6]. CAC testing is useful for the purpose of determining statin therapy initiation and therefore generally not

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helpful in the setting of patients with active symptoms of chest pain or who are already on statin. The exception would be to consider the addition of Ezetimibe and further with Paraprotein Convertase Subtilisin/Kexin 9 serine protease (PCSK9) inhibitor in stepwise fashion if LDL was still not within the recommended range in patients at very high-risk ASCVD [5].

The objective of this study was to compare patients who self-referred CAC testing to those who were provider-referred. We hypothesized that there would be a statistical difference between groups where self-referred patients would have fewer baseline risk predictors than provider-referred patients. We presumed that providers would have higher preventive risk awareness than patients who would otherwise pursue testing on their own with self-perceived ASCVD risk. If our study resulted in a predicted difference, we could pursue improved primary screening strategies with general providers. If no difference, patients were reliable at self-prediction and the CAC initiative would be considered successful with further insight into how such community initiatives contribute to public health.

2. Materials & methods

The study was approved by the Wright State University Institutional Review Board and entailed a retrospective chart review of patients who received CAC CT between 1 January 2019 to 30 June 2019 at seven southwest Ohio hospitals. Subjects were either (1) self-referred patients influenced by a community campaign and having one or more cardiovascular risk factors (i.e., family history of coronary artery disease [CAD], premature CAD or stroke, history of hypertension, hyperlipidemia, diabetes, or smoking) or (2) cardiology-referred patients identified as having CVD risk factors and the benefit that therapy would be optimized based on testing. All patients were aged 18 years or older, asymptomatic, at intermediate cardiovascular risk, and amenable to $99 self-pay of the CAC CT study [7,8].

The absolute CAC score, rather than percentile, was used both as a continuous variable and for categories of coronary artery calcification: absent = 0, discrete = 1–100, moderate = 101–400, and accentuated >400 [9]. Three demographic characteristics, 11 risk factors, 4 values obtained from lab tests, 6 anti-lipid prescriptions and 6 antihypertensive prescriptions within the trial period, as well as referral status and CAC score were obtained (Figs. 1-4). Prescription information was gathered from 1 June 2018 to 30 June 2019, 6 months prior and till date of CAC, in order to capture this primary study of who was on designated hyperlipidemia and hypertension medications prior to the CAC test. Lipid level was obtained within a 6-year period from 1 October 2013 to 30 September 2019 in order to capture a representative number of patients who had any previous lipid evaluation. Sufficient lipid levels were not obtainable within a shorter period of time. These details were gathered from the Epic electronic medical record (EMR) using the Microsoft SQL Server Manager. Date range means were also obtained (Figs. 5-6).

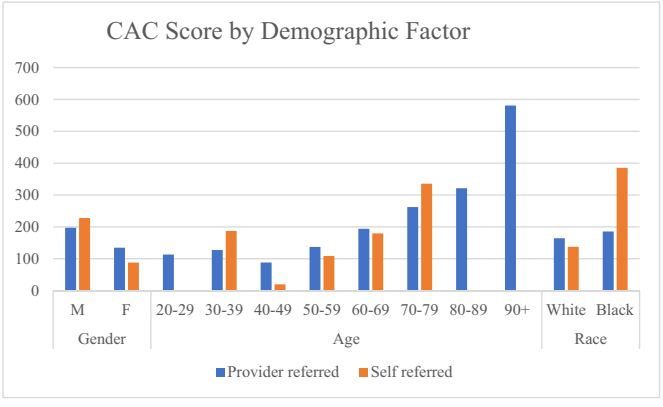

Fig. 1. CAC score by demographic factor.

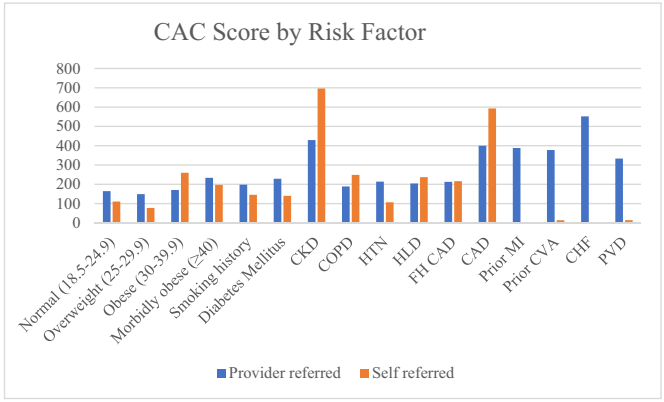

Fig. 2. CAC score by risk factor.

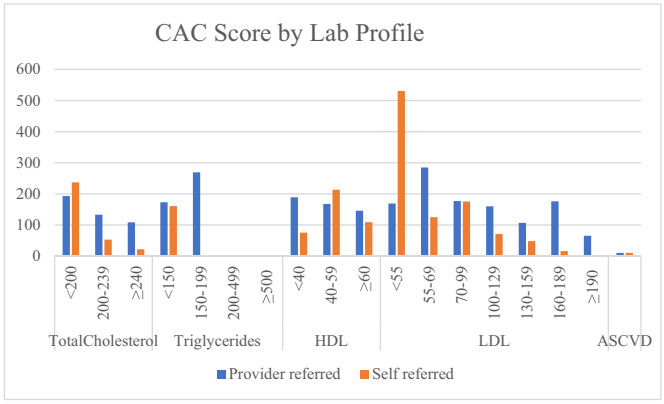

Fig. 3. CAC score by lab profile.

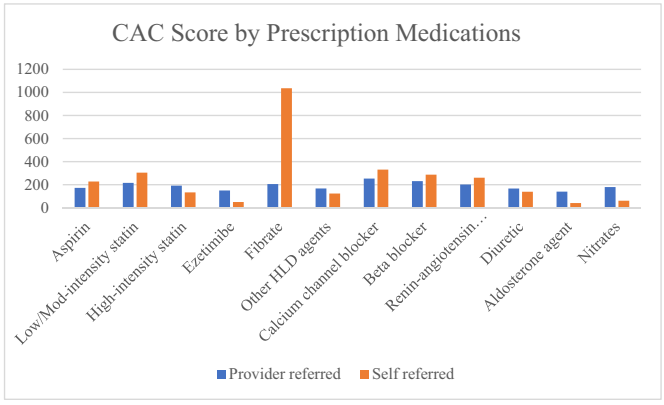

Fig. 4. CAC score by prescription medications.

Five races were identified in the social history of the EMR and obtained: White, Black, Pacific Islander, Asian, and Native American/Alaskan. Interestingly there was no Hispanic/Latino representation. Due to low numbers of patients in certain racial groups, only White and Black patients were included in the analysis. Specifically, only White and Black races had statistical representation for race differences with 92% Caucasian, 6.4% Black. Pacific Islander represented only 1.5% of the study group and for other races this value was <1%. Therefore Pacific Islander, Asian, and Native American/Alaskan categories were excluded.

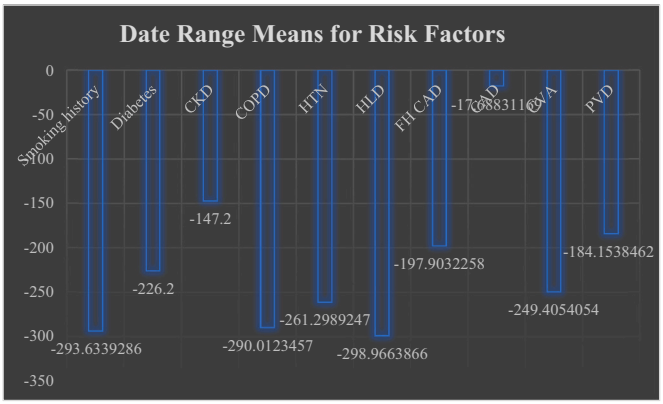

Fig. 5. Date range means for risk factors.

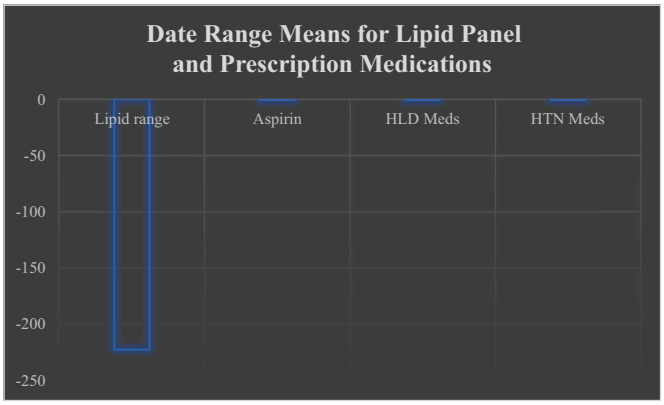

Fig. 6. Date range means for lipid panel and prescription medications.

SAS version 9.4 (SAS Institute, Inc., Cary, NC) was used for all analyses and a level of significance of alpha = 0.05 was used throughout to assess statistical significance. A multiple logistic regression was run to answer this research question with CAC Status as the response variable and all variables of interest as predictor variables. The model predicts the odds of being in the moderate/accentuate CAC category. With any type of regression that includes more than one predictor variable, predictor variables must not be too highly correlated with each other to avoid multicollinearity with artificially high *p*-values, which could mask significant relationships. For this reason, total cholesterol was excluded as a function of other cholesterol variables. The model controlled for the effects of all other variables in the model, so that odds ratios displayed are adjusted odds ratios. Another multiple logistic regression was run to answer this research question with Referral Status as the response variable and all variables of interest as predictor variables. The model predicts the odds of being in the self-referral category. Total cholesterol was again excluded due to multicollinearity.

3. Results

A total of 2124 patients, aged 18 to 89, qualified for the study, 163 of whom were self-referred and 1961 were provider-referred. Chronic kidney disease (CKD), chronic obstructive pulmonary disease (COPD), and coronary artery disease (CAD) were independent predictors for moderate/accentuated CAC score in our model.

With only White and Black races represented in our analysis, we saw no association. This was also true for body mass index (BMI), smoking history, diabetes mellitus (DM), hypertension (HTN), hyperlipidemia (HLD), family history (FH) of CAD, cerebrovascular accident (CVA) including stroke and transient ischemic attack (TIA), and peripheral vascular disease (PVD). Individual lipid levels such as triglycerides, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) had no association, and therefore neither did ASCVD. HLD and HTN prescription medications for the group of 2124 patients was not associated with a moderate/accentuated CAC score. Three predictors for moderate/accentuated CAC score remained significant after multiple logistic regression: CKD (OR 0.24, CI 0.008–0.68, $p < 0.05$), COPD (OR 0.39, CI 0.19–0.80, $p < 0.05$), and CAD (OR 0.46, CI 0.22–0.98, $p < 0.05$) (Table 1).

Table 2 compares self- vs provider-referred patients on 30 demographic and clinical risk factors. When referral groups were compared there were four differences which include PVD, higher triglyceride levels, higher LDL, as well as beta blocker (BB) prescription with higher odds ratio for elevated CAC score in the self-referred group. For compared groups there was still no differences in body mass index (BMI), smoking history, diabetes mellitus (DM), hypertension (HTN), hyperlipidemia (HLD), family history (FH) of CAD, or cerebrovascular accident (CVA) including stroke and transient ischemic attack (TIA). HLD prescription medications were not associated with a moderate/accentuated CAC score. However the self-referred group had higher rates of PVD (OR 0.21, CI 0.05–0.86, $p < 0.05$), higher triglyceride (OR 1.004, CI 1.00–1.01, $p < 0.05$), higher LDL levels (OR 0.991, CI 0.98–1.00, $p < 0.05$), and prescription of beta blocker (OR 4.38, CI 1.49–12.85, $p < 0.05$) compared to provider-referred patients.

Table 1
Multiple logistic regression results for CAC Status.

Variable	Odds ratio	95% CI	p-Value
Referral status	1.11	0.60–2.05	0.75
Demographic			
Gender	0.70	0.47–1.05	0.08
Age	1.03	0.99–1.06	0.06
Race	0.49	0.23–1.02	0.05
Risk factor			
BMI	1.02	0.99–1.05	0.33
Smoking history	0.95	0.48–1.87	0.87
Diabetes mellitus	1.71	0.79–3.71	0.17
CKD	0.24	0.08–0.68	<0.05
COPD	0.39	0.19–0.80	<0.05
HTN	1.15	0.71–1.85	0.57
HLD	0.88	0.60–1.28	0.49
Family history CAD	0.99	0.49–1.98	0.97
CAD	0.46	0.22–0.98	<0.05
CVA	1.35	0.40–4.56	0.62
PVD	1.03	0.30–3.50	0.96
Lab values			
Triglycerides	0.999	0.99–1.00	0.41
HDL	0.99	0.97–1.00	0.18
LDL	0.996	0.99–1.00	0.18
ASCVD	0.997	0.97–1.03	0.82
Prescription medications			
HLD agents			
Aspirin	1.25	0.78–2.00	0.35
Low/moderate statin	0.92	0.62–1.37	0.68
High statin	0.93	0.49–1.76	0.82
Ezetimibe	0.51	0.10–2.60	0.42
Fibrate	0.81	0.31–2.10	0.67
Other HLD agent	0.96	0.60–1.55	0.88
HTN agents			
BB	0.92	0.58–1.46	0.72
ACEi/ARB	1.17	0.76–1.78	0.48
Diuretic	0.97	0.60–1.55	0.88
CCB	0.96	0.55–1.66	0.87
Aldosterone antagonist	0.72	0.34–1.50	0.38
Nitrates	1.88	0.38–9.3	0.44

Key: ACEi, angiotensin-converting enzyme inhibitor. ARB, angiotensin receptor blocker. ASCVD, atherosclerotic cardiovascular disease. BB, beta blocker. BMI, body mass index. CAD, coronary artery disease. CCB, calcium channel blocker. CI, confidence interval. CKD, chronic kidney disease. COPD, chronic obstructive pulmonary disease. CVA, cerebrovascular accident; including stroke and transient ischemic attack (TIA). HTN, hypertension. HDL, high-density lipoprotein. HLD, hyperlipidemia. PVD, peripheral vascular disease.

Table 2
Multiple logistic regression results for Referral Status.

Variable	Odds ratio	95% CI	p-Value
CAC status	1.09	0.59–2.03	00.78
Demographic			
Gender	0.86	0.46–1.63	0.65
Age	1.01	0.96–1.06	0.80
Race	0.60	0.17–2.19	0.44
Risk factor			
BMI	1.01	0.97–1.06	0.55
Smoking history	1.04	0.33–3.23	0.95
Diabetes mellitus	0.91	0.27–3.07	0.88
CKD	0.96	0.11–8.23	0.97
COPD	3.70	0.48–28.28	0.21
HTN	1.66	0.74–3.72	0.22
HLD	1.08	0.58–2.02	0.81
Family history CAD	0.71	0.26–1.96	0.51
CAD	1.36	0.30–6.24	0.69
CVA (TIA or stroke)	1.85	0.20–17.03	0.59
PVD	0.21	0.05–0.86	<0.05
Lab values			
Triglycerides	1.004	1.00–1.01	<0.05
HDL	1.00	0.98–1.02	0.92
LDL	0.991	0.98–1.00	<0.05
ASCVD	1.002	0.96–1.05	0.94
Prescription medications			
HLD agents			
Aspirin	1.06	0.50–2.22	0.88
Low/moderate statin	1.43	0.75–2.74	0.28
High statin	1.43	0.46–4.42	0.54
Ezetimibe	3.34	0.52–21.54	0.20
Fibrate	0.81	0.31–2.10	0.67
Other HLD agent	0.59	0.31–1.15	0.12
HTN agents			
BB	4.38	1.49–12.85	<0.05
ACEi/ARB	0.83	0.43–1.57	0.56
Diuretic	0.73	0.36–1.49	0.38
CCB	0.86	0.38–1.95	0.71
Aldosterone antagonist	1.12	0.35–3.59	0.85
Nitrates	0.75	0.09–6.55	0.79

Key: ACEi, angiotensin-converting enzyme inhibitor. ARB, angiotensin receptor blocker. ASCVD, atherosclerotic cardiovascular disease. BB, beta blocker. BMI, body mass index. CAD, coronary artery disease. CCB, calcium channel blocker. CI, confidence interval. CKD, chronic kidney disease. COPD, chronic obstructive pulmonary disease. CVA, cerebrovascular accident; including stroke and transient ischemic attack (TIA). HTN, hypertension. HDL, high-density lipoprotein. HLD, hyperlipidemia. PVD, peripheral vascular disease.

Ideally, patients would not be prescribed a statin within 6 months leading up to date of CAC as the purpose of CAC is to optimize statin and hyperlipidemia therapies. We found that this was mostly true for both groups and the overall sample. There was a higher odds ratio for prescription of aspirin and other HLD agents like niacin, fish oil, and omega-3 fatty acids, but these did not affect CAC value.

4. Discussion

We accomplished the objective of the study which was to identify independent risk factors for moderate/accentuated CAC as well as to compare self- and provider-referred patients for differences regarding their CVD risk as demonstrated by an elevated CAC score. For the full sample of 2124 patients, they were more likely male, older aged ≥59 years, with no differences between White and Black race when they had higher CAC. Those with the risk factors CKD, COPD, and CAD were likely to have higher CAC. There were not differences in demographics, lab values, or prescription medications. There was also not a difference in CAC score between referral groups (Table 1). When our sample was compared by referral status, self-referred patients were similarly male, mean age ≥59 years, without race differences and higher CAC. Self-referred patients compared to provider-referred patients, however, were more likely to have PVD, higher levels of triglycerides and LDL as well as prescription for BB when their CAC score was elevated (Table 2).

Providers and patients in a Southwest Ohio population seem to have similar awareness of risk factors for primary prevention concerns when reminded with a community initiative. Such community initiatives may have a public health benefit for primary prevention for early detection of cardiac risk and may be repeated in other communities. It is not believed that different eligibility criteria should be applied to the self- than provider-referred group. Self-referred patients were actually more reliable to self-refer. The data show this is true for self-referred patients who had peripheral vascular disease, previous abnormal cholesterol levels, or who were being treated for blood pressure with a typical antihypertensive. When these factors were present, they were likely to have a higher CAC score.

Male gender and older age as risk factors for CVD are consistent with the Multi-Ethnic Study of Atherosclerosis (MESA) cohort study [4]. MESA identified elevated glucose (DM) and family history of MI (family history of CAD) to be related to higher CAC score, as did our initial data when we used more expanded date ranges through 30 September 2019 [10]. Patients seemed to be evaluated more closely after they had CAC CT as demonstrated by more comorbidities identified in the months following the community initiative. Other literature evaluations found obesity [11], hypertension, diabetes [12], and reduced renal function [13] as risk factors for higher CAC score, so that our data is consistent. COPD of note is found to be a significant comorbidity alongside CVD. Patients with COPD are more vulnerable to cardiac disease [14], the two diseases often coexist together and COPD serves as a worse prognostic risk factor for CVD [14–16].

We examined 30 demographic and clinical variables and found four differences between groups (PVD, higher triglyceride and LDL levels, prescription BB) in which these factors were associated with moderate/accentuated CAC in self-referred patients (Table 2). PVD is the peripheral manifestation of CVD that can progress or be preceded by CAD. Triglycerides are generally related to CAD and CVD as a previously acclaimed independent risk factor. It is postulated that it may be the high triglyceride-like proteins that are more culprit than the entire molecule [17–19]. Further lending argument to this controversy of the triglyceride molecule as an independent risk factor, Xia et al. discuss an inverse association between triglyceride levels and mortality risk in CAD, calling it the “triglyceride paradox” [19]. This is of little clinical importance, however, as treating triglycerides with statins effectively lowers LDL as well as culprit particle-cholesterol. Therefore. statin remains standard of care for both triglyceride and LDL lowering [18]. LDL as an independent CVD risk factor is well established and is alone an indication for initiating statin with levels ≥190 mg/dL [5]. BB association appears to be purely incidental.

Our study had limitations. First, the study was conducted within a single hospital network, limiting the generalizability to other clinical settings. However, the seven hospitals vary to some degree in patient populations and median household income. Second, our sample was not representative of the race composition of Southwest Ohio or the US population. Patients were predominantly White (92%) than Black (6.2%), which may be a reflection of patient access to care, availability based on life responsibilities that may be related to financial status, or for any nondescript number of reasons. Third, revisions to the ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease were published in March 2019 and then updated throughout the remainder of the year, the time period that corresponded with the CAC testing of our sample [5,20]. The new 2019 guideline may have had little impact on the decision of self-initiated patients to have CAC testing. In contrast, physicians may have been influenced more substantially by the mid-study ACC/AHA guideline revisions, both in their management of patients (e.g., change in the role of aspirin in primary prevention) and in referral for CAC testing. Lastly and of important note, the self- and provider-referred groups were unbalanced in sample size, 163 vs. 1961, respectively. The investigators checked the statistical requirements for each inferential procedure to assure that this discrepancy did not yield *p* values that were untrustworthy and thus threaten validity.

As medical knowledge and therapies advance and patients live longer, a focus on preventive medicine can address risk factors associated with disability or death. CAC CT is a noninvasive tool for differentiation of CVD risk among asymptomatic patients. Patients with any of the CVD risk factors we include are likely to benefit from CAC testing [3,5,6,13,21]. We plan to continue adding patients to our CAC testing database and explore relationships among patients with these comorbidities. Early CAC CT testing can lead to expedited risk classification, appropriate treatment, reduced disability and mortality, and lower healthcare costs for coronary artery disease, a major healthcare problem in the US and worldwide.

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CRediT authorship contribution statement

The primary author contributed to the entirety of IRB protocol, data collection, discussion with statisticians, creation of figures, manuscript writing, and editing. Other authors contributed in decreasing order to data analysis, writing, and review. Ronald Markert provided editing feedback for our primary manuscript as the facility biostatistician and also professional editor. Our faculty advisor provided oversight for the project. We wish to acknowledge the hours invested in reviewing and revising code from the Microsoft SQL Manager to ensure accurate data to the authors' satisfaction by our IT data analyst, Patrick Siler. A second statistician was involved in the later revisions to the manuscript whom we especially wish to thank, Michael Bottomley, for his tenacity and education through this important material.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

The late Mukul Chandra, MD, was a beloved friend and mentor to his patients, colleagues, and learners. He contracted the pandemic SARS-CoV19 virus in March 2020 during the work of this project and passed away on 18 October 2020. Even in illness, he served his community by being the impetus for research grants focused on new COVID drug therapies in the early months of the pandemic. He was instrumental in the adoption of CAC CT in southwest Ohio to improve patient health outcomes. It was a goal of Dr. Chandra that this CAC CT database contribute to the cardiology literature. We are honored to continue this work with Dr. Chandra's dedication to preventive cardiology as our inspiration. There were no primary or grant funding contributions.

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