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● *Original Contribution*

PROFOUND INCREASE IN LONGITUDINAL DISPLACEMENTS OF THE PORCINE CAROTID ARTERY WALL CAN TAKE PLACE INDEPENDENTLY OF WALL SHEAR STRESS: A CONTINUATION REPORT

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Abstract—The mechanisms underlying longitudinal displacements of the arterial wall, that is, displacements of the wall layers *along* the artery, and the resulting intramural shear strain remain largely unknown. We have already found that these displacements undergo profound changes in response to catecholamines. Wall shear stress, closely related to wall shear rate, represents the viscous drag exerted on the vessel wall by flowing blood. The aim of the work described here was to study possible relations between the wall shear rate and the longitudinal displacements. We investigated the carotid arteries of five anesthetized pigs in different hemodynamic situations using in-house developed non-invasive ultrasound techniques. The study protocol included administration of epinephrine, norepinephrine and β-blockade (metoprolol). No significant correlation between longitudinal displacement of the intima–media complex and wall shear rate was found. This result suggests that one or multiple pulsatile forces other than wall shear stress are also working along arteries, strongly influencing arterial wall behavior. (E-mail: Asa.ryden_ahlgren@med.lu.se) **© 2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Wall shear rate, Wall shear stress, Longitudinal movement, Arterial wall, Epinephrine, Norepinephrine, Catecholamines.**

INTRODUCTION

Cardiovascular disease is still a major cause of morbidity and mortality in the Western world. It is, therefore, essential to increase our knowledge of the cardiovascular system and cardiovascular diseases. Hemodynamic forces are considered important modulators of vascular tone and vascular remodeling and are increasingly implicated in atherogenesis. The longitudinal displacement of arteries, that is, the displacement *along* the artery, has for many years been assumed to be negligible compared with the radial displacement, that is, the diameter change (Nichols and O'Rourke 2005). However, by using modern ultrasound scanners it can be observed that in large human arteries, the inner layers of the arterial wall, that is, the intima–media complex, move not only in the radial direction, but also in the longitudinal direction, that is, along the artery, during the cardiac cycle (Persson et al. 2002, 2003). To study this phenomenon, our group developed a non-invasive ultrasonic method for simultaneous high-resolution recording of both the longitudinal and radial movements of the arterial wall *in vivo* (Cinthio et al. 2005a, 2005b). Using this method, we have found that the longitudinal displacement of the intima–media complex is of the same magnitude as the well-known diameter change during the cardiac cycle (Cinthio et al. 2006). Importantly, we have also illustrated that the adventitial region exhibits the same basic pattern of longitudinal displacement, although the magnitude of the displacement is smaller. This means that intramural shear strain, and thus shear stress, is present (Cinthio et al. 2006). We have reported that this phenomenon can be detected in the carotid, popliteal and brachial arteries, as well as in the abdominal aorta, and thus seems

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to be a general phenomenon in large human arteries (Cinthio et al. 2006). Substantial longitudinal displacements of the human carotid artery wall have recently been confirmed with other in-house developed ultrasonic techniques (Idzenga et al. 2012; Yli-Ollila et al. 2013; Zahnd et al. 2011).

We have also recently reported that the longitudinal displacement of the common carotid artery (CCA) of healthy humans at rest can exhibit dramatically different patterns, also in patients of the same age and gender, and that these patterns of displacement are stable over a 4-mo period (Ahlgren et al. 2012a), thus raising the question: Is the pattern of the longitudinal displacement of the arterial wall a valuable marker for future risk for cardiovascular disease (Ahlgren et al. 2012a)? Recent studies reporting that the amplitude of the longitudinal displacement of the arterial wall is reduced in patients with carotid plaques, suspected coronary artery disease and type 2 diabetes (Svedlund and Gan 2011; Svedlund et al. 2011; Zahnd et al. 2011), as well as in patients with periodontal disease (Zahnd et al. 2012), suggest a positive answer to such a question.

Changes in longitudinal displacement and intramural shear strain of the arterial wall have the potential to alter endothelial shear (Cinthio et al. 2006; Halliwill and Minson 2010) and to influence the circulation of the vasa vasorum, as well as the smooth muscles and the extracellular matrix in the media (Cinthio et al. 2006). In a study on the porcine carotid artery, we recently reported that the longitudinal displacements and intramural shear strain undergo profound changes in response to catecholamines, that is, our stress hormones epinephrine (adrenalin) and norepinephrine (noradrenalin), and changes in blood pressures (Ahlgren et al. 2012b). In many cases, the longitudinal displacement of the intima–media complex increased more than 200%. These findings might have important implications for vascular disease in both the short term and the long term, constituting a possible link between mental stress and cardiovascular disease and also indicating a possible influence in the context of atherosclerotic plaque rupture (Ahlgren et al. 2012b). However, the mechanisms underlying the longitudinal displacement and resulting intramural shear strain of the arterial wall are largely unknown, and the possible implications for cardiovascular disease are still unclear.

Wall shear stress (WSS), given by the product of wall shear rate (WSR), that is, the blood velocity gradient at the vessel walls, and blood viscosity, represents the viscous drag exerted on the vessel wall by the flowing blood. WSS has important roles in acute adaptations to flow changes and vascular remodeling and in the development of atherosclerosis. Because WSS acts along the arteries, an obvious hypothesis is that WSS is an important factor in the longitudinal displacement of the arterial wall. The mechanical events within the arterial wall under the forces of pulsatile flow are currently being studied using mathematical models and simulations (Bukač and Čanić 2013; Bukač et al. 2013; Fukui et al. 2007, Hodis and Zamir 2008, 2011a, 2011b; Warriner et al. 2008). The relation between WSS and the longitudinal displacement of the arterial wall has, however, not been addressed *in vivo*. Further, there are few non-invasive *in vivo* studies of WSR, and WSS, during different hemodynamic situations. The aim of the present work was, therefore, to study possible relations between WSR and longitudinal displacement of the arterial wall by investigating the response of the porcine common carotid artery to different hemodynamic situations. WSR was measured using the multigated spectral Doppler technique (Tortoli et al. 2006, 2011), implemented in the research system ULA-OP (Boni et al. 2012). The study protocol included intravenous infusion of epinephrine, intravenous boluses of norepinephrine, as well as β-blockade (using the β_1-selective receptor antagonist metoprolol). The results of the WSR measurements are analyzed in relation to the recently presented data from measurements of the longitudinal displacement of the arterial wall (Ahlgren et al. 2012b).

METHODS

Material

As recently reported (Ahlgren et al. 2012b), five 4-mo-old pigs weighing 25 kg were used for this study. The study was approved by the Animal Research Ethics Committee, Lund University. Anesthesia was induced with an intramuscular injection of ketamine (30 mg/kg) and xylasin (4 mg/kg). Sodium thiopental (5–8 mg/kg) and atropine (0.015 mg/kg) were given intravenously before tracheotomy. Anesthesia and muscular paralysis were maintained with a continuous infusion of 10 mL/h NaCl (0.9%) solution containing ketamine (16 mg/mL) and pancuronium (0.6 mg/mL). After induction of anesthesia, the animals were tracheotomized and ventilated with pressure-regulated, volume controlled normoventilation (Servo Ventilator 300, Siemens, Solna, Sweden). Electrocardiogram (ECG), PaO_2, PCO_2 and O_2 saturation were monitored. Blood pressure was continuously recorded intra-arterially (TestPoint, Capital Equipment, Billerica, MA, USA) in the right CCA. Body temperature was monitored using a thermistor in the esophagus. The temperature in the laboratory was kept constant.

Measurements of wall shear rate

Measurements were performed using ULA-OP, an advanced open platform for ultrasound research (Tortoli et al. 2009), connected to the LA523 probe (Esaote,