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Wall shear stress in the human common carotid artery as function of age and gender

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Abstract

Objectives: It has been postulated that in the arterial system mean wall shear stress is maintained at a constant value. The present study was performed to investigate the level of wall shear stress in the common carotid artery (CCA) as function of age and possible interactions between diameter and storage capacity, defined as the absolute area change per heart beat, with mean wall shear stress. **Methods**: Wall shear stress (wall shear rate multiplied by whole blood viscosity) was assessed in the right CCA of 111 presumed healthy male ($n=56$) and female ($n=55$) volunteers, varying in age between 10 and 60 years. Wall shear rate was measured with a high resolution ultrasound system. Simultaneously, arterial diameter and storage capacity were determined. Whole blood viscosity was calculated from haematocrit, plasma viscosity and shear rate. **Results**: From the second to the sixth age decade peak wall shear stress was significantly higher in males than in females and decreased from 4.3 Pa to 2.6 Pa ($r=-0.56$, $p<0.001$) in males and from 3.3 Pa to 2.5 Pa ($r=-0.54$, $p<0.001$) in females. Mean wall shear stress tended to decrease from 1.5 Pa to 1.2 Pa ($r=-0.26$, $p=0.057$) in males and decreased significantly from 1.3 Pa to 1.1 Pa ($r=-0.30$, $p=0.021$) in females. No significant difference in mean wall shear stress was found between males and females in any age decade. The diameter of the CCA increased significantly in both males ($r=0.26$, $p<0.05$) and females ($r=0.40$, $p<0.003$). Storage capacity decreased significantly in both sexes (males: $r=-0.63$, $p<0.001$; females: $r=-0.68$, $p<0.001$). **Conclusions**: These observations suggest that the reduction in mean wall shear stress with age results from the concomitant increase in diameter in an attempt of the arterial system to limit the reduction in storage capacity of the arterial system with increasing age.

Keywords: Ageing; Blood flow; Carotid artery; Gender; Ultrasound; Wall shear rate; Wall shear stress

1. Introduction

Wall shear stress is the drag exerted by flowing blood on the vessel wall. This stress is thought to play an important role in adaptational processes of the vascular wall by inducing the production by endothelial cells of substances such as nitric-oxide, [1,2] prostacyclin [3] and endothelin [4,5].

Based on the assumption that the arterial tree is an optimally designed conduit system mean wall shear stress can be expected to be the same for all vessels to achieve minimal expenditure of energy for flowing blood (minimum work model) [6,7]. Under physiological circumstances this value was estimated to be on the order of 1.5 Pa (15 dyne/cm^2), irrespective of calibre and function of the vessel [8,9]. Indeed, in the monkey iliac artery Zarins et al. found mean wall shear stress to be regulated around this value through diameter adaptations [10]. Similar observations were made by Langille and O' Donnell in the rabbit common carotid artery [11]. These investigators also showed the diameter adaptation response to be age dependent, i.e. less efficacy at older age. These studies indicate that mean wall shear stress is regulated around a certain

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constant value by adapting the internal diameter of the vessel to the quantity of blood flowing through it.

Studies in humans showed an increase of luminal diameter and stiffening of the vessel wall with advancing age [12–17]. The diameter increase throughout life may be attributed to an effort of the arterial system to maintain storage capacity with increasing age [15]. Assuming that the blood flow per unit of tissue is independent of age, estimated mean wall shear stress would decrease with age due to the age-dependent increase in diameter [18–20]. This, however, would be at variance with the hypothesis that wall shear stress is maintained at the same level through diameter adaptations.

It was the aim of the present study to investigate the age and sex dependent changes in wall shear stress, if any, in the common carotid artery of presumed healthy male and female volunteers varying in age between 10 and 60 years. The diameter and the storage capacity of this artery were assessed as well. Wall shear stress was calculated from wall shear rate and whole blood viscosity. Wall shear rate was determined with a specially designed ultrasonic Shear Rate Estimation System developed at our institute [21,22]. This system also allows the simultaneous assessment of arterial diameter and storage capacity using a wall tracking algorithm [23]. Whole blood viscosity was estimated from haematocrit, plasma viscosity and mean wall shear rate.

2. Material and methods

2.1. Subjects

Two hundred (100 males and 100 females) subjects, varying in age between 10 and 60 years and living in the Maastricht city and environment, were contacted between September 1995 and August 1996. Their names and addresses were randomly selected from the population register of Maastricht. Respondents who smoked and/or used medication were excluded, leaving 129 subjects for further analysis. From these subjects 18 had to be excluded from the study: eleven subjects because of diagnosed hypertension ($>$140 mmHg systolic and/or $>$90 mmHg diastolic blood pressure) and/or cholesterol levels higher than 6.4 mmol/l, 2 subjects because of elevated glucose levels ($>$10 mmol/l) and 5 subjects because of detected plaques in the carotid artery bifurcation, leaving 111 subjects (55 females and 56 males) for further analysis. None of these participants had a history of cardiopulmonary or other major diseases and all were clinically free of cardiovascular symptoms. All subjects had normal levels of haemoglobin, haematocrit, glucose, cholesterol, HDL, LDL, triglycerides and plasma viscosity. According to institutional guidelines, all subjects, including the parents of the subjects younger than 18 years, were aware of the investigational nature of the study and gave written informed consent. The study was approved by the joint medical ethical committee of the Academic Hospital Maastricht and Maastricht University.

2.2. Wall shear rate assessment: the shear rate estimation system

The ultrasonic system to measure wall shear rate has been described in detail before [21,24,25]. In short, for the present study the Shear Rate Estimation System (SRES) consisted of an Ultramark 9 plus (Advanced Technology Laboratories, Bellevue, WA, USA) with a broad band (5–9 MHz) curved array transducer (C9–5 ICT, beamwidth 1.1 mm at a depth of 20 mm) and an ultrasonic processing system in a personal computer. The received raw digitised (20 MHz) radio-frequency (rf) signals were transferred to the personal computer (486DX4/100) through an interface configuration consisting of an internal card in the ATL-system in combination with a custom built plug-in card for the PC. The latter card makes it possible to selectively capture segments of the rf-signals starting at a preselected depth and with a preselected width. To assess the instantaneous blood velocity distribution along a selected line of observation (in B-mode) with a high axial resolution, the echo system was switched to a wide band pulsed Doppler mode with short transducer activation. The returned acoustic signals have an effective pulse length of 3 periods at 5.3 MHz equivalent to a spatial resolution of 375 μm. Each velocity estimate is based on overlapping data segments of 300 μm in depth and 10 ms in time and is obtained using a modelled cross correlation function for the rf-signal [26]. Data acquisition is initiated synchronously with a trigger derived from the top of the R-wave of the ECG, facilitating the detection of the maximum (systolic), mean and minimum (diastolic) velocity (in mm s^{-1}) as well as the initial (diastolic) arterial diameter. The available PC memory presently limits the recording time to 1.2 s, which is sufficient to capture data of one complete heart beat.

Processing of the received rf-signals as function of time provides both the time dependent change of arterial diameter (distension waveform) [23] and the velocity distribution as function of depth (Fig. 1a) [21]. The peak value of the distension waveform gives the distension (ΔD), allowing the calculation of relative distension ($RD = \Delta D/D$ in %) and the storage capacity SC ($SC = \Delta A \cong \pi \Delta D.D/2$). The latter is comparable to compliance but is independent of acting pulse pressure. The velocity waveform as recorded in the centre of the lumen provides peak systolic velocity (PSV in mm s^{-1}) and mean velocity (MV in mm s^{-1}). The latter is comparable with the mean velocity as detected with conventional pulsed Doppler systems in the centre of the lumen.

The instantaneous shear rate distribution follows from the radial derivative of the velocity profile at each time instant. A typical recording of a shear rate distribution is shown in Fig. 1b. The maximum value of the derivative,

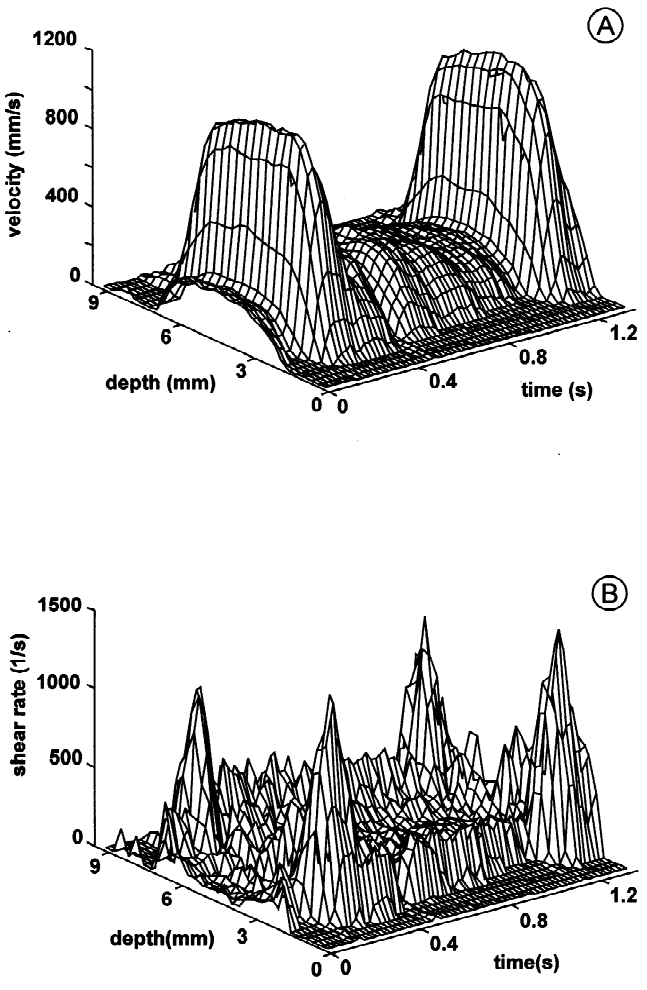

Fig. 1. (a) The velocity distribution across the diameter as function of time in the common carotid artery of a presumed healthy male volunteer. The velocity profile is a flattened parabola. (b) The instantaneous shear rate distribution as function of time in the common carotid artery of the same volunteer showing the highest values near the vessel walls with the peak values in systole.

averaged for the anterior and posterior wall of the vessel, is considered as an estimate of wall shear rate. The averaging procedure is performed to minimise possible effects induced by secondary flows [21]. The peak wall shear rate in systole (PWSR in s^{-1}) and shear rate averaged over one cardiac cycle, i.e., mean wall shear rate (MWSR in s^{-1}), are used for further analysis. For a young population the intrasubject intrasession reproducibility of the SRES is about 15% for the PWSR and 13% for the MWSR [25].

2.3. Haemodynamic monitoring

Brachial artery blood pressure and heart rate were determined with a semi-automated oscillometric device (Dinamap; Critikon, Tampa, Florida, USA) which was set to take a recording every 5 min.

2.4. Biochemical analysis

Blood samples were obtained without stasis from an antecubital vein for determination of haematocrit, haemoglobin, glucose, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides and cholesterol using standard auto-analysing techniques. Plasma viscosity was determined using an Ostwald micro-viscometer (Schott Gerate GMBH, Hofheim, Germany).

2.5. Wall shear stress assessment

From plasma viscosity, haematocrit and mean wall shear rate whole blood viscosity (WBV) can be estimated using the approximation proposed by Weaver [27]:

$$\log(\mathrm{WBV}) = \log(\eta 0) + \alpha.\mathrm{Ht}$$

$$\alpha = 0.030 - 0.0076\log(\mathrm{MWSR})$$

where WBV is whole blood viscosity in mPa.s, $\eta 0$ plasma viscosity in mPa.s, Ht haematocrit, and MWSR mean wall shear rate in s^{-1}. This approximation circumvents the practical problems associated with the direct measurement of whole blood viscosity.

To asses wall shear stress (WSS), wall shear rate (WSR) was multiplied by the estimated whole blood viscosity, employing the relationship:

$$\mathrm{WSS} = \mathrm{WBV}^{*}\mathrm{WSR}$$

A previous study [25] in a young population has demonstrated that the estimated peak wall shear stress and mean wall shear stress had an intrasession intrasubject variation on the order 15% and 12%, respectively.

2.6. Measurement procedure

The measurements were performed in the morning. The subjects were examined in supine position in a climatised room with a temperature of 22°C–24°C. A history on symptoms related to atherosclerosis was taken, after which a physical examination was performed. Blood was collected and after an acclimatisation period of at least 10 minutes the blood pressure and ultrasound measurements started. The echosystem was switched to B-mode to verify if both common, internal and external carotid arteries were free of plaques and to select the site of measurement. Wall shear rate measurements were performed only in the right common carotid artery as preliminary studies have shown that there are no differences in haemodynamics between the left and right common carotid arteries [13,25,28,29]. A line of observation was selected crossing the right common carotid artery (CCA) 2 to 3 cm proximal to the tip of the flow divider at an angle of 70 degrees with the longitudinal axis of the artery (Fig. 2). Hereafter a recording during 1.2 s of the received rf-signals was made and stored on the

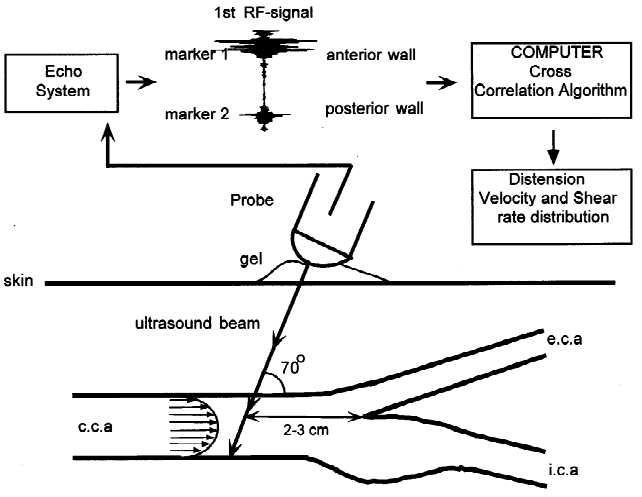

Fig. 2. Schematic representation of the shear rate measurement procedure. After a measurement is recalled the end-diastolic lumen boundaries are manually identified with markers, whereupon calculation of the distension waveform, velocity and shear rate distribution is started. c.c.a = common carotid artery; e.c.a = external carotid artery; i.c.a = internal carotid artery.

hard disk of the computer. The measurement procedure was repeated 20 times with a time interval of 2 to 3 min. After these measurements, each recording was recalled whereafter the vessel walls were manually identified by placing sample volumes, indicated by markers, on the reflections of the anterior and posterior vessel wall (Fig. 2). The distance between both markers, corrected for the angle of observation, is considered as the initial (end-diastolic) diameter (D in μm) of the vessel.

At the end of the measurement session the SRES was set to calculate artery wall distension, and the velocity and wall shear rate distributions in the artery, taking about 2 min per measurement with the computer employed. From the 20 independent measurements per subject only recordings with a symmetrical velocity profile were included. Within each session, on average, one to two recordings had to be excluded, because they did not meet the criteria.

2.7. Statistical analysis

Data are expressed as mean ± standard deviation (SD). The unpaired Student's *t*-test was employed to explore whether differences in the parameters measured with the SRES were statistically significant between males and females. To investigate age dependency linear regression was performed. Regression coefficients (slope) are expressed with their standard error (rc ± se). The significance level was set at $p<0.05$. All statistical analyses were performed with the statistical software package SPSS for Windows, release 6.0.

3. Results

3.1. Wall shear stress as function of age.

Between 10 and 60 years of age PWSS and MWSS decreased in both the female and the male group. (Tables 1 and 2; Figs. 3 and 4). In the female group PWSS decreased by 26% (3.33 to 2.48 Pa, $rc=-0.024\pm0.005$) and MWSS by 19% (1.29 to 1.05 Pa, $rc=-0.005\pm0.002$). In the male group these parameters decreased by 40% (4.27 to 2.56 Pa, $rc=-0.035\pm0.007$) and 18% (1.45 to 1.19 Pa, $rc=-0.005\pm0.002$), respectively. PWSS was significantly higher in males than in females, up till the sixth age decade. The regression coefficients for this parameter were similar for both groups (Fig. 3). MWSS decreased slightly but significantly in the female group and was similar to the male group, although the latter descent just did not reach the level of significance (Fig. 4).

3.2. Wall shear rate and blood flow velocity as function of age.

Between 10 and 60 years of age in the female group PWSR (Table 1) decreased by 31% (1150 to 793 s^{-1}, $rc=-9.82\pm1.68$, $r=-0.63$, $p<0.001$), MWSR by 24% (450 to 341 s^{-1}, $rc=-2.40\pm0.87$, $r=-0.35$, $p<0.008$) and PSV by 27% (848 to 621 $mm.s^{-1}$, $rc=-6.74\pm1.23$, $r=-0.60$, $p<0.001$). MV decreased by 10%, but this descent did not reach the level of significance (315 to 282 $mm.s^{-1}$, $rc=-0.72\pm0.52$, $r=-0.19$, $p=0.17$). In the male group (Table 2) PWSR decreased with age by 45% (1389 to 767 s^{-1}, $rc=-11.79\pm2.41$, $r=-0.55$, $p<0.001$), MWSR by 25% (475 to 357 s^{-1}, $rc=-1.79\pm0.88$, $r=-0.30$, $p<0.025$), PSV by 32% (976 to 667 $mm.s^{-1}$, $rc=-7.08\pm1.41$, $r=-0.56$, $p<0.001$), and MV by 13% (347 to 301 $mm.s^{-1}$, $rc=-0.94\pm0.58$, $r=-0.27$, $p<$

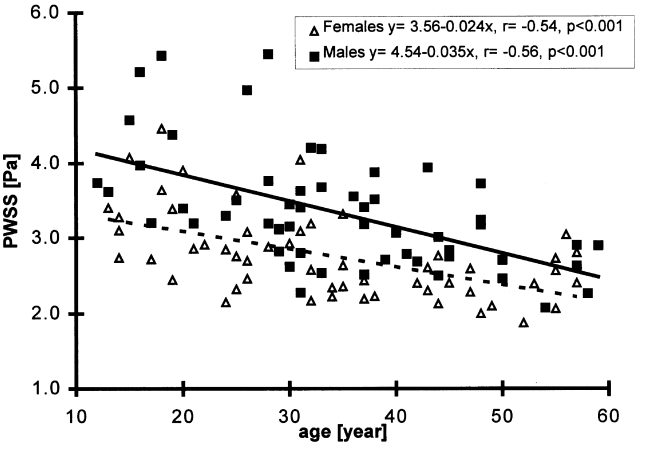

Fig. 3. Peak wall shear stress (PWSS) in the right common carotid artery as function of age in the female and male groups.

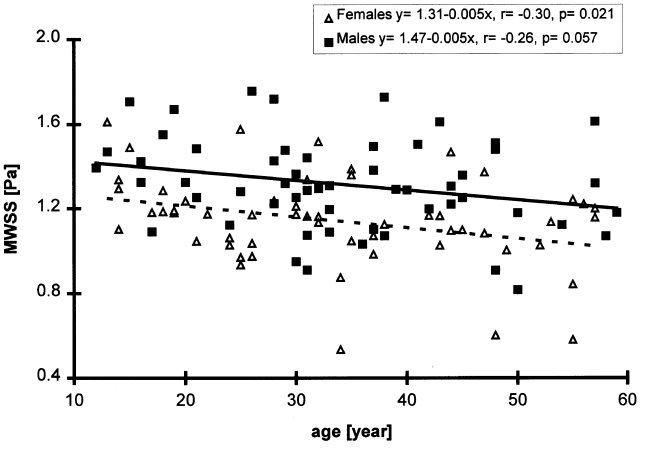

Fig. 4. Mean wall shear stress (MWSS) in the right common carotid artery as function of age in the female and male groups.

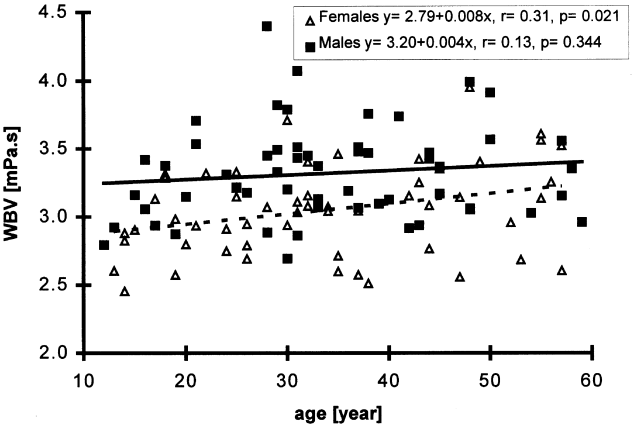

Fig. 5. Whole blood viscosity (WBV) as function of age in the female and male groups.

0.111). The regression coefficients for either of these parameters were not significantly different between the male and the female group.

3.3. WBV as function of age

In the female group WBV showed a significant increase of 10% (2.89 to 3.18 mPa.s, rc = 0.008±0.003, $r = 0.31$, $p < 0.021$) between 10 and 60 years of age. In the male group WBV tended to increase about 6% (from 3.03 to 3.22 mPa.s, rc = 0.004±0.004, $r = 0.13$, $p = 0.34$), but this change did not reach the level of significance (Fig. 5).

3.4. D, ΔD, RD and SC as function of age.

In both sexes the diameter of the CCA increased significantly about 7% (females from 5.92 to 6.31 mm and males from 6.02 to 6.44 mm) from the second to the sixth age decade. The diameter increase (Fig. 6) with age was similar for both sexes (females: rc = 12.9±4.1, $r = 0.40$, $p = 0.003$; males: rc = 10.5±5.3, $r = 0.26$, $p = 0.05$). ΔD decreased significantly by 46% (from 757 to 398 μm, rc = −9.2±1.1, $p < 0.001$) in the female group and by 62% (from 848 to 341 μm, rc = 11.9±1.6, $p < 0.001$) in the male group. RD decreased significantly ($p < 0.001$) from 13% to 6% in the female group and from 14% to 5% in the male group. SC decreased significantly by 45% (7.5

Table 1
Diameter (*D*), Distension (Δ*D*), Relative Distension (RD), mean (MV), peak (PV) blood flow velocity, peak (PWSR), mean (MWSR) wall shear rate, peak (PWSS) and mean (MWSS) wall shear stress as function of age per decade in the right common carotid artery in the female group ($n = 55$)

Age	*n*	*D* [mm]	Δ*D* [μm]	RD [%]	PSV [mm.s^{-1}]	MV [mm.s^{-1}]	PWSR [s^{-1}]	MWSR [s^{-1}]	PWSS [Pa]	MWSS [Pa]
10–19 y	10	5.9±0.3	758±123	13±2	848±149	315±59	1150±191	450±85	3.33±0.62*	1.29±0.16
20–29 y	12	6.0±0.3	611±72	10±1	762±136	267±40	965±182	375±52	2.87±0.49*	1.12±0.18
30–39 y	15	6.2±0.5	473±106	8±2	706±133	289±43	906±152	379±80	2.75±0.57*	1.14±0.24
40–49 y	10	6.4±0.6	455±105	7±2	592±76	266±55	748±138	357±111	2.36±0.25*	1.11±0.23
50–59 y	8	6.3±0.3	398±125	6±2	621±88	282±52	793±136	341±99	2.48±0.38	1.05±0.23

* denotes significant difference compared to the male group.

Table 2
Diameter (*D*), Distension (Δ*D*), Relative Distension (RD), mean (MV), peak (PV) blood flow velocity, Peak (PWSR) and mean (MWSR) wall shear rate, peak (PWSS) and mean (MWSS) wall shear stress as function of age per decade in the right common carotid artery in the male group ($n = 56$)

Age	*n*	*D* [mm]	Δ*D* [μm]	RD [%]	PSV [mm.s^{-1}]	MV [mm.s^{-1}]	PWSR[s^{-1}]	MWSR[s^{-1}]	PWSS[Pa]	MWSS[Pa]
10–19 y	8	6.0±0.3	848±198	14±3	976±130	347±37	1389±219	475±68	4.27±0.78	1.45±0.20
20–29 y	12	6.5±0.6	659±153	10±2	904±113	319±47	1050±264	408±83	3.59±0.80	1.39±0.19
30–39 y	18	6.5±0.5	565±137	9±2	848±143	297±57	983±188	375±74	3.26±0.58	1.24±0.21
40–49 y	10	6.5±0.4	416±90	6±2	767±136	297±51	942±193	410±83	3.07±0.44	1.33±0.20
50–59 y	7	6.4±0.5	341±151	5±2	667±104	301±67	767±114	357±81	2.56±0.31	1.19±0.24

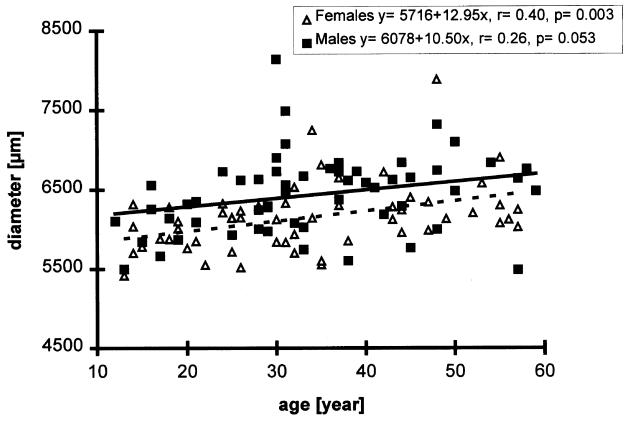

Fig. 6. Internal diameter of the right common carotid artery (CCA) as function of age in the female and male groups.

to 4.1 mm^2, rc = −0.08±0.013, $r = -0.68$, $p < 0.001$) in the female group and by 60% (8.9 to 3.6 mm^2, rc = −0.12±0.02, $r = -0.63$, $p < 0.001$) in the male group (Fig. 7). The observed decrease in SC with increasing age can be attributed to a loss of elasticity of the arterial wall.

3.5. Blood pressure as function of age

From the second to the sixth age decade systolic blood pressure increased significantly in females (rc = 0.36±0.09, $r = 0.50$, $p < 0.001$), but not in the males (rc = 0.08±0.09, $r = 0.11$, $p = 0.40$). With increasing age diastolic blood pressure increased significantly in females (rc = 0.27±0.08, $r = 0.44$, $p < 0.001$), as well as in the males (rc = 0.45±0.08, $r = 0.60$, $p < 0.001$). From the second to the sixth age decade pulse pressure decreased significantly in males (rc = −0.37±0.07, $r = -0.54$, $p < 0.001$), but did not change in the females (rc = 0.10±0.08, $r = 0.17$, $p = 0.21$).

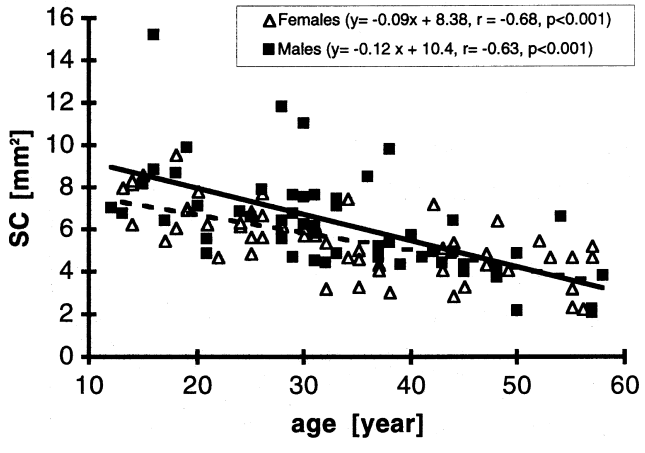

Fig. 7. The storage capacity (SC) of the right common carotid (CCA) artery in the female and male groups as function of age.

4. Discussion

In this study peak and mean wall shear stress in the right common carotid artery of humans, varying in age between 10 and 60 years were determined with a non-invasive system based on ultrasound technology. In both sexes peak and mean wall shear stress decreased with age. The decrease in peak wall shear stress is more pronounced in males than in females up to the sixth age decade. No significant difference in mean wall shear stress could be found between males and females.

The scatter in the main results (Figs. 3 and 4) may be contributed to inter subject variations and to measurement errors. The selected angle of observation (70 degrees) is quite critical: a minor deviation causes a large relative error in the assessed shear rate. A consistent angle of observation within and between subjects is only possible for straight arterial segments like the common carotid artery. The measurement error and the effect of physiological variation are reduced by taking the average of more than 15 heart beats. Moreover, shear rates on opposite sides are averaged, reducing both the variance of shear rate estimates and the contribution of radial velocities. Radial velocity gradients will be suppressed most effectively if both walls move symmetrically in opposite directions, but in the practical situation the anterior wall moves more than the posterior wall. Radial velocity gradients, however, are quite small: an assumed peak wall speed of only the anterior wall of 6 mm/s induces an additional gradient of 1 s^{-1} for an artery diameter of 6 mm. Because of the angle of observation the velocity gradients considered do not originate exactly from opposite sides of an artery. For a vessel diameter of 6 mm the spatial shift will be less than 0.5 mm which converts to a time delay of 0.08 ms for a pulse wave velocity of 6 m/s. The temporal (and spatial) skewness can be neglected considering a temporal sample width of 10 ms.

For both sexes the decrease in peak wall shear stress with age can be explained by the descent of peak wall shear rate due to a decrease in peak systolic blood flow velocity. The latter is in agreement with previous studies in which blood flow velocity was also found to decrease with age [13,29]. The higher peak wall shear stress in males than in females can be attributed to the higher peak wall shear rates (although not significantly different per decade) combined with the higher whole blood viscosities in males. The higher blood viscosity in males than in females as observed in the present study is in agreement with observations of de Simone et al [30]. The physiological implication of a difference in peak wall shear stress due to gender for the vessel wall is as yet unknown and needs further investigation.

The descent of mean wall shear stress with age in both sexes was surprising, because we expected this parameter to be regulated around the same value. This hypothesis was based on the minimum work theory, proposing a constant

value of mean wall shear stress irrespective of diameter [6,7,9]. On the other hand, assuming no change in volume flow with age, the increase in diameter with increasing age, which is in agreement with earlier observations, [13,14,16,31]. will result in a reduction of mean wall shear rate and, hence, a decrease of mean wall shear stress when the increase in blood viscosity with age is limited as is the case in the present study. Despite the decrease of mean wall stress with increasing age the measured values still remain in the range compatible with the minimum work theory according to Kamiya et al [32]. These investigators concluded that mean wall shear stress in the arterial tree should be within the range of 0.75 to 2.25 Pa. The mean wall shear stress values found in the present study varied between 0.53 Pa and 1.61 Pa in females and between 0.82 Pa and 1.76 Pa in males between the second and sixth decade.

In a recent study, Gnasso et al. found a more pronounced decrease of mean wall shear stress with age than in the present study [33]. In their study the subjects at older age appeared to be overweighed (BMI$>$25 kg/m^2), which was not the case in the younger population. It is known that in obese subjects blood flow velocities are underestimated as compared to lean subjects, explaining partly the lower range of mean wall shear stress values at older age and, thereby, confounding the correlation between wall shear stress and age. Moreover, wall shear stress was estimated indirectly based on the Poiseuille equation, assuming a steady parabolic velocity profile. The shape of the velocity profile, however, varies with the phase of the cardiac cycle (Fig. 1) and has a flattened rather than a parabolic profile [14–25]. Thus the time dependent change of the velocity gradient in the spatial direction is not taken into account in their study. In a former study of our group it has been shown that the approximation of wall shear stress based upon Poiseuille results in an underestimation, especially at higher blood flow velocities [24]. This will affect the outcome of age dependency studies because blood flow velocities decreases with age.

Although in both sexes mean wall stress remains within the physiological range, as far as the minimum work theory is concerned, it can not be excluded that the lower wall shear stress at older age negatively influences endothelial cell function and, hence, the properties of the arterial wall. Low wall shear stress, after all, has been associated with the initiation of atherosclerosis [34] and arterial wall thickening [35,36]. It may quite well be that the impaired endothelial cell function at older age [37–41] is related to the reduced wall shear stress.

To tentatively investigate the relations between mean wall shear stress, age, BMI, blood pressure and vessel wall structure (diameter) and function (distension, relative distension, storage capacity), if any, a multiple stepwise forward regression analysis [42] was performed. The analysis indicates a strong negative correlation between mean wall shear stress and diameter (females $r=-0.62$, $p<0.0001$; males $r=-0.55$, $p<0.0001$), dominating the contribution of age. This suggests that the reduction of mean wall shear stress as function of age can be attributed to an increase of vessel diameter. The latter induces a decrease of mean wall shear rate, which in combination with a relatively small increase in whole blood viscosity results in a decrease of mean wall shear stress. The increase of vessel diameter concomitant with a reduced distension can be seen as an attempt to retain storage capacity with increasing age, [15] suggesting that pulsatile volume flow is an important parameter. Incorporation of storage capacity in the minimum work theory might reveal that at a lower distension a shift to a larger diameter is necessary to attain minimum cost. The latter concept needs theoretical exploration.

Our results show that with increasing age regulation of mean wall shear stress is not fully attained via adjustments of lumen diameter. Studies which do show direct interaction between wall shear stress and diameter pertain to experiments in which wall shear stress is changed acutely by alternating volume flow [10,11]. These and our findings indicate that mean wall shear stress is adjusted by vessel diameter in case of acute and subacute changes in volume flow, but that in chronic processes, such as ageing, other factors are involved.

In conclusion, the present investigation indicates that in the common carotid artery of human males and females peak and mean wall shear stress decrease with age. The decrease of peak wall shear stress results from a decrease in peak wall shear rate with increasing age. The decrease of mean wall shear stress results from the age dependent change in diameter of the artery in an attempt to limit the loss of storage capacity under these circumstances.

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