Focused Vascular Ultrasound for the Assessment of Atherosclerosis: A Proof-of-Concept Study

Amer M. Johri, MD, Catherine M. Calnan, RAH, Murray F. Matangi, MBChB, Jimmy MacHaalany, MD, and Marie-France Hétu, PhD, Kingston, Ontario, Canada

Background: Current decisions to refer for angiographic coronary assessment are based on pain character, risk scores, stress testing, and occasionally calcium scoring. Carotid plaque has emerged as an effective vascular biomarker, but the cost and time of a full carotid ultrasound examination are disadvantageous. Focused vascular ultrasound (FOVUS) is a rapid limited assessment of carotid plaque that can be conducted by non-vascular-trained operators. The objective of the study was to determine the test characteristics of FOVUS for the assessment of significant coronary atherosclerosis in symptomatic patients referred for cardiac assessment.

Methods: In this prospective study, FOVUS was performed in 208 outpatients at low to intermediate risk undergoing same-day angiography. Carotid artery maximal plaque height was measured in each participant. A previously established receiver operating characteristic curve determined that a value of ≥1.5 mm was the threshold for significant angiographic coronary artery disease. FOVUS scan results, alone or combined with stress testing, were analyzed for the prediction of significant coronary artery disease.

Results: The negative predictive value and sensitivity of plaque height alone by FOVUS were found to be 77% and 93%, respectively. Adding the FOVUS scan result to stress testing significantly increased the negative predictive value and sensitivity of these traditional risk stratification tools.

Conclusions: Rapid carotid plaque height measurement by FOVUS enhanced atherosclerosis risk prediction in patients referred for cardiac assessment. Rapid plaque quantification had good negative predictive value and high sensitivity alone or in combination with stress testing. FOVUS may serve as a potential point-of-care ultrasound tool in the integrated assessment of cardiac pain. (J Am Soc Echocardiogr 2016; DOI: 10.1016/j.echo.2016.05.003)

Keywords: Carotid ultrasound, Plaque, Stress test, Angiography

Coronary angiography, an invasive procedure with low but important risks, remains the clinical standard for the diagnosis of coronary artery disease (CAD) in symptomatic patients. Recent studies have shown that up to 40% of angiographic examinations may have normal findings, resulting in low-risk patients’ being unnecessarily referred for angiography. In this era of cost restraints, there are calls for enhanced screening strategies with better negative predictive value (NPV) to minimize unnecessary procedures and better identify symptomatic patients with significant disease. On the other hand, a screening test for CAD must maximize the true-positive rate and have a cut point with high sensitivity to avoid missing this potentially fatal disease.

A formal, full carotid ultrasound test is deemed a class D indication by the US Preventive Services Task Force in asymptomatic patients as a screening tool for endarterectomy. However, this guideline is limited to the assessment of asymptomatic patients in the context of stroke and does not consider evidence demonstrating the utility of carotid plaque assessment as a vascular biomarker for cardiac risk screening. In a recent position paper by the European Society Cardiology Working Group on Peripheral Circulation, carotid ultrasound and plaque assessment was compared with established vascular biomarkers and recommended to be a highly effective method of cardiac risk screening given its high incremental value, clinical utility, and ease of use. Compared with coronary artery calcium scoring, carotid ultrasound is less costly, carries lower risk, and is highly correlated with coronary calcium. Carotid plaque burden is more closely related to coronary disease and more predictive of cardiovascular risk than carotid intima-media thickness (IMT) and it has previously been shown (along with plaque height) to predict coronary stenosis more accurately than IMT. Plaque height has previously been reported to predict cardiovascular risk. Some practitioners use real-time carotid atherosclerosis assessment as an
a focused vascular ultrasound (FOVUS) protocol may serve as a
cost-effective screening method with high sensitivity and/or NPV for
ruling out clinically significant coronary atherosclerosis in symptom-
atic patients. In this proof-of-concept study, we define the test charac-
teristics of FOVUS for predicting important coronary atherosclerosis
in a symptomatic population presenting for cardiac assessment.

METHODS

Human and Animal Rights and Informed Consent

Informed consent was obtained for all participants in this study for
FOVUS and the use of data for publication. This study conforms to
the ethical guidelines of the 1975 Declaration of Helsinki, as reflected
in a priori approval by the institution’s human research committee.
The Queen’s University Health Sciences Research Ethics Board
approved this study. The study was designed and implemented using
the 14-item original Quality Assessment of Diagnostic Accuracy
Studies tool to ensure the quality of diagnostic accuracy studies.19

FOVUS

Focused cardiac ultrasound (FCU) is defined by the American
Society of Echocardiography guidelines as a cardiac ultrasound using
a protocol limited to a few specific views and conducted by operators
without formal echocardiography training, usually using handheld or
portable devices.20 The FOVUS protocol proposed is analogous to
FCU in that it is conducted by non-vascular-trained operators and is
limited to a few views (long- and short-axis views of the right and
left carotid bulb) to rapidly screen for the presence of plaque. A single,
simple measurement (maximal plaque height in the carotid bulb from
the long axis) is conducted (Figure 1). The FOVUS protocol does
not include assessment of IMT, Doppler velocity, and calculation
of percentage stenosis as described by the American Society of
Echocardiography guidelines for a formal full diagnostic carotid ultra-
sound study.21

The FOVUS scan was approximately 7 min in length and was
limited to the long- and short-axis views of the right and left carotid
bulb only. As a proof-of-concept study, scans were conducted by a
single sonographer who received 15 hours of informal training in
the FOVUS protocol and was not accredited in vascular imaging.
Specifically, this was a typical midcareer registered cardiac sonogra-
pher (~10 years’ experience) who conducts echocardiographic
examinations on a daily basis but conducts no vascular imaging
and has no formal vascular training. Scans were conducted using a
vascular device (Vivid E9 Cardiovascular Ultrasound System, GE
Healthcare, Mississauga, Canada) equipped with an 9L transducer
for two-dimensional imaging. Scans were interpreted by a non-
vascular-trained cardiologist. Additionally, images obtained were re-
viewed by a specialist with extensive expertise in vascular imaging
and full carotid ultrasound performance (M.F.M.).

For each participant, the maximal plaque height (thickness) in the
left and right carotid artery bulb was measured as previously
described.22,23 Receiver operating characteristic curve analysis
plaques height cutoff values specific to the total enrolled population
(n = 318) have been previously established.23 In this study, the previ-
ously derived threshold of ≥1.54 mm was used to indicate angiographic-
significantly CAD. These values were nearly identical to the
Atherosclerosis Risk in Communities definition for plaque height
(≥1.5 mm).24 Patients were thus stratified for CAD using a plaque
height ≥1.5 mm and were considered to have positive FOVUS
results. All procedures were conducted and interpreted by investiga-
tors blinded to the other procedure results.

Study Design

This was a prospective study designed from its inception to test the
incremental value of FOVUS to stress testing for the assessment of
atherosclerosis. All stress tests in question were critical components
of the patients’ index assessments leading to angiographic evaluation.
Enrollment in the study occurred only after referral for angiography in
order to generate a clinical standard (finding of atherosclerosis present
or not).

Study Population

Three hundred eighteen outpatients for clinically indicated coro-
nary angiography were approached prospectively from the Cardiac
Catheterization Laboratory at Kingston General Hospital during a
6-month period in 2011 for FOVUS. In the participants recruited
(n = 208), indications for coronary angiography included angina,
abnormal results on resting or exercise electrocardiography (ECG),
and/or positive results on functional imaging stress tests. Inclusion
criteria were age ≥18 years and no clinical contraindications to angi-
ography or FOVUS. Recruited participants underwent same-day angi-
ography and FOVUS to assess for plaque only. Participants who had
complete scans and who had undergone stress tests within 3 months
before angiography were studied.

Patients’ pretest likelihood (probability) of CAD was calculated
on the basis of age, sex, and type of angina, according to the
American Heart Association combined Forrester-Diamond and
Coronary Artery Surgery Study data.25 If records had Canadian
Cardiovascular Society angina pectoris grades of 1 to 3, patients
were classified as having typical angina. To be conservative, patients
with no grades (0) or who were not experiencing chest pain at referral
were classified as having atypical angina. Symptoms other than chest
pain requiring cardiologic assessment and leading to both invasive
and noninvasive investigation included dyspnea, syncope, and palpita-
tion (53 of 208 patients [25%]).

Coronary angiography was performed using the standard Judkins
method with a GE System 2000 (GE Healthcare, Milwaukee, WI)
by experienced interventional cardiologists.22 Luminal narrowing of
coronary arteries was analyzed using a 16-segment model to produce
an overall score, as previously defined.22,26-28 Angiographic scoring
was as follows: 0 = no or minimal disease (0%-19% narrowing
in any segment), 1 = mild disease (20%-49% narrowing in
any segment), 2 = moderate disease (luminal narrowing of at least one

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>CAD</td>
<td>Coronary artery disease</td>
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<tr>
<td>ECG</td>
<td>Electrocardiography</td>
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<tr>
<td>FCU</td>
<td>Focused cardiac ultrasound</td>
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<tr>
<td>FOVUS</td>
<td>Focused vascular ultrasound</td>
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<td>IMT</td>
<td>Intima-media thickness</td>
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<td>NPV</td>
<td>Negative predictive value</td>
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