Atherosclerosis 221 (2012) 118–123

Contents lists available at SciVerse ScienceDirect

Atherosclerosis

journal homepage: www.elsevier.com/locate/atherosclerosis

# High-resolution radial artery intima-media thickness and cardiovascular risk factors in patients with suspected coronary artery disease – Comparison with common carotid artery intima-media thickness

Charlotte Eklund[a,b], Peter Friberg[a,b], Li-Ming Gan[a,b,c,*]

[a] The Department of Clinical Physiology, Sahlgrenska University Hospital, S-41345 Gothenburg, Sweden
[b] Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy at the University of Gothenburg, S-41345 Gothenburg, Sweden
[c] Translational Sciences, CVGI innovative Medicine Unit, AstraZeneca R&D, S-43183 Mölndal, Sweden

ARTICLE INFO

*Article history:*
Received 16 June 2011
Received in revised form
20 December 2011
Accepted 22 December 2011
Available online 29 December 2011

*Keywords:*
Atherosclerosis
Cardiovascular disease
Ultrasound
Intima-media thickness
Radial artery

ABSTRACT

*Objective:* The radial artery wall structure can be measured with non-invasive very high-resolution ultrasound with great feasibility and high accuracy. In the present study, we aim to explore clinical correlates of radial artery intima-media thickness (rIMT), in a relatively large patient cohort with suspected coronary artery disease, and further compare those to common carotid artery IMT (cIMT) that is an accepted surrogate marker of atherosclerosis.
*Methods:* Four hundred and sixteen patients referred to myocardial perfusion scintigram (MPS) were recruited, and cIMT and rIMT were scanned using conventional and very high-resolution ultrasound (55 MHz transducer), respectively. A number of plasma biomarkers were also measured.
*Results:* Both cIMT and rIMT were similarly correlated with disease history, MPS-verified ischemia, carotid plaque burden, and lipid status. Repeated measurement of rIMT showed acceptable variability.
*Conclusion:* Radial artery IMT may constitute a novel feasible imaging biomarker for systemic atherosclerosis burden, which may be used in future imaging trials to evaluate, e.g. anti-atherosclerotic treatments.



## 1. Introduction

The atherosclerotic process starts in the intima layer of the arterial wall [1]. It is a systemic disease that begins in childhood, and remains asymptomatic for decades, before any clinical manifestations occur. Although the progression rate of atherosclerosis is variable dependent on arterial site, a correlation between the degree of atherosclerosis in coronary and carotid artery has been reported, i.e. intima-media thickness in carotid artery (cIMT) has been shown to correlate with coronary artery atherosclerosis burden as measured by intravascular ultrasound [2,3]. IMT in the carotid artery is also known to be associated with a number of cardiovascular (CV) risk factors in older, young and middle-aged populations [4,5], and has been shown to predict coronary events [6,7]. Carotid IMT is a well known marker of atherosclerosis and is accepted in clinical trials for assessing vascular effects of various therapies [8,9,10].

By using very high-resolution ultrasound, originally developed for imaging small animals, it is possible to image human superficial arteries with a resolution down to 20 μm, in comparison to 200–400 μm with the 7–15 MHz transducer that is used in the clinic today [11,12]. One of the vessels readily assessable is the radial artery. Even though lumen occlusive lesions are rare in this vessel segment, autopsy data have shown that intima hyperplasia and atherosclerosis frequently occur in the radial artery and are related to several traditional CV risk factors [13]. Thus, rIMT may be an equivalent vascular structural biomarker as cIMT.

We have previously shown that both rIMT and radial intima thickness (rIT) can be accurately measured from childhood to old age [11]. Also, increased rIT has been reported in different small groups of patients with hypertension, peripheral artery disease and end-stage renal disease [14–16]. Using this imaging approach, superior image quality of the radial artery can be obtained, which facilitates accurate and reproducible measurement of the wall structure.

The present study examines, by means of very high-resolution ultrasound, whether rIMT may be used as a surrogate marker of atherosclerosis, in a relatively large patient cohort with suspected

*Abbreviations:* CABG, coronary artery bypass graft; CAD, coronary artery disease; cIMT, carotid intima-media thickness; CV, cardiovascular; MI, myocardial infarction; MPS, myocardial perfusion scintigram; PCI, percutaneous coronary intervention; rIMT, radial intima-media thickness; rIT, radial intima thickness.

* Corresponding author at: Department of Molecular and Clinical Medicine, Institute of Medicine, Sahlgrenska Academy at the University of Gothenburg, S-41345 Gothenburg, Sweden. Tel.: +46 0 709154922.
*E-mail addresses:* charlotte.eklund@vgregion.se (C. Eklund), peter.friberg@mednet.gu.se (P. Friberg), li-ming.gan@gu.se (L.-M. Gan).

0021-9150/$ – see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.atherosclerosis.2011.12.035

coronary artery disease (CAD). We aim to investigate the relationship between rIMT and clinical CV risk markers, and further compare the results directly with those for cIMT.

## 2. Materials and methods

### 2.1. Study population

This study included 416 patients (mean age 62 ± 9 years, range 56–68 year, 233 female and 183 male). All patients undergoing clinical radionuclide MPS due to suspected CAD and evaluation of chest pain, at the department of Clinical Physiology, Sahlgrenska University Hospital, Gothenburg, (February 2006 to April 2008), were asked about participation in the study. Written informed consent was obtained before entry into the study. The study was approved by the local ethics committee at the Sahlgrenska Academy in Gothenburg. All study patients were examined within four weeks after the performed MPS. Both patients and investigators were blinded to the outcome of clinical MPS and the output from this study was also blinded to the referring physician.

### 2.2. High-resolution ultrasound of radial artery

Left and right radial arteries were examined non-invasively in longitudinal view, with near and far walls clearly visible, using a 55 MHz transducer with a resolution down to 20 μm (RMV708, Vevo 770, Visualsonics, Toronto, Canada) and frame rate 45 Hz. In Fig. 1 images of the same radial artery acquired with different transducers are shown. As evident, the 55 MHz transducer gives superior image quality. To standardize rIMT image acquisition, the transducer was placed at 1–2 cm proximal to the skinfold separating the palma manus from regio antebrachi anterior according to the earlier standardized protocol [11]. Digital cine-loops in B-mode of four consecutive heartbeats were stored.

### 2.3. Ultrasound of carotid artery

Left and right carotid arteries were examined in longitudinal view, with near and far walls visible, using an 8 MHz linear transducer (Siemens, Acuson Sequoia 512, Mountainview). ECG-signals were simultaneously recorded. Digital cine-loops in B-mode of three consecutive heartbeats were stored in a format of Digital Imaging and Communications in Medicine (DICOM) for further analysis. Image acquisition and definitions of IMT and plaque was performed according to the recommendations in "Mannheim Carotid IMT consensus update (2004–2006)" [17]. Plaque screening was performed with and without color Doppler. Only plaques in the carotid bulb were included. Plaque was defined as lesion with 50% greater thickness than surrounding IMT or IMT >1.5 mm. Plaque area was measured offline (workstation Tomtec, Image-Arena 2.9.1, Germany), with manual tracing of the lesion. The total sum of plaque area in left and right carotid bulb was used in the analysis.

### 2.4. Offline IMT measurement

IMT, defined as the distance between the leading edges of the lumen-intima and media-adventitia interface, was measured in the far wall. Two measurements in systole in two different heartbeats were averaged, and mean values between left and right artery were used in the analysis. IMT measurements were standardized and performed in peak systole; defined as the frame in systole where the artery had its largest diameter in a cine loop.

All offline measurements were done by a single reader who was blinded to the clinical characteristics of the patients.

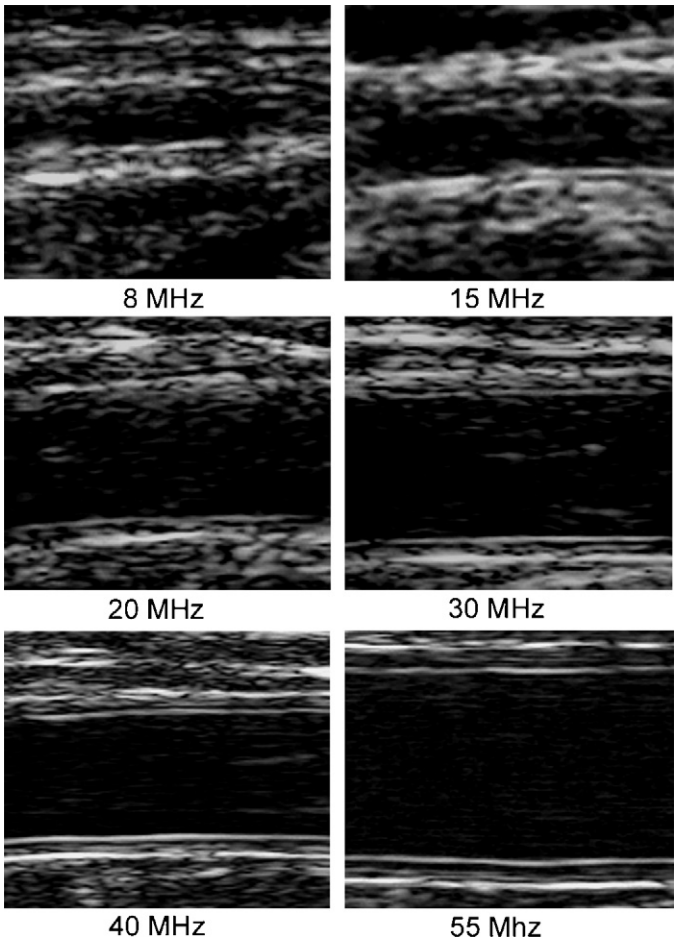


**Fig. 1.** Ultrasound images of a radial artery acquired with transducers ranging from 8 to 55 MHz, illustrating significant differences in image quality when using very high resolution ultrasound.

Offline measurements of rIMT were performed using workstation VisualSonics Vevo 770 (Version 3.0.0). Offline measurements of cIMT were performed in the common carotid artery, 1 cm proximal to the bifurcation (workstation Image-Arena, version 2.9.1, Tomtec, Germany).

### 2.5. Laboratory analyses

Blood sampling was performed in all patients. All biochemical analyses were performed using commercially available kits, according to the manufacturer's protocols.

Triglycerides and cholesterol in serum were measured using reagent systems from Roche (Triglycerides/GB kit No; 12146029216, Cholesterol kit no. 2016630, Roche Diagnostics GMBH, Mannheim Germany).

The Apolipoprotein A1 (ApoA1) concentration was measured with turbidimetric technique, using polyclonal rabbit anti-human antibodies (Q 0496 and Q 0497, Daco Cytomation, Glostrup, Denmark).

HDL in plasma was measured using an enzymatic colorimetric method (Direct HDL-Cholesterol, RANDOX cat no CH2652). The assay was performed on a Cobas Mira Analyser (Hoffman-La Roche & Co., Basel Switzerland).

The value of LDL was calculated with Friedewalds equation (only in patients with triglyceride <4 mmol/l): "LDL = Total Cholesterol − HDL − (0.45 × Triglycerides)". For all patients, the ratio "Total cholesterol/HDL" was also calculated.