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ORIGINAL PAPER

The association of carotid plaque burden and composition and the coronary artery calcium score in intermediate cardiovascular risk patients

Georgia Kersche[1] · Dathan Liblik[2] · Marie-France Hétu[1] · Murray F. Matangi[3] · Laura Mantella[4] · Raveen S. Pal[1] · Michael J. Blaha[5] · Amer M. Johri[1]

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Abstract

Both the carotid ultrasound and coronary artery calcium (CAC) score quantify subclinical atherosclerosis and are associated with cardiovascular disease and events. This study investigated the association between CAC score and carotid plaque quantity and composition. Adult participants ($n=43$) without history of cardiovascular disease were recruited to undergo a carotid ultrasound. Maximum plaque height (MPH), total plaque area (TPA), carotid intima-media thickness (CIMT), and plaque score were measured. Grayscale pixel distribution analysis of ultrasound images determined plaque tissue composition. Participants then underwent CT to determine CAC score, which were also categorized as absent (0), mild (1–99), moderate (100–399), and severe (400+). Spearman correlation coefficients between carotid variables and CAC scores were computed. The mean age of participants was 63 ± 11 years. CIMT, TPA, MPH, and plaque score were significantly associated with CAC score ($\rho=0.60$, $p<0.0001$; $\rho=0.54$, $p=0.0002$; $\rho=0.38$, $p=0.01$; and $\rho=0.49$, $p=0.001$). Echogenic composition features %Calcium and %Fibrous tissue were not correlated to a clinically relevant extent. There was a significant difference in the TPA, MPH, and plaque scores of those with a severe CAC score category compared to lesser categories. While carotid plaque burden was associated with CAC score, plaque composition was not. Though CAC score reliably measures calcification, carotid ultrasound gives information on both plaque burden and composition. Carotid ultrasound with assessment of plaque features used in conjunction with traditional risk factors may be an alternative or additive to CAC scoring and could improve the prediction of cardiovascular events in the intermediate risk population.

Keywords Carotid ultrasound · Coronary calcium score · Plaque vulnerability · Plaque composition · Intermediate risk · Risk stratification

Introduction

The development of enhanced screening tools for coronary artery disease is paramount for the prediction and prevention of major adverse cardiovascular events (MACE). Current screening tools are moderately useful for predicting events for those who fall in the high- and low-risk categories by the Framingham Risk Score (FRS). The intermediate-risk population, however, is at the highest risk of being misclassified by existing tools[1]. Optimizing the screening protocol for this population may reduce both healthcare costs and the incidence of MACE. Carotid artery ultrasound is a promising risk stratification tool that addresses these goals. Further, plaque composition analysis from carotid ultrasound imaging has been underutilized and could improve the prediction of events making carotid ultrasound a valuable tool in this population [1–3].

The CAC score is a sensitive and reliable tool for predicting the presence of coronary artery disease (CAD) and long-term risk of MACE [4, 5]. CAC scoring uses non-contrast

✉ Georgia Kersche
georgia.kersche@gmail.com

1 Queen's University, Kingston, ON, Canada

2 Ferko Liblik Inc., Markham, ON, Canada

3 Kingston Heart Clinic, Kingston, ON, Canada

4 University of Toronto, Toronto, ON, Canada

5 Johns Hopkins Ciccarone Centre, Baltimore, MD, USA

cardiac-gated computed tomography (CT) to quantify calcified lesions of the coronary arteries according to the Agatston method. A CAC score of > 400 is associated with a > 20% risk of 10-year MACE [5]. Studies consistently show that the CAC score has a greater predictive value than risk factor formulas including the FRS [4, 6–8]. When considered in conjunction with the FRS, its performance is marginally improved [8]. It is generally accepted as a useful risk stratification tool and relevant in deciding treatment courses for adults with subclinical atherosclerosis. However, CT may underestimate the burden of non-calcified lesions and is rarely used for long-term repeated follow-up [9]. Plaque with a greater proportion of low-density tissue is more likely to rupture and cause MACE [10–14]. Thus, CAC scores have been reported to underestimate risk in certain populations, including females and Black patients [15, 16]. Hence, investigation into the alternative tools to maximize the value of tests is warranted. Additionally, CT is expensive and has limited accessibility, especially in the outpatient setting, necessitating the development of risk stratification tools that are readily available and cost-effective.

Previously we and others have established the relationship between carotid plaque assessment by ultrasound and CAD and MACE in at-risk patients [17, 18]. This relationship needs further examination in the low to intermediate risk population. The strengths of carotid ultrasound include its relative low-cost, speed, simplicity of performance, and ease of interpretation. An abbreviated carotid ultrasound can offer quantification of plaque burden including measures such as total plaque area (TPA), maximum plaque height (MPH), carotid intimal-medial thickness (CIMT), and plaque score. More recently, there has been widespread interest in the utility of plaque composition analysis as a method to predict plaque rupture, a precursor to most cardiovascular events [19]. Plaque composition analysis has been used by our lab to predict 5-year MACE and stenosis severity on angiography in the high-risk population [20]. The proportion of calcium, fibrous, lipid, and bloody tissue may provide similar insights in the intermediate risk population as well. The absence of carotid plaque also has a good negative predictive value for the absence of CAD [2, 21].

CAC score was found to be a similar predictor of stroke and a better predictor of cardiovascular events and CAD than carotid plaque score in the Multi-Ethnic Study of Atherosclerosis [22]. Another study found that carotid ultrasound was more sensitive for detecting asymptomatic atherosclerosis than CAC scoring in a cohort of a similar age to the sample studied here [23]. The American Heart Association listed carotid ultrasound and CAC scoring at the same level of treatment effect (IIa, Benefit > > Risk) in their guidelines [24]. In this pilot study, we sought to clarify the association between carotid ultrasound measures and the CAC score. We hypothesized that carotid plaque burden (TPA, MPH, plaque score, and CIMT) is associated with CAC score in the low to intermediate risk population. Additional comparisons of carotid plaque %Calcium and %Fibrous tissue were also assessed.

Materials and methods

Study design

This study was approved by the Queen's Health Sciences Research Ethics Board. We performed a cross-sectional, 2-centre study assessing the association between carotid ultrasound and CAC scoring for an assessment of subclinical atherosclerosis in stable outpatients. We enrolled adults with no history of significant coronary artery disease and cardiovascular events who were referred for stress echocardiography for cardiovascular risk stratification. Patients were recruited from the Kingston Health Sciences Centre and Kingston Heart Clinic. At Kingston Health Sciences Centre, this sub-study ran concurrently under an ongoing parent project, the CIRCE Study (Combining Intraplaque Neovascularization with Risk Stratification by Carotid Stress Echo). Briefly, the CIRCE study investigates the additive value of an abbreviated carotid ultrasound applied to patients receiving stress echo for the prediction of events and the need for angiography. The present sub-study enrolled a subset of CIRCE participants to undergo cardiac CT for calcium scoring within 6-months of their carotid ultrasound and stress echo. This window was chosen based on studies which found that significant increases in CAC scores can be found at time points > 6 months [25].We selected a purposeful population with a ranging extent of plaque in the carotid arteries based on their carotid ultrasound. We also included eligible data sets from the Kingston Heart Clinic database of adults who had received both carotid ultrasound and CAC scoring assessment within 6-months prior to the commencement of the CIRCE Study a part of their standard of care.

CIRCE Inclusion Criteria: (1) Males or females aged ≥ 18 years; (2) Referred for an assessment of ischemia and risk stratification; (3); and the ability and willingness to give informed written consent. **CIRCE Exclusion Criteria**: (1) Emergency procedure, or active acute coronary syndrome (active chest pain, ischemic electrocardiogram changes, or cardiac enzyme elevation); (2) Referral for viability, pulmonary hypertension, or valve assessment; (3) Referral outside of the normal working hours; (4) History of significant CAD: percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG], or coronary angioplasty; (5) History of stroke or myocardial infarction (MI); (6) Known or documented hypersensitivity or allergy

to perflutren (DEFINITY® contrast agent); (7) Known or documented allergy to Polyethylene Glycol (Peg) a component of DEFINITY®; (8) History of carotid surgery (endarterectomy or stenting); (9) Any serious medical condition or complication from the stress test that according to the investigator could interfere with the carotid scan or optimal care; (10) Currently pregnant or breastfeeding; and (11) Previous enrolment into the study. **Additional Sub-Study Exclusion Criteria**: (1) Incomplete CIRCE study images; (2) Any contraindication for receiving a cardiac CT; and (3) Weight > 675lb, abdominal width > 70 cm, or other physical inhibition from using the CT.

Carotid ultrasound protocol and interpretation

A focused carotid ultrasound protocol was carried out for all participants at the time of their stress echo. The sensitivity, and intra- and inter-rater reliability of this protocol has been validated by our lab to be 0.86 and 0.99 respectively [26]. Carotid ultrasounds were performed by cardiac sonographers trained in the vascular scan and supervised by a research delegate. An example of the images captured for each participant is presented in Fig. 1. The abbreviated scan included a cross-sectional sweep of the common carotid artery up to the bifurcation into the internal and external carotid arteries to screen for lesions. Longitudinal still images of the common carotid, bulb, and internal carotid arteries were obtained for plaque measuring and composition analyses. Care was taken to ensure that any focal protrusions were captured at their maximal height. This process was repeated for both the left and right sides of each participant. For all participants, plaque height, plaque area, and CIMT were collected manually using calipers on EchoPAC software (v. 113, GE healthcare) on longitudinal images by an experienced reader. Regular quality check of measurements by a secondary reader took place throughout data collection and analysis. Plaques are defined as focal protrusions > 1.5 mm in height or 50% greater than the adjacent CIMT. Where multiple plaques are present, all plaque areas were summed to define the TPA. MPH was recorded as the greatest single plaque height measurement between both sides taken at a perpendicular angle to the associated adventitia. The mean CIMT between the measurements for the left and right sides was considered as the CIMT for analysis. For the plaque score, carotid arteries were scored according to the Rotterdam method. The result of the stress echo was also recorded, and inconclusive tests were categorized as negative.

Carotid composition analysis

Carotid plaque composition was determined using pixel distribution analysis. An example of composition analysis is shown in Fig. 2. B-mode DICOM images were exported and uploaded to Intelliplaque © (Ferko Liblik Inc.). Images were normalized so that the lumen had a greyscale median value of 0 and the far wall adventitia had a value of 190. Ranges established and validated by histological analysis by Lal et al. in 2002 have been widely used, they are as follows: 0–4 (Blood), 8–26 (Fat), 41–76 (Muscle), 112–196 (Fibrous), and 211–255 (Calcium) [27]. The total proportion of analyzed pixels that fall within each category between both sides for a patient was recorded and used in data analysis. For those with no plaque detected all values were 0.

CAC score interpretation

CAC scoring and ultrasound image analysis was performed at Queen's University by experienced readers. The absolute Agatston score was determined by an experienced cardiac CT reader who was blinded to the participant's stress echo and carotid ultrasound results. An example of one slice of the CT imaging and pixel attenuation is shown in Fig. 3. Raw scores were categorized to be Absent (0), Mild (1–99),

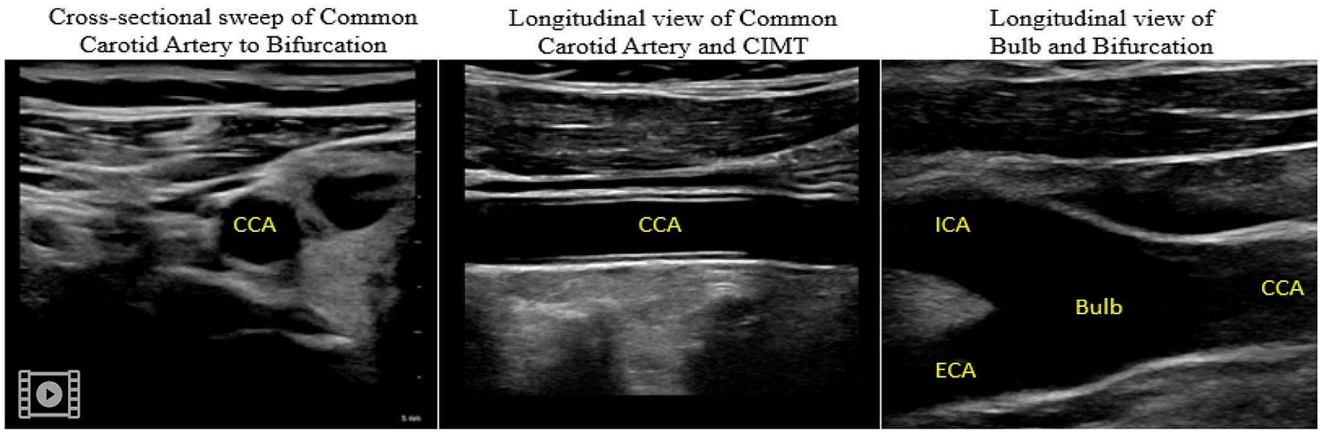

Fig. 1 Summary of views with example carotid ultrasound images

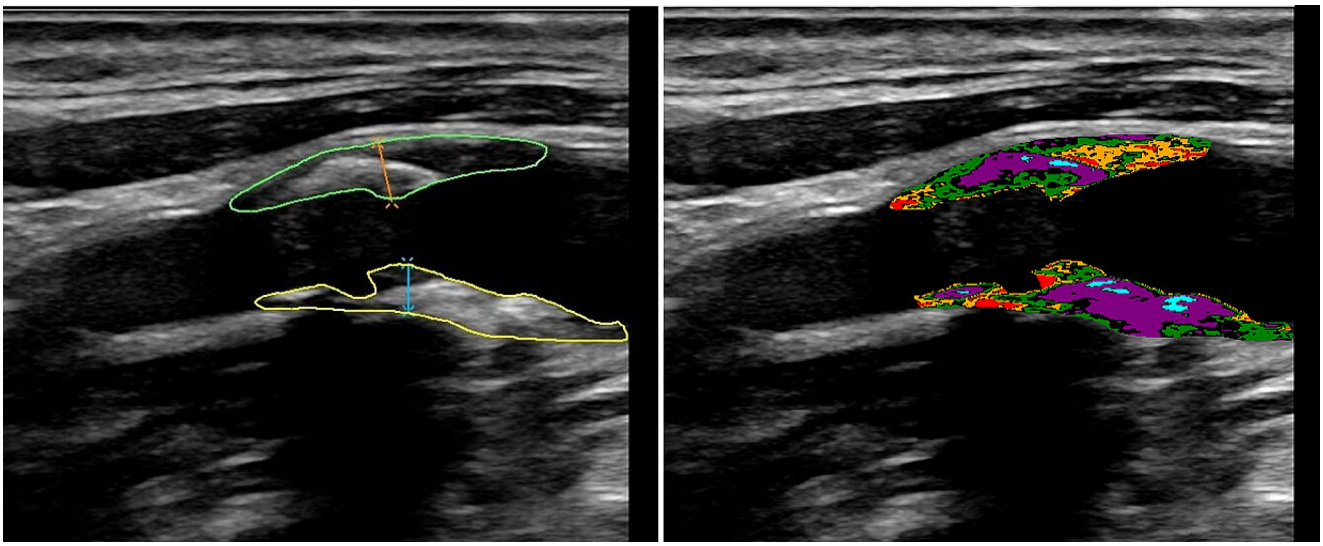

Fig. 2 Example of plaque size and composition analysis. Blue and orange calipers describe the plaque height, and the green and yellow outlines measure plaque areas (left). Intelliplaque composition analysis shows colour-coded pixels to describe the makeup of each lesion based on the greyscale median ranges by Lal et al. Red = Blood, Yellow = Fat, Green = Muscle, Purple = Fibrous, and Blue = Calcium (right)

Moderate (100–399), or Severe (400+) [28]. CAC scores were then compared to published reference values according to each participant's age, sex, and race to define their CAC percentile (https://www.mesa-nhlbi.org/CACReference.aspx) [29]. CAC percentiles are useful for providing context to overall risk based on a patient's demographics, and appear frequently in guidelines [30].

Statistical analysis

We ran paired analyses to determine the Spearman correlation coefficient (ρ) for burden measures TPA, MPH, plaque score, and CIMT to CAC score. Similar analyses were carried out for all composition parameters, including %Calcium, and %Fibrous. The same variables were compared to CAC categories (absent, mild, moderate, and severe) using the Kruskal-Wallis ANOVA test and post-hoc Dunn's test where relevant. These factors were also compared to CAC score age- and sex-based percentiles. Correlation coefficients that are 0.70–0.99 were considered very strong, 0.50–0.69 were substantial, 0.30–0.49 were fair, 0.10–0.29 were low, and 0.01–0.09 were negligible [31]. A correlation of > 0.60 is commonly considered to be clinically relevant, and a p-value < 0.05 was considered statistically significant [31].

Results

A total of 21 participants were enrolled from Kingston Health Sciences Centre June 2022 to May 2023. An additional 22 participant datasets were identified from the Kingston Heart Clinic database from 2012 to 2022. B-mode carotid ultrasound scans took an average of 5-minutes to complete. The enrollment process is detailed in Fig. 4.

The baseline characteristics of participants with complete ultrasound and CT imaging ($n = 43$) are described in Table 1. The mean age of participants was 62.8 ± 11.3 years old, and 53.5% were female. Carotid plaque was found in 90% of participants, and 67% of participants had a non-zero CAC score (Table 2). CAC scores ranged from 0 to 3059.

The correlations found between carotid plaque features and CAC scores are summarized in Table 3. CIMT showed the strongest correlation to CAC score at $\rho = 0.60$ ($p < 0.0001$). TPA, MPH, and plaque score were also significantly associated with CAC score ($\rho = 0.54$, $p = 0.0002$; $\rho = 0.38$, $p = 0.01$; and $\rho = 0.49$, $p = 0.001$). The TPA, MPH, and plaque scores of those with severe CAC scores are significantly different than those with CAC scores of 0.

Plaque composition features were not associated with the CAC score (Table 3). %Fibrous tissue was mildly correlated ($\rho = 0.19$, $p = 0.006$), but this association is unlikely to impact clinical decision-making. The primary feature of interest, %Calcium of carotid plaques, had no clear relationship with coronary calcium within this sample.

We repeated the analysis with the same plaque burden and composition measures compared to CAC percentiles (Table 4). We found similar correlation trends to the raw CAC score. The association with plaque score was strongest ($\rho = 0.52$, $p = 0.0002$), and associations with composition features did not reach significance. Plaque composition features did not hold significant relationships with CAC percentiles (Table 4).

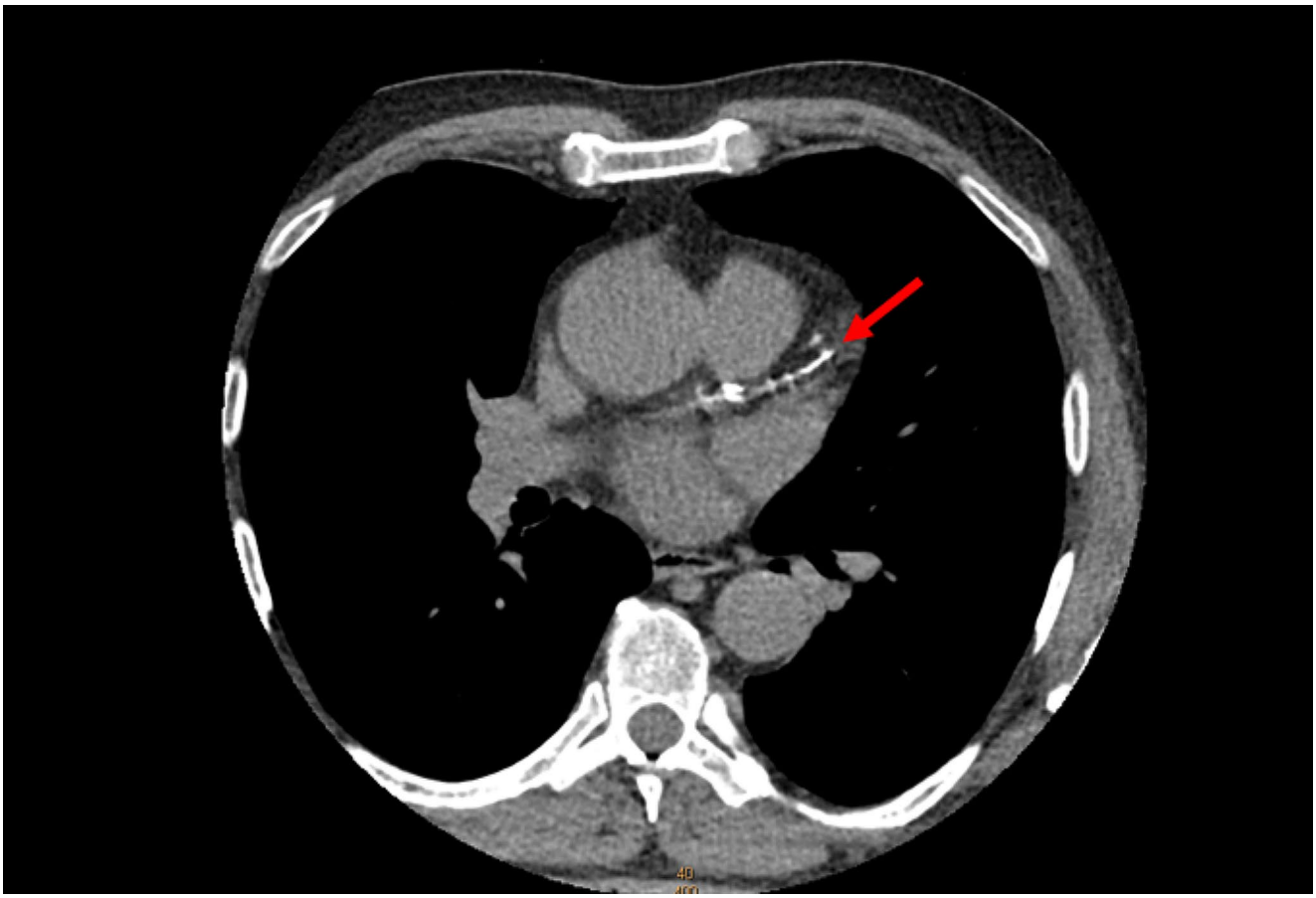

Fig. 3 A single transverse slice of an example patient's coronary calcium scan. The red arrow points toward the left anterior descending artery (LAD). The bright white areas represent calcium. This patient had a total Agatston score of 343

Discussion

In this pilot study we used carotid ultrasound and cardiac CT imaging to examine the relationship between carotid plaque burden and composition and coronary calcified plaque burden. Carotid plaque burden features appear to show moderate correlations with CAC score in adults with no history of significant cardiovascular disease. The strongest correlation found in this study was between CIMT and CAC score, consistent with findings in prior studies. The relationship between elevated CIMT and CAC scores > 0 has been well documented [32–34]. Comparisons to measures of plaque burden are not as well documented, however, this study suggests that TPA and MPH also correlate with CAC score. The correlations of the measures of plaque burden and CAC score ranged from 0.38 to 0.60, which are generally considered to indicate a moderately strong relationship [31]. This modest correlation suggests that ultrasound of the carotid arteries and calcium scoring of the coronary arteries should not be used to infer one another in most cases. Instead, these findings provide some initial evidence that carotid ultrasound may complement other assessments to contribute to a full picture of a patient's risk. The association between CIMT and CAC percentile was notably lower than CIMT and raw CAC score, potentially in part due to CIMT's strong association with age. As CAC percentiles compare scores to those of the same age, we do not expect CAC percentile to increase over time linearly as CIMT typically does.

Our study found that the strongest correlations were between CAC score and CIMT. Literature has shown that CIMT has less predictive value for clinical outcomes compared to TPA and MPH [35, 36]. While elevated CIMT and carotid plaques are distinct, it is well established that elevated CIMT is strongly associated with the development of carotid plaque across ages, sexes, and time course [37]. They are often understood as different stages of atherogenesis [38, 39]. The fact that CAC score aligns best with CIMT may be indicative of a gap in risk assessment. Unlike CIMT and plaque score, TPA and MPH are direct measures of the amount of plaque in the carotid arteries. As TPA has a greater predictive accuracy for MACE than CIMT, this may suggest that plaque identification and composition analysis will be a better predictor of events than CAC score, and further research is required to confirm this. Vulnerable plaques

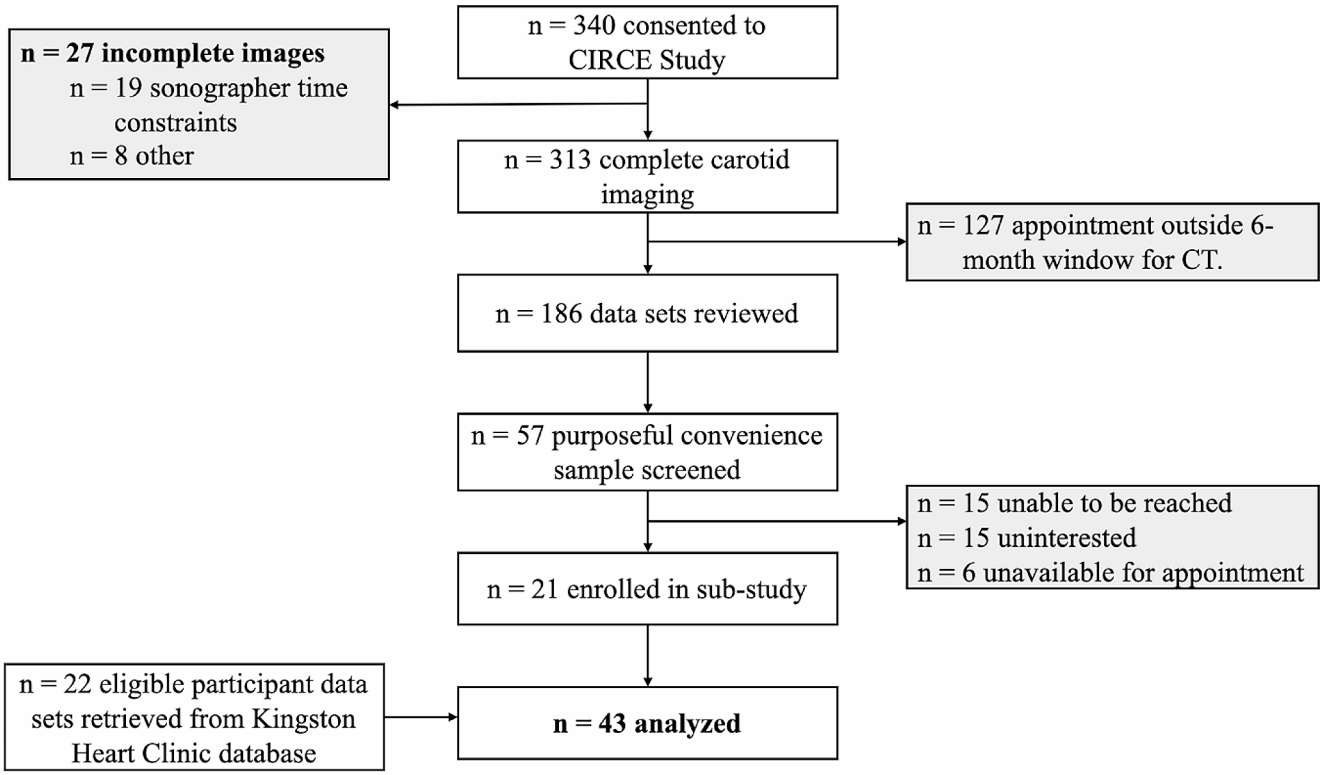

Fig. 4 Study participant recruitment flow chart

Table 1 Baseline characteristics of participants

	Overall Cohort ($n=43$)
Male Sex	20 (46.5%)
Mean Age, y	62.8 ± 11.3
Obesity (BMI > 30 kg/m^2)	16 (37.2%)
Diabetes Mellitus	7 (16.3%)
Hypertension	21 (48.8%)
Hyperlipidemia	21 (48.8%)
Smoking History	19 (39.9%)
Family History of CAD	27 (62.8%)
History of CVD	2 (4.7%)
History of PVD	2 (4.7%)
Current statin use	13 (30.2%)
Current ACE inhibitor use	9 (20.9%)
Current ARB use	8 (18.6%)
Current antiplatelet use	20 (46.5%)
Carotid plaque present (Plaque Score > 0)	39 (90.7%)
Median CAC Score (IQR)	88 (0, 289)

BMI indicates body mass index; CAD, coronary artery disease; CVD, cerebrovascular disease; PVD, peripheral vascular disease; ACE, angiotensin converting enzyme; and ARB, angiotensin receptor blocker.

Table 2 Summary of imaging data

Imaging Data	Overall Cohort ($n=43$)
Mean Total Plaque Area (mm^2)	41.64 ± 33.7
Mean Maximum Plaque Height (mm)	2.45 ± 1.21
Mean Plaque Score	2.65 ± 1.63
Mean Carotid Intima Media Thickness	0.84 ± 0.36
Absent Calcium (CAC Score = 0)	14 (32.6%)
Mild CAC (1–99)	11 (25.6%)
Moderate CAC (100–399)	10 (23.3%)
Severe CAC (400+)	8 (18.6%)

Table 3 Summary of carotid plaque associations with CAC scores

Factor	Association to CAC Score (CI)	*p*-value
Total Plaque Area	0.54 (0.29, 0.72)	**0.0002**
Maximum Plaque Height	0.38 (0.08, 0.61)	**0.01**
Plaque Score	0.49 (0.22, 0.69)	**0.001**
Carotid Intima Media Thickness	0.60 (0.18, 0.66)	**< 0.0001**
Composition		
Total %Calcium	0.09 (-0.22, 0.38)	0.59
Total %Fibrous Tissue	0.19 (-0.11, 0.47)	**0.006**
Total %Muscle	0.06 (-0.25, 0.35)	0.71
Total %Fat	0.01 (-0.29, 0.31)	0.95
Total %Blood	0.07 (-0.24, 0.36)	0.65

can be present in the absence of clinically significant coronary stenosis [40]. While angina and ischemic symptoms are credited to coronary stenosis, acute coronary syndromes are most often caused by spontaneous plaque rupture which is not entirely associated with the degree of stenosis [40].

Table 4 Summary of carotid plaque associations with CAC percentiles

Factor	Association to CAC Percentile (CI)	*p*-value
Total Plaque Area	0.46 (0.16, 0.66)	**0.0018**
Maximum Plaque Height	0.42 (0.11, 0.63)	**0.0047**
Plaque Score	0.52 (0.25, 0.71)	**0.0002**
Carotid Intima Media Thickness	0.29 (-0.02, 0.55)	**0.007**
Composition		
Total %Calcium	0.18 (-0.13, 0.46)	0.2463
Total %Fibrous Tissue	0.28 (-0.03, 0.54)	0.0540
Total %Muscle	0.22 (-0.09, 0.49)	0.0939
Total %Fat	-0.03 (-0.34, 0.27)	0.8364
Total %Blood	0.05 (-0.26, 0.35)	0.6841

Since CAC score is primarily used to predict coronary plaque burden, there remains a role for other assessments of plaque vulnerability. Carotid composition analysis can provide useful insight in terms of mortality and cardiovascular outcomes [10, 41–43]. For example, carotid calcium was found to be associated with a lower probability of survival than coronary calcium [44]. Ultrasound-based assessments also carry additional advantages including shorter duration of assessment, lower cost, portability, and serial assessment capabilities [26, 41]. This study has demonstrated that consideration of several carotid features together is possible and may improve accuracy of event prediction. When considered alongside FRS, it contributes to the body of work that suggests that low and intermediate risk patients may be reclassified by CAC scoring and carotid assessment [45–47].

Our results did not support the hypothesis that echogenic plaque composition features are correlated to CAC score. In fact, the incidence of calcium deposits in carotid plaques was low, with only 7 (16%) participants with a carotid %Calcium > 0. These findings suggest that the deposition of calcium is far greater in the coronary system than the carotid system. Atherosclerosis is generally thought of as a systemic disease, but carotid and coronary arteries do not develop plaque in a phenotypically identical manner, especially prior to the advanced lesion stage [48, 49]. Other works have assigned this discrepancy in part to the difference in pressure and augmentation index, as well as the inherent distinction with which atherosclerosis impacts different vascular beds through variances in inflammatory pathways [48]. Coronary arteries are predisposed to calcium deposition due to their tortuousness, bifurcations, and expression of pro-calcific processes activated by mechanical stimulus from pulsatile pressure in the coronary system [49]. Greater coronary calcium deposition was also found in a study of a high-risk cohort using Agatston scoring across both coronary and carotid sites [48]. A meta-analysis concluded that while plaque builds in both the coronary and carotid systems simultaneously, plaque calcification, lipid-rich necrotic core, and intraplaque hemorrhage as detected by MRI imaging did not share a strong link [34]. However, they reported an r of 0.61 comparing carotid calcification and CAC scores > 400 [34]. This describes a complex relationship between plaque composition variables but confirms that those with severe CAC scores are more likely to have calcified plaques throughout the body, which is supported by our findings [20, 48]. Taken together, our results support findings that suggest calcium in separate vascular beds in those with less than advanced disease are not predictive of one another, and carotid assessment may reveal otherwise undetected vulnerabilities.

The differences in plaque morphology and development have been attributed to several factors and pathways [49, 50]. The most widely reported factors dictating development include redox signaling pathways, vascular tone and endothelial function, wall shear stress, and vessel circumference [49]. For example, detectable plaque tends to develop first in large-diameter vessels, and only in smaller distal vessels with more advanced disease and aging [51]. Wall shear stress exerts a great frictional force on large vessels at points of curvature and bifurcation. Interestingly, in human carotid arteries at the common carotid bifurcation, low wall shear stress promotes vulnerable lesion development, whereas plaque develops slower and with a less vulnerable phenotype in areas of high shear stress [51, 52]. Some studies do, however, discuss how high shear stress exerted on plaque can trigger inflammatory processes that can increase the vulnerability of a plaque [53]. High shear stress is present in areas of bifurcation or tortuous vessels, triggering vascular smooth muscle cells to switch to a more fibrous phenotype which may contribute to the coronary bed appearing more calcified than carotid arteries. This in part explains why the lipid-rich core and fibrous cap features are expected to appear differently between beds. Altogether, carotid arteries will most likely show detectable plaque sooner than coronary arteries, and these plaques are more likely to be larger and exhibit a thin fibrous cap, neovascularization, and a lipid core as signs of vulnerability. Coronary arteries, on the other hand, tend to develop more diffuse plaque, vascular remodeling, and calcification [40]. The association found within our sample between CIMT and CAC score is consistent with these theories, as both CIMT and calcification processes increase as a result of vascular smooth muscle remodelling [54, 55].

While this pilot study did not support a large enough sample to adequately power subgroup analyses, future analyses should examine differences in correlations between sexes, statin use history, and smoking history. Females tend to have smaller and more echogenic plaques than males [56, 57]. It is well-acknowledged throughout the literature that cardiovascular risk assessment of females must consider the

physiological differences and disproportionate late diagnosis of cardiovascular disease. Screening tests and risk calculators that do not account for females specifically lead to elevated morbidity and mortality for this population. Secondly, statin use is associated with a more stable clinical presentation of both coronary and carotid plaques including greater calcium content and smaller plaque burden [12, 58]. Cigarette smoking has a nonlinear relationship with plaque morphology but increasing pack years is associated with echogenicity and markers of vulnerability [59]. Smoking appears to have a similarly complex relationship with CAC score, with both an association to greater CAC score and high-risk coronary plaque in low CAC scoring patients having been reported [60, 61]. Considerations for factors that are known to impact atherosclerosis development may lend further insight of how each screening tool should be applied when considering invasive testing and medical therapies.

To conclude, CAC scoring is a strong indicator of clinically significant CAD but does not directly assess the presence of vulnerable plaques. The use of traditional risk scores and CAC scoring alone may underestimate some patients' risk of acute coronary and cerebrovascular syndromes. Our results in consideration with related literature point towards carotid ultrasound not replacing CAC scoring, but instead contributing to a more holistic picture of a patient's likelihood of developing CAD and MACE. For example, in low-risk patients with a CAC score of 0, carotid plaque presence was independently associated with the development of CAD and MACE over 10 years [62]. Our results show that carotid plaque burden modestly correlates with CAC score, indicating that plaque does develop throughout the body at similar rates. They also emphasize that the composition of plaques in the carotid arteries is not predictive of the calcium content in coronary vessels, thus plaque composition should be considered as an additive risk stratification tool that may be helpful for the detection of vulnerable lesions throughout the body.

Limitations

A small and majority Caucasian sample limits the applicability of these results for immediate incorporation into practice. Since this study was designed and funded as a pilot study, a sufficiently powered sample size was not the priority at this stage. The design also prioritized enrolling a majority sample with detectable carotid plaque, thus random sampling was not employed for this study to maximize the value of limited CT use and funding. As a result, the sample is expected to have a higher proportion of plaque present than the general population of interest. This design was also unable to accommodate the administration of both imaging procedures at the same study visit, and thus there is potential for some minor remodelling of the coronary or carotid arteries to have taken place between image captures. Finally, the limited duration of this study did not allow us to collect outcomes data for sensitivity analysis. Future work should aim to follow-up over 10 years to investigate if one method has greater sensitivity and specificity for MACE. This study does, however, confirm that further investigation into the comparison of carotid and coronary atherosclerosis screening is warranted.

Author contributions Conceptualization: GK, MH, RP, AJ; Methodology: GK, MH, RP, AJ; Formal analysis and investigation: GK, MH; Writing - original draft preparation: GK; Writing - review and editing: GK, LM, MJB, RP, AJ; Funding acquisition: MH, AJ; Software: DL; Supervision: AJ.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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