



Post-processing reproducibility of the structural characteristics of the common carotid artery in a Flemish population

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Received 12 December 2016; received in revised form 28 February 2017; accepted 26 April 2017

KEYWORDS

Reproducibility study;
Carotid artery;
Intima-media
thickness;
Carotid plaques

Abstract *Introduction:* Common carotid artery (CCA) intima-media thickness (IMT), lumen diameter, and maximum plaque thickness were assessed on ultrasound images. The objective of the study was to evaluate the intra- and inter-reader reproducibility of the measurements following a standardised protocol.

Methods: Two readers performed the off-line measurements on B-mode ultrasound images of the distal CCA, in a randomly selected subset ($n = 60$) from a Flemish population cohort (FLEMENGHO). We calculated the coefficient of variation, the interclass correlation coefficient (ICC) and reproducibility according to the Bland–Altman method.

Results: The intra-reader bias for the measurements of left and right side CCA IMT were -0.003 ± 0.04 mm ($p = 0.55$) and 0.01 ± 0.04 mm ($p = 0.03$), respectively. The intra-reader bias of the lumen diameter was -0.04 ± 0.25 mm ($p = 0.27$) for the left and 0.02 ± 0.22 mm ($p = 0.45$) for the right side. The measurements for the maximum plaque thickness showed no intra-reader differences with bias 0.07 ± 0.2 mm ($p = 0.26$) for the left and -0.03 ± 0.2 mm ($p = 0.55$) for the right side. The inter-reader analysis showed good reproducibility for the left and right side CCA IMT with bias 0.004 ± 0.06 mm ($p = 0.57$) and -0.008 ± 0.05 mm ($p = 0.19$), respectively, but the lumen diameter measurements showed inter-reader differences, with bias 0.17 ± 0.27 mm ($p < 0.0001$) for the left and 0.10 ± 0.21 mm ($p = 0.0006$) for the right side. The inter-reader bias for the maximum plaque

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thickness were 0.07 ± 0.2 mm ($p = 0.21$) and -0.1 ± 0.4 mm ($p = 0.26$) for the left and right side, respectively.

Conclusion: The results demonstrated a reliable reproducibility of carotid wall structural measurements, allowing for an adequate further analysis of the entire population cohort.

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Introduction

Ischaemic heart disease and stroke remain the two leading causes of cardiovascular death according to the Global Burden of Disease study 2015.¹ The same underlying arterial pathology, atherosclerosis, underlines both diseases.

The carotid artery, with its size and superficial position in the neck, presents an important target for arterial ultrasound screening in asymptomatic individuals.^{2,3} B-mode sonography, being non-invasive and wide available,^{4,5} is the most often used technique for measuring several arterial characteristics. The common carotid artery (CCA) intima-media thickness (IMT) reflects the subclinical atherosclerotic burden and, in addition, it presents an independent risk factor for cardiovascular disease.^{6,7} It has been strongly related to the presence of atherosclerotic lesions in the coronary^{8,9} and peripheral arteries.¹⁰ Higher IMT predicts fatal and non-fatal myocardial infarction and stroke.¹¹ A meta-analysis incorporating 11 population studies has shown that carotid plaques are a distinctive phenotype of atherosclerosis, more indicative of the atherosclerotic burden and cardiovascular risk, and not a continuum of IMT progression.¹² Even though rarely measured, lumen diameter is an important addition to carotid measurements, since it serves as an indicator of the non-atherosclerotic adaptive response to the effects of pressure and flow on the arterial wall.¹³

Even though the use of semi-automated measurement software provides a highly reproducible and accurate way for measuring morphologic characteristics,^{14,15} the sonographer and/or reader can still introduce measurement error. The objective of the current study was to assess the intra- and inter-reader post-processing reproducibility of carotid arterial characteristics, such as CCA IMT, lumen diameter and maximal carotid plaque thickness, by off-line analysis of ultrasound images, in a random sample of 60 subjects drawn from FLEMENGHO, a population study conducted in Flanders, Belgium.

Methods

Study population

The Flemish Study on Environment, Genes and Health Outcomes (FLEMENGHO) was approved by the Ethics Committee of the University of Leuven, Belgium. It complies with the Helsinki declaration for research in human subjects and the Belgian legislation for the protection of privacy (<http://www.privacycommission.be>). Initial recruitment for the FLEMENGHO study started in 1985 and continued until 2004.¹⁶ A random sample of families living in a

geographically defined area of Northern Belgium was investigated. All selected family members aged 20 years or older were invited to join the cohort. From June 1996 until January 2004, recruitment of families continued using the former participants (1985–1989) as index persons, also including teenagers. At enrolment, the participation rate was 78%.¹⁷ The participants were repeatedly followed up. At each contact, participants renewed informed consent.

Arterial ultrasound imaging started in 2005 and is still ongoing. At the first examination 1446 enrolled participants underwent ultrasound imaging of the heart, renal and carotid artery. From this population, we randomly selected 60 subjects, stratified by sex and three age strata (<40, 40–59, ≥60 years).

Measurements

Before the examination at the field centre, the participants were asked to refrain from smoking, heavy exercise, and drinking alcohol or caffeine-containing beverages for at least 3 h. At each contact, trained nurses administered the same questionnaire to collect information about the participants' medical history, smoking and drinking habits, and intake of medications. In addition, they measured each participants' blood pressure using a standard mercury sphygmomanometer (Riester, Jungingen, Germany), height, weight and heart rate. Body mass index was body weight in kilogram divided by body height in metres squared. Hypertension was a blood pressure (average of five consecutive readings) of at least 140 mmHg systolic or 90 mmHg diastolic BP or use of antihypertensive drugs. Obesity was a body mass index of 30 kg/m² or more. Venous blood samples were drawn and plasma glucose, serum total cholesterol, high-density lipoprotein (HDL), triglycerides and serum creatinine were measured by automated methods in a single certified laboratory. Dyslipidaemia was a low-density lipoprotein (LDL)-cholesterol higher than 4.11 mmol/L or a total cholesterol exceeding 6.21 mmol/L or a fasting triglyceride serum level of 2.0 mmol/L or more. Diabetes mellitus was fasting blood glucose higher than 7.0 mmol/L or random blood glucose higher than 11.1 mmol/L or anti-diabetic drug intake.

Carotid ultrasound

Image acquisition. Carotid artery ultrasound was performed by an experienced observer (T.K.) using a commercially available ultrasound system (Vivid E9, GE Vingmed, Horten, Norway) interfaced with a linear transducer (9L-D, 3.1–10 MHz). The participants were studied in the supine position after at least 5 min of rest. With the

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