Non-invasive assessment of wall shear rate (WSR) in humans by means of ultrasound

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Abstract: An ultrasound technique is described to accurately assess non-invasively near wall shear rate (WSR) in humans. From near WSR and whole blood viscosity near wall shear stress (WSS) is estimated. The first studies indicate that near mean WSS is regulated when acutely changing whole blood viscosity, even under pathological conditions albeit at a lower level, but that the regulation is less optimal in chronic processes as ageing.

INTRODUCTION

Wall shear stress \( WSS = \text{WSR} \times \text{whole blood viscosity} \) is the drag of the flowing blood exerted on the vessel wall. In a variety of studies it has been shown that WSS is an important determinant of endothelial cell function, among others, influencing the production of such vasoactive substances as NO, prostacycline and endothelium, and, hence, vessel wall function. Although much progress has been made in unraveling the mechanisms underlying the interaction between WSS and endothelial cell function, the consequences for the human situation are less well known, mainly because of the lack of techniques to assess non-invasively WSR.

ULTRASOUND TECHNIQUE TO ASSESS WSR

Recently we developed a noninvasive ultrasound system to directly estimate dynamic WSR, i.e., the velocity gradient \( \Delta v/\Delta r \) at the wall during the cardiac cycle, in humans. Reliable assessment of \( \Delta v/\Delta r \) at the wall requires accurate determination of the low blood flow velocities close to the vessel wall. In ultrasound systems accurate determination of the low, near wall velocities is hampered by contamination due to the high power signals reflected by the slowly moving artery walls. Until recently suppression of these artery wall reflections was generally achieved by static high-pass filtering, also eliminating the scattering as induced by the blood cells flowing at low velocities along the vessel wall. A major breakthrough in solving this problem has been the introduction of adaptive filtering (1). Adaptive filtering requires accurate identification and tracking of the artery walls, providing also information about the arterial diameter and its changes during the cardiac cycle (distension waveform). Our system consists of an ultrasound echo system combined with dedicated signal processing (1, 2).

To assess WSR the artery is first visualized in B-mode (operating frequency 5 to 9 MHz) whereupon an M-line is positioned. After positioning the M-line, the ultrasound system is switched to echo M-mode with a high pulse repetition frequency. A registration starts synchronously with a trigger derived from the R-top of the ECG, facilitating the detection of the maximum (systolic) and minimum (diastolic) velocity as well as the initial diameter. The captured radio frequency (rf) signals (reflected and scattered ultrasound signals) are digitized at 20 MHz and transferred to the memory of the computer. The present size of the memory allows the recording during 1.2 s, normally sufficient to capture one complete heart beat. The first digitized rf-line as function of depth is displayed on the computer screen. From the shape and the position in depth of the reflections, the wall-lumen interfaces on both sides are identified manually by placing sample volumes, indicated by markers, on the reflections of the anterior and posterior vessel walls. The distance between both markers, corrected for the angle of observation (70°), is considered as the initial (end-diastolic) diameter of the vessel. Processing of the rf-data within the sample volumes as function of time, with the sample volumes adaptively tracking the observed displacement, results in the time-dependent change of the artery wall position (displacement waveform). The difference between the displacement curves of both walls reflects the pulsatile change in diameter over time. To obtain the time-dependent blood flow velocity distribution, a modelled cross-correlation function is employed to the rf-data between the markers to estimate the mean velocity over time segments of 10 ms spaced at 5 ms (50% overlap) time intervals. The length of the rf-segments corresponds to 300 \( \mu \text{m} \) in depth and the segments are spaced at 150 \( \mu \text{m} \) intervals (50% overlap). Calculating the mean velocity of all rf-segments results in a time-dependent velocity profile, which is corrected for the angle of observation (70°). The shear rate distribution
follows from the radial derivative of the velocity profile at each time instant \((\Delta v/\Delta r)\). The peak value of the derivative is considered as the estimate of the instantaneous longitudinal near WSR. Near peak WSR (PWSR) is defined as the near WSR at peak systole and near mean WSR (MWSR) as the time averaged shear rate over one cardiac cycle. The average intrasubject intrasession variability per measurement is about 15% for near PWSR and about 12% for near MWSR (3). The intrasubject intersession variability for averaged values \((n=15)\) is about 3% for near PWSR and about 2% for near MWSR (3).

**ESTIMATION OF WSS**

To calculate near WSS one has to be informed of the viscosity close to the wall. At the present state of the art it is impossible to obtain this information in vivo. Because the peak value of the \((\Delta v/\Delta r)\) is reached 300-400 \(\mu\)m from the wall whole blood viscosity, estimated from plasma viscosity, hematocrit and corrected for local near MWSR, is used to calculate near WSS.

**APPLICATIONS**

Based upon the assumption that the arterial tree is an optimally designed conduit system mean WSS can be expected to be the same for all vessels to achieve minimal expenditure of energy for flowing blood. Under physiological circumstances this value is estimated to be on the order of 1.5 Pa (15 dyne cm\(^{-2}\)), irrespective of calibre and function of the vessel (4). In acute animal studies MWSS was found to be regulated around a certain value by adapting the internal diameter of the vessel (5) to regulate blood flow velocity. Recent studies on the common carotid artery in humans, as performed in our institute, however, showed that near MWSS decreases linearly between the second and sixth age decade from 1.5 to 1.2 Pa in males and from 1.3 to 1.1 Pa in females, mainly due to an increase in arterial diameter with age (6). As could be expected arterial compliance also decreased with age in this study. These findings indicate that in chronic processes, as with increasing age, the reduction of arterial compliance is limited through an increase in arterial diameter, which is at the cost of a decrease in mean near WSS. In patients with end-stage renal failure - in whom near MWSS in the common carotid artery is significantly lower as compared with age-matched control subjects \((0.71 \pm 0.20 \text{ versus } 1.24 \pm 0.20 \text{ Pa, } \pm \text{sd})\) due to both a lower mean near MWSR and a lower whole blood viscosity - however, near MWSS was regulated following acute changes in whole blood viscosity of 33% as induced by hemodialysis. All together these findings indicate that MWSS in the common carotid artery is regulated around a certain value when acutely changing whole blood viscosity, even under pathological conditions albeit at a lower level, but that in chronic processes this regulation is less optimal.

In the common carotid artery reflections, originating from the periphery and the flow divider, affect the shape of the flow velocity profile and, hence, near WSS differently just before the bifurcation and 20-30 mm more upstream. Near MWSR is significantly lower near the bifurcation, as compared with more upstream, and is associated with a larger intima-media thickness than at the more proximal site (7).

**REFERENCES**