



Handheld versus conventional vascular ultrasound for assessing carotid artery plaque

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ABSTRACT

Background: Coronary Artery Disease (CAD) is the leading cause of death worldwide. Ultrasound-detected carotid plaque has been previously shown to predict significant CAD. Despite this evidence, carotid plaque assessment has not been implemented in cardiac risk screening, likely due to the cost associated with a formal carotid ultrasound examination. This study sought to determine whether a handheld vascular ultrasound device could be used as an accurate point-of-care imaging tool for the assessment of carotid artery plaque.

Methods: We performed a focused vascular ultrasound of the carotid arteries of 200 patients referred for coronary angiography using a handheld ultrasound device as well as a full-size conventional ultrasound system. For each participant, the maximum plaque height (MPH) and total plaque area (TPA) of the carotid artery bulbs were measured.

Results: Carotid plaque assessment using the handheld device was comparable to that of the conventional ultrasound system. We found a good correlation and no relevant bias between handheld and conventional ultrasound systems in measuring MPH ($r = 0.84$, $p < 0.0001$) and TPA ($r = 0.94$, $p < 0.0001$). Furthermore, there was good inter-rater reliability for online and offline measurements of MPH and offline measurements of TPA by handheld ultrasound (0.79, 0.76 and 0.85, respectively).

Conclusions: This study demonstrates that a focused ultrasound of the carotid artery using a handheld device can be used to accurately measure MPH and TPA. This protocol has the potential to provide an expedited point-of-care assessment of carotid plaque.

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1. Introduction

Coronary Artery Disease (CAD) is the leading cause of death worldwide and can lead to ischemic events such as unstable angina, myocardial infarction (MI), and cardiac death [1]. Coronary angiography is the current clinical standard for the diagnosis of CAD [2]. However, this costly and invasive procedure is not recommended as an initial screening tool for CAD. Thus, many risk-stratification strategies are implemented prior to coronary angiography to determine which patients require angiography as a diagnostic test. These less invasive procedures include exercise stress tests, vasodilator and dobutamine nuclear myocardial perfusion imaging, and exercise and dobutamine

echocardiography [3]. Despite these tests, previous studies have demonstrated that coronary angiograms return normal results up to 40% of the time [4]. Thus, to prevent unnecessary exposure to this invasive test, as well as to reduce associated costs, researchers continue to develop prediction models and methods to risk stratify patients at risk of coronary artery disease.

It has been found that ultrasound-based measurements of carotid plaque height and area are able to predict CAD [5–8]. Despite this evidence, carotid plaque assessment has not been implemented as a vascular biomarker for cardiac risk screening [9]. As a result, we must provide evidence of feasible methods to introduce this technology into cardiovascular disease screening and risk-assessment.

The use of point-of-care ultrasound (POCUS) in emergency and critical care settings has aided in decision-making and interventional guidance [10]. Many subspecialties, including respiriologists, emergency physicians and cardiologists, have adopted bedside procedures using POCUS to assess certain conditions [11–13]. The creation of handheld ultrasound scanners has made it easy to bring carotid assessment at the point-of-care. However, concerns about image resolution remain. In this study, we determined the utility of a focused carotid ultrasound

Abbreviations: BMI, body mass index; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; MI, myocardial infarction; MPH, maximum plaque height; POCUS, point-of-care ultrasound; TPA, total plaque area.

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using a handheld ultrasound device for the quantification of carotid plaque, in order to increase the portability and accessibility of the test. We hypothesized that there would be no difference in plaque height and area measurements using handheld and standard ultrasound devices.

2. Methods

2.1. Study design and population

This prospective, observational study was designed to compare handheld ultrasound-derived measurements of carotid plaque height and area with those from a conventional ultrasound system. We included 200 patients referred for coronary angiography at the Kingston Health Sciences Center between January 2017 and February 2018. This population was chosen due to a higher prevalence of carotid plaque, which was required in order for quantification to be possible. To be eligible for the study, patients met the following inclusion criteria: 1) ≥ 18 years of age; 2) referred for clinically indicated angiography for assessment of CAD; 3) absence of clinical contraindication to angiography; and 4) able and willing to give informed consent. Patients with previous carotid endarterectomy were excluded. The primary endpoints of our study were maximum plaque height (MPH) and total plaque area (TPA).

The study was approved by Queen's University Health Sciences and Affiliated Teaching Hospitals Research Ethics Board. All participants provided informed consent to participate in the study.

2.2. Focused carotid ultrasound

Focused carotid ultrasound was carried out as previously described [7]. Briefly, long- and short-axis scans of the left and right carotid bulbs were conducted by a non-vascular-trained operator first using a handheld ultrasound device (Vscan with Dual Probe Handheld Ultrasound Scanner, GE Healthcare, Mississauga, Canada) and followed by a standard full-size ultrasound system (Vivid E9 Cardiovascular Ultrasound System with 9-L transducer, GE Healthcare, Mississauga, Canada). Plaque height was measured on the handheld ultrasound at the bedside (Supplementary Fig. 1A). In addition, plaque height and area were measured offline using each device's respective software (EchoPac Software and Gateway software, GE Healthcare) (Supplementary Fig. 1B, C) according to published literature [7].

2.3. Statistical analysis

Bland-Altman plots were created to determine any relevant bias in plaque height and area measurements between conventional and handheld ultrasound, as well as between observers. Pearson correlation was assessed to determine the correlation of measurements between handheld and conventional ultrasound devices. To determine inter-rater reliability, we calculated the intraclass correlation coefficient using a two-way ANOVA random effects model. JMP13 was used to perform the statistical analyses. $P < 0.05$ were considered significant.

3. Results

3.1. Patient baseline characteristics

Of 217 patients screened, 208 met the inclusion and exclusion criteria of the study. Scans were completed on 200 patients (139 males and 61 females). Loss of consented patients was due to withdrawn consent or time constraints. Patients ranged in age from 37 to 89 years (mean age 64 ± 11 years). The mean BMI was 31 ± 6 kg/m². Many participants had a history of hypertension (72%), hyperlipidemia (63%), or were current tobacco users or had a history of cigarette use (72%). A large proportion of patients were on anti-platelet or anti-coagulant medications (79%) as well as HMG-Co reductase inhibitors (62%) (Table 1).

3.2. Measurements of MPH and TPA using handheld vs. standard ultrasound systems

To assess whether a focused carotid ultrasound could be accurately carried out with the handheld ultrasound device, we compared plaque height and area measurements from the device with those from the conventional ultrasound system. Online measurements of MPH on the handheld device and offline measurements of MPH using the software correlated well to the conventional ultrasound system ($r = 0.84$, $p < 0.0001$ and $r = 0.83$, $p < 0.0001$, respectively, Fig. 1A, C). Bland-

Table 1
Study sample baseline characteristics.

Variable	Study participants (N = 200)
Age	64 \pm 11
Females	61 (31%)
Caucasian	197 (99%)
eGFR	77 \pm 19
BMI	31 \pm 6
Diabetes	56 (28%)
Hypertension	143 (72%)
Hyperlipidemia	126 (63%)
Smoking history	143 (72%)
Family history of CVD	127 (64%)
Medications	
HMG-Co reductase inhibitors	124 (62%)
ACE inhibitors	90 (45%)
Angiotensin receptor blockers	15 (8%)
Alpha-blockers	15 (8%)
Beta-blockers	102 (51%)
Calcium channel blockers	42 (21%)
Anti-platelet/anti-coagulants	158 (79%)
Diuretics	39 (20%)
Non-insulin diabetes medications	35 (18%)

eGFR, estimated glomerular filtration rate; BMI, body mass index; ACE, angiotensin converting enzyme; CVD, cardiovascular disease.

Altman analysis revealed no relevant bias and a normal variation between online handheld ultrasound and conventional ultrasound measurements of MPH (0.19 mm; $1.96 * SD = 1.54$ mm, Fig. 1B) as well as between offline handheld ultrasound and conventional ultrasound measurements of MPH (0.14 mm; $1.96 * SD = 1.61$ mm, Fig. 1D). Likewise, offline measurements of TPA using the handheld ultrasound software correlated well to the conventional ultrasound system ($r = 0.94$, $p < 0.0001$, Fig. 1E). Bland-Altman analysis revealed no relevant bias and a normal variation between handheld ultrasound software and conventional ultrasound TPA measurements (9.7 mm²; $1.96 * SD = 35$ mm², Fig. 1F).

3.3. Inter-rater reliability of MPH and TPA on handheld ultrasound device

To determine the reproducibility of our vascular ultrasound protocol using a handheld device, two operators performed scans and measurements on a subset of 30 patients. Bland-Altman analysis indicated no relevant bias and a normal variation for online and offline MPH measurements as well as offline measurements of TPA between operators (0.69 mm; $1.96 * SD = 2.03$ mm; 0.33; $1.96 * SD = 2.17$; 5.07 mm²; $1.96 * SD = 41.9$ mm², Fig. 2A–C). The Intraclass correlation coefficients for online MPH measurements by handheld ultrasound, offline MPH measurements by handheld ultrasound and offline TPA measurements by handheld ultrasound were 0.79, 0.76 and 0.85, respectively (Table 2). These values correspond to good reliability for this handheld ultrasound protocol [14,15].

4. Discussion

In this study, we have shown that carotid artery plaque can be assessed using a handheld ultrasound device at the bedside with good reliability. Compared to a conventional ultrasound system, the Vscan portable device had good correlations and no relevant bias between online and offline measurements of plaque height and area taken using each device. We also found that there was good inter-rater reliability for online and offline measurements of MPH and offline measurements of TPA by handheld ultrasound.

Point-of-care ultrasound is rapidly evolving as a diagnostic modality. This is largely due to increased portability of ultrasound machines, which allows physicians to make diagnoses in a timely matter and perform procedures at the bedside [16]. Many medical and surgical subspecialties have adopted bedside procedures using POCUS to assess

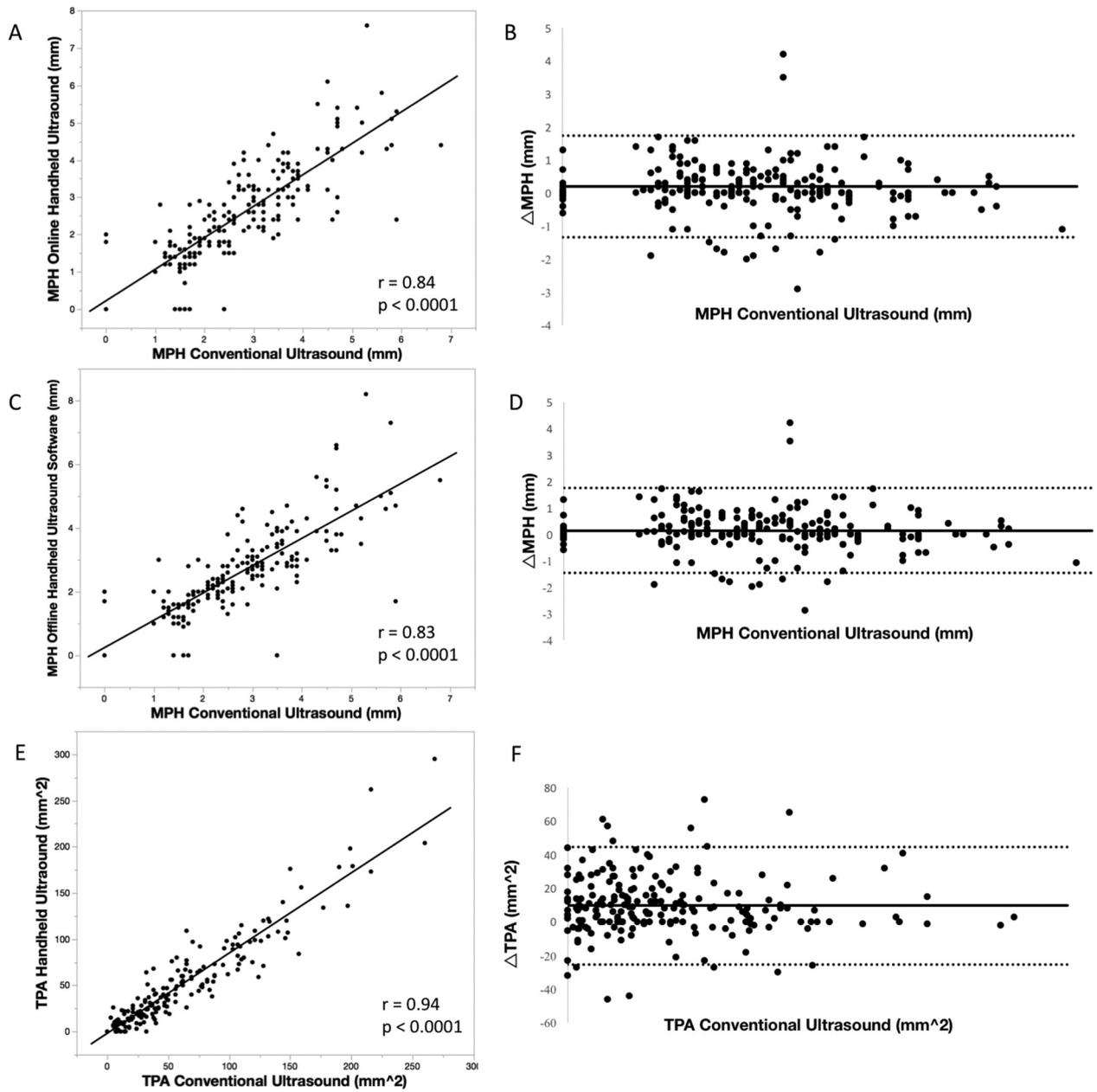


Fig. 1. Handheld ultrasound measurements of MPH and TPA are correlated to conventional ultrasound. A) Correlation between MPH measured using conventional (x-axis) and online using handheld ultrasound (y-axis). B) Bland-Altman plot shows no relevant bias between online handheld and conventional ultrasound assessments of MPH. C) Correlation between MPH measured using conventional (x-axis) and offline using handheld ultrasound software (y-axis). D) Bland-Altman plot shows no relevant bias between offline ultrasound assessments of MPH. MPH – maximum plaque height. E) Correlation between TPA measured using conventional (x-axis) and handheld ultrasound (y-axis). F) Bland-Altman plot shows no relevant bias between ultrasound assessments of TPA. TPA – total plaque area.

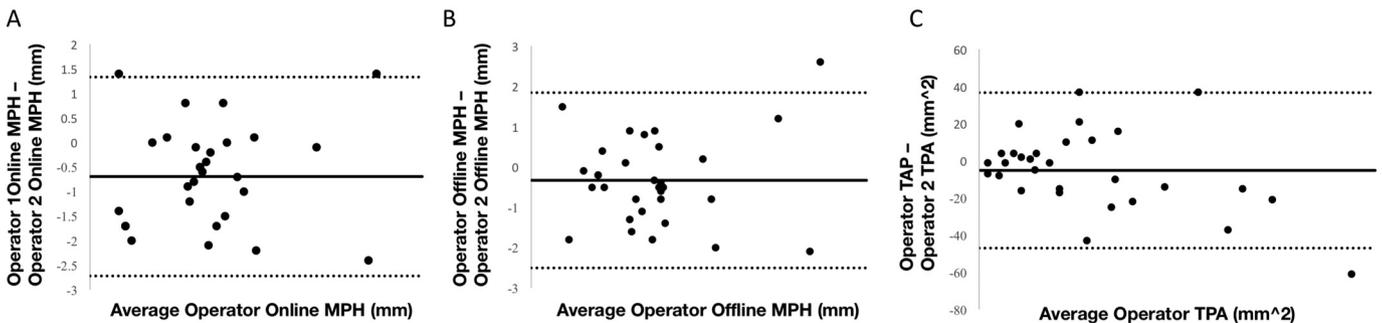


Fig. 2. Good inter-rater reliability for MPH and TPA using handheld and conventional ultrasound. Bland-Altman plot shows no relevant bias between raters for A) online MPH measurements using handheld ultrasound, B) offline MPH measurements using software and C) TPA using software. MPH – maximum plaque height, TPA – total plaque area.

Table 2
Inter-rater reliability for handheld ultrasound measurements.

Test	ICC	Lower 95% confidence bound	Level of reliability
MPH (online handheld ultrasound)	0.79	0.48	Good
MPH (offline handheld ultrasound software)	0.76	0.58	Good
TPA (offline handheld ultrasound software)	0.85	0.73	Good

ICC, intraclass correlation coefficient.

certain conditions. For example, the Bedside Lung Ultrasound in Emergency (BLUE) protocol is used to assess respiratory failure [11,12], the Focused Assessment with Sonography in Trauma (FAST) protocol is employed to look for peritoneal free fluid [12], the Rapid Ultrasound for Shock and Hypotension (RUSH) protocol assesses shock [17] and the Cardiovascular Limited Ultrasound Examination (CLUE) evaluates heart failure [13]. Similarly, our focused carotid ultrasound protocol using a handheld ultrasound device can be performed by a non-sonographer. The handheld ultrasound itself is a low-cost device that is becoming more common in clinical practice. The results from this study demonstrate the accuracy of POCUS in assessing carotid artery plaque, and position this technique as a useful tool for risk-assessment in settings such as the primary care office or the emergency department.

Previous studies have demonstrated the utility of carotid maximum plaque height and total plaque area in predicting significant CAD and cardiovascular risk [6,18–20]. Adams et al. have shown that carotid plaque burden and plaque height can predict coronary stenosis more accurately than carotid intima-media thickness [6]. Moreover, prior studies have indicated that carotid plaque measurements, including plaque height, can predict cardiovascular risk [18,19]. In addition, carotid plaque thickness has been associated with CAD lesions assessed by coronary angiography [20,21]. These studies provide evidence of the utility of carotid ultrasound in the prediction of significant CAD and cardiovascular events. We have previously shown that carotid plaque height can predict significant CAD [7]. We now demonstrate that both plaque height and area can be measured accurately on a handheld ultrasound device. Taken together, this suggests that measurements of plaque height and area can be performed at the bedside using a handheld device to stratify patients based on their risk for CAD. Thus, this protocol has the potential to provide a more accessible screening tool or imaging biomarker for CAD and cardiovascular risk.

A major hurdle when using a handheld vascular ultrasound device to assess plaque burden is the lower resolution compared to conventional ultrasound. In addition, concerns about the narrower sector, smaller field of view, and simplified transducer technology have been raised [10,16,22]. In this study, we did find discrepancies in height and area measurements between devices, likely due to the lower resolution of the handheld machine and the thick tracing lines on the offline software, which make outlining small lesions difficult. There is also no “zoom” function on the handheld device's software, again making measuring a challenge. Despite these limitations, we have shown that handheld vascular ultrasound system-derived measurements of carotid plaque height and area can be measured with good accuracy. In addition, the smaller transducer size on the handheld device was useful in patients with limited neck mobility, and detected plaques that were not obvious when using the larger transducer on the conventional ultrasound system. Moreover, many have pointed to operator training as a major limiting factor in all POCUS protocols [23–26]. Operator training is crucial when using a handheld device due to the lower resolution of the image. Inadequate image optimization during acquisition can lead to significant variations in plaque height and area measurements. In addition, an ability to recognize artifacts in each image during acquisition and interpretation can largely improve diagnostic accuracy.

The use of focused carotid ultrasound at the point-of-care by means of handheld ultrasound devices will not only lend itself to increased accuracy of cardiovascular risk-stratification prior to angiography, but

also improve health outcomes. In this study, scans were conducted and interpreted by a non-sonographer who received 15 h of informal training in the protocol and was not accredited in vascular imaging. A subset of 30 scans was conducted and interpreted by two non-sonographers with the same informal training to assess inter-observer reliability. It is important to note that all ultrasound examinations were carried out in the catheterization laboratory, mimicking the challenging conditions of bedside use. These challenges include confined space and suboptimal lighting.

4.1. Limitations

Our patient population was taken from those undergoing angiography for the assessment of CAD, thus they had a greater likelihood of having plaque. It would be important to assess this protocol in an intermediate risk population, where this tool would be used, and assess accuracy and usefulness in detecting and measuring carotid plaque. Follow-up for CV events would also validate the utility of this tool. Estimates of inter-rater reliability were based on only two raters. It is important to note that these estimates could vary if other or additional raters were used. Lastly, the handheld focused carotid ultrasound protocol needs to be tested by an emergency physician or cardiologist to assess its impact on their practice.

5. Conclusions

To our knowledge, this is the first study demonstrating the accuracy in measuring carotid plaque using a handheld ultrasound device. The portability and feasibility of this protocol make it particularly interesting as a tool that can be used at the bedside to assess cardiovascular risk. This procedure can provide expedited, safe, and accurate care and has the potential to be used by emergency physicians and hospitalists as a stratification tool in routine clinical practice.

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijcard.2018.12.014>.

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Conflicts of interest

The authors report no relationships that could be construed as a conflict of interest.

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