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● *Original Contribution*

LONGITUDINAL MOVEMENT OF THE COMMON CAROTID ARTERY WALL: NEW INFORMATION ON CARDIOVASCULAR AGING

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Abstract—Putative changes in the multiphasic pattern of longitudinal movement of the common carotid artery wall in the normal aging process are unknown. The aim of this study was to explore the phases, and resulting patterns, of the longitudinal movement of the intima–media complex of the human common carotid artery with respect to age and gender. One hundred thirty-five healthy non-smoking patients of different ages were investigated using in-house-developed ultrasound methods. The patterns of longitudinal movement seen in middle-aged and older patients were markedly different from those commonly seen in young patients, including the appearance of two additional phases of motion and, thus, new complex patterns. The displacement and maximum velocity of one of the phases, occurring at the time of aortic valve closure, increased quadratically with age in both men and women. (E-mail: magnus.cinthio@bme.lth.se)

Key Words: **Aging, Ultrasound, Biomarkers, Physiology, Hemodynamics, Clinical studies, Atherosclerosis, Vascular disease.**

INTRODUCTION

Hemodynamic forces acting on the arterial wall are important modulators of vascular tone and remodeling and are increasingly implicated in the development of atherosclerosis. Wall shear stress (WSS) and the diameter change of arteries, caused by the pulsatile blood pressure, have been largely investigated. WSS is an important determinant of endothelial cell function (Nichols and O'Rourke 2011) and is among the factors that influence the production of vasoactive substances such as nitric oxide, prostacyclin and endothelin. Measurements of diameter change form the basis for the estimation of arterial wall stiffness (Nichols and O'Rourke 2011). Increased stiffness of central arteries has been reported to be an independent risk factor for cardiovascular mortality (Nichols and O'Rourke 2011). In addition, ultrasound measurement of carotid intima–media thickness is a widely used marker for atherosclerosis, associated with future cardiovascular events (O'Leary and Bots 2010).

Longitudinal displacement of the arterial wall, that is, movement of the wall along the arteries, has not until recently attracted attention. Using in-house-developed ultrasonic methods, we have reported that in both large predominantly elastic arteries and large muscular arteries, there is a distinct bidirectional displacement of the arterial wall during the cardiac cycle (Cinthio et al. 2006). Further, we found that the intima–media of these arteries exhibits a longitudinal displacement that is larger than that of the adventitial region (Cinthio et al. 2006; Nilsson et al. 2010). Thus, there is shear strain and shear stress within the arterial wall, later confirmed by others in studies on the common carotid artery (CCA) (Idzenga et al. 2012; Zahnd et al. 2011). Furthermore, in a study on the porcine carotid artery, we recently reported that longitudinal movement and intramural shear strain undergo profound changes in response to the important circulatory hormones adrenalin and noradrenalin

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(Ahlgren et al. 2012b). These findings indicate that the longitudinal movements and resulting intramural shear strain constitute an important but overlooked mechanism in the cardiovascular system. Smooth muscle cells and extracellular matrix components, which are important for vascular function, are sensitive to mechanical stress (Hunt et al. 2002). Further, there is increasing evidence suggesting that the circulation in the vasa vasorum has a role in the development of atherosclerosis (Mulligan-Kehoe 2010). Longitudinal movement and the resulting intramural shear stress might affect all of these components of the arterial wall.

Studies on longitudinal movement of the arterial wall are sparse, and the mechanical behavior of arteries is not thoroughly characterized. Recent studies have indicated that the maximal amplitude of the longitudinal displacement of the CCA is reduced in patients with cardiovascular risk factors (Zahnd et al. 2012) and suspected and manifest atherosclerotic disease (Svedlund and Gan 2011; Svedlund et al. 2011), suggesting that the maximal longitudinal displacement of the arterial wall during a cardiac cycle might prove to be a valuable marker for future risk of cardiovascular disease. We previously reported that in young healthy humans, the pattern of longitudinal movement of the CCA at rest was distinctly multiphasic and stable over a 4-month-period (Ahlgren et al. 2012a). Furthermore, the pattern of movement can differ dramatically between patients of similar age and sex (Ahlgren et al. 2012a). We hypothesize that not only the total amplitude of movement, but also the pattern of longitudinal movement can provide important information on cardiovascular function.

Despite indications that there is a link between longitudinal movement of the CCA and cardiovascular health, the changes in longitudinal movement in the normal aging process of the arterial wall are unknown. Characterization of the complex bidirectional multiphasic pattern of movement of the CCA during aging can provide important new information both on the aging process of the arterial wall and the coupling of the left ventricle with the systemic circulation, and it might also serve as a basis for studies on risk factors and vascular disease. Further, characterization of the pattern and amplitude of longitudinal movement in the aging process of the arterial wall might also provide new insights into the mechanisms underlying the longitudinal movements.

The aim of the present study was to explore the phases and resulting patterns of the longitudinal movement of the intima−media complex of the human CCA wall in relation to age and sex. For this purpose, the CCAs of healthy, non-smoking men and women of different ages were investigated using in-house-developed, non-invasive ultrasound methods.

METHODS

Patients

We recruited 150 healthy non-obese (body mass index <30) Caucasian patients: 65 men (20−76 years of age) and 85 women (22−73 years of age). None of the patients reported previous cardiopulmonary disease, hypertension, diabetes or smoking, and none were taking any medication. All patients gave informed consent according to the Helsinki Declaration, and the study was approved by the ethics committee of Lund University.

Ultrasonic examinations of the arterial wall

B-Mode ultrasound was used to measure the longitudinal movement, maximum lumen diameter, distension (*i.e.,* diameter change) and intima−media thickness of the right CCA wall 2−3 cm proximal to the bifurcation. Before the recordings were obtained, the carotid arteries were scanned to evaluate the possible presence of atherosclerotic plaques. All examinations were performed in a quiet room (temperature: 21°C−23°C) with the subject in the supine position after ≥10 min of rest. The artery was scanned in the longitudinal direction, oriented horizontally in the image. Zoomed cine loops were saved for offline analysis. To avoid the introduction of false movements, the operator held the transducer steady and gently while the subject shortly paused breathing. Brachial blood pressure was measured with the auscultatory method using a sphygmomanometer and standard cuff on the left upper arm immediately after the ultrasound recordings were obtained.

Examinations were carried out by one of two experienced ultrasound technicians and were performed using one of two commercial ultrasound systems (Models HDI 5000 and IU22, Philips Medical Systems, Bothell, WA, USA), each equipped with a 38-mm, 5- to 12-MHz linear-array transducer. A frame rate close to 60 Hz was used. The image data were transferred to a personal computer for post-processing and offline cine-loop analysis in MATLAB (The MathWorks, Inc., Natick, MA, USA), in which the algorithms for measurement of longitudinal movement (Albinsson et al. 2014, 2017), lumen diameter, diameter change and intima−media thickness (Nilsson et al. 2014) were implemented. Two or three 5- to 6-second cine loops were recorded for each subject. The first recording with acceptable quality from each subject was chosen. Quality was evaluated based on visual inspection, ensuring that the double-line pattern of the intima−media complex of the far wall was clearly visible, that the kernel followed the wall movements and that the resulting movement curve had a repeatable pattern during the entire recording.

To suppress measurement noise and to enhance real longitudinal movement of the arterial wall, an average