Common carotid wall shear stress and carotid atherosclerosis in end-stage renal disease patients

Jan Malik[1], Jaroslav Kudlicka[1], Vladimir Tuka[1], Eva Chytilova[1], Josef Adamec[2], Katarina Rocinova[3], Vladimir Tesar[3]

1) Third Department of Internal Medicine, First Faculty of Medicine, Charles University in Prague and General University Hospital

2) Department of Fluid Dynamics and Power Engineering, Faculty of Mechanical Engineering, Czech Technical University in Prague

3) Department of Nephrology, First Faculty of Medicine, Charles University in Prague and General University Hospital

Short title: Wall shear stress in ESRD

Corresponding author:

Dr. Jan Malik

3rd Dept. of Internal Medicine,General University Hospital

U nemocnice 2

12808 Prague 2

Czech Republic

Tel/fax: +420 224 962 765 E-mail: malik.jan@vfn.cz

Abstract

Background: Decrease of arterial wall shear stress (WSS) is associated with higher probability of atherosclerotic plaque development in many disease conditions. End-stage renal diseases (ESRD) patients suffer from vascular disease frequently, but its nature differs from general population. This study was aimed at proving an association between common carotid wall shear stress and the presence of carotid bifurcation plaques in a group of ESRD patients.

Methods: ESRD subjects, planned for the creation of a dialysis access and therapy were included. Wall shear rate (WSR) was used as a surrogate of WSS and was analyzed in the common carotid arteries by duplex ultrasonography. Intima media thickness (IMT) was measured at the same site. The presence/absence of carotid bifurcation plaques was recorded. The endothelial function was estimated by the levels of vonWillebrand factor (vWf).

Results: 35 ESRD patients were included (19 females, 17 diabetics). Atherosclerotic plaque was present in 53% of bifurcations. Wall shear rate was lower in arteries with plaques (349 ± 148 vs. 506 ± 206 s^{-1}, p = 0.005) and was directly related to the height of IMT and inversely to the activity of vWf (r = -0.65, p = 0.016).

Conclusion: Lower wall shear rate in the common carotid arteries is linked to the endothelial dysfunction and to the presence of atherosclerotic plaques in carotid bifurcations in ESRD subjects. Faster arterial dilatation may facilitate this process in ESRD subjects.

Key words: atherosclerosis; dialysis; end-stage renal disease; wall shear stress

Introduction

More than 50% of end-stage renal disease (ESRD) patients die from cardiovascular diseases (Collins 2003). Arteries of ESRD patients are affected by atherosclerosis, but also by large artery (medial and intimal) calcifications (Coll *et al.* 201, Ballanti *et al.*, 2011). Many risk factors of these diseases have been identified. They include traditional risk factors known from the non-ESRD population (diabetes mellitus, smoking, hypertension etc.), but also factors specific for renal failure, such as increased phosphate concentrations, inflammation, oxidative stress, malnutrition and increased levels of circulating ADMA (asymmetric di-methyl-arginine, endogenous inhibitor of nitric-oxide synthase). Despite these findings, the use of traditional risk scoring underestimates atherosclerosis burden (Coll *et al.* 2010). All these factors act in the entire organism and, indeed, atherosclerosis is a systemic disease. However, atherosclerotic plaques predominantly occur in some specific areas, such as along the internal curve of aortic arch and bifurcation outer walls. It can be explained by the local character of blood flow and by the inability of arterial wall to adapt to blood flow changes. Hemodynamically, this interaction of blood flow and arterial wall is described by the wall shear stress (WSS).

Wall shear stress is directly related to the blood velocity and viscosity and indirectly to the arterial radius. More precisely, it is proportional to the velocity gradient (wall shear rate, WSR) near the vessel wall and the dynamic viscosity of the blood (Malek et al. 1999). Its physiological role is to dilate the artery in response to increased tissue metabolic demands - higher blood flow volume. Local vascular resistance is decreased by the arterial and arteriolar dilatation, which leads to increased blood flow volume. When the metabolic demands decrease, slower blood velocity leads to arterial

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constriction, which helps to direct cardiac output to metabolically more active organs and to save energy. Straight segments of arteries keep the value of WSS within a narrow limit (15-30 dyne/cm2) (Malek *et al.* 1999). Aforementioned sites of arteries prone to atherosclerosis are not able to adapt to slower blood velocity and thus area of low or even zero WSS develops there, as was documented by the study by Schirmer and Malek (2007) using non-Newtonian flow model. It is associated with increased endothelial permeability for molecules and white blood cells, which facilitates development of atherosclerosis.

Others (Irace *et al.* 1999) and we (Chytilova *et al.* 2009) have observed that some diseases, such as type 2 diabetes mellitus or carotid atherosclerosis are associated with lower WSS also in straight arterial segments, such as in the common carotid arteries. Irace et al.(1999) demonstrated that subjects suffering from carotid atherosclerosis, but with low calculated cardiovascular risk have lower WSS of the common carotid artery than controls. Investigation on patients affected by unilateral carotid atherosclerosis demonstrated, that shear stress is lower in the carotid arteries with plaques than in contralateral plaque-free arteries (Gnasso *et al.* 1997). In a study of patients affected by single large-artery atheroembolic stroke, the hemodynamic conditions were worse (lower wall shear stress, higher wall tension and Peterson´s elastic modulus) at the affected side than in the other side even in the absence of significant stenosis (Carallo et al*.* 2006). In a recent study (Irace, et al. 2011), it has been shown that common carotid WSS decreases with age, which is accompanied by the increase of intima-media thickness. Less is known about the carotid WSS in ESRD patients, who have very high prevalence of cardiovascular complications. However, the nature of these complications and of the atherosclerotic plaques differs from the general population (Kono K, 2011). Therefore,

we performed this study, which was aimed at proving an association between common carotid WSS and the extent of carotid atherosclerosis in a group of ESRD subjects just before the initiation of a chronic hemodialysis therapy.

Methods

Thirty-five subjects with ESRD, planned for the surgical creation of a vascular access within 1 month and for the hemodialysis therapy within 3 months were asked to participate in this study. Selection criteria were the following: clinically stable condition (no overt inflammatory or other acute disease), left ventricle ejection fraction assessed by echocardiography more than 50%, absence of significant valvular disease and absence of any clinical manifestation of vascular disease. Basic history was recorded, blood samples for basic biochemistry, blood count and von Willebrand factor (blood glycoprotein involved in hemostasis, which higher levels or activity correspond to endothelial dysfunction and activation) (Malik *et al.* 2002) were drawn and carotid ultrasonography performed. All subjects gave their informed consent. The study was approved by the local Ethical committee and conforms to the Declaration of Helsinki.

Ultrasound examination was performed by the use of a linear-array 3-11 MHz probe of SONOS 5500 (Philips, Andover, Massachusetts, USA). The examinations were performed during morning hours after 10 minutes rest at the examination bed and after overnight fast. The subjects were kept in supine position with their heads slightly extended. We scanned common carotid arteries (CCA), carotid bifurcations and the origins of the internal carotid arteries in longitudinal and transverse planes. Subjects with >50% stenosis of the carotid tree were excluded. Plaque was defined as a focal structure encroaching into the arterial lumen by at least 0.5 mm or 50% of the surrounding carotid

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intima-media thickness (CIMT), or as CIMT >1.5 mm, which corresponds to the Mannheim intima-media consensus (Touboul et al. 2004).

Ultrasound measurements were performed in the common carotid arteries within 10 mm proximal to the bifurcation. The distal segments of CCA were recorded digitally for further analysis. Blood flow velocity was detected with the sample volume placed in the center of CCA. Peak systolic (V_{max}) , end-diastolic (V_{min}), and mean velocity (V_{mean}) were recorded using the outer envelope of the spectral Doppler curve got by pulse wave Doppler (mean of 3 heart cycles).

Both internal diameter (ID) and CIMT were analyzed off-line by the specialized software Image Pro-Plus version 4.0 (Media Cybernetics, Silver Spring, Maryland, USA) using the B-mode records with ECG gating and automatic border detection function. The reader was the same throughout the study and was blinded with regard to the subject investigated. CIMT, defined as the distance between two parallel lines: the lumen-intima and media-adventitia boundaries, was measured on the far wall of CCA. Internal diameter, defined as the distance between the leading edge of the echo produced by the intima-lumen interface of the near arterial wall and to the leading edge of the echo produced by the lumen-intima interface of the far wall, was measured during end- diastole (ECG gating). Three measurements of CIMT and of ID were performed and their mean value was used for further analysis.

Wall shear rate (WSR) was used as a measure of WSS and was calculated using the Poiseuillian parabolic model of velocity distribution across the arterial lumen based on the assumption of laminar blood flow, according to the following formula (Jiang *et al.* 2000):

$$WSR_{max} = 4 \times V_{max} / ID$$

$$WSR_{mean} = 4 \times V_{mean} / ID$$

where WSR is wall shear rate (s^{-1}), V_{max} and V_{mean} represent the maximum (systolic) and mean velocity (time-averaded velocity of the spectral Doppler outer wall)(cm. s^{-1}) and ID is the arterial diameter (cm). WSR was calculated separately for maximal, mean blood velocity.

Statistical analysis

Left and right carotid arteries were analyzed separately for the analysis of WSR effect on atherosclerosis, which doubled the number of cases. The carotid arteries were divided into 2 groups according to the presence/absence of atherosclerotic plaque. The studied variables had normal distribution, so the differences between the carotids were analyzed by the unpaired t-test; p-value <0.05 was considered significant.

Results

A total of 35 ESRD patients were included (19 females, 17 diabetics), see Table 1 for more details. Atherosclerotic plaque was present in 53% of bifurcations (in 36 of 68, which were adequately visible by ultrasonography). All but 2 plaques were echogenic. Laboratory data (Table 1) correspond to the usual findings in the ESRD population – note higher triglycerides, uric acid, fibrinogen and von Willebrand factor. All included subjects had compensated hypertension with the use of angiotensin converting enzyme inhibitors and calcium channel blockers.

Wall shear rate was lower and CIMT higher in arteries with plaques (see Table 2). There was no statistical difference in the potential risk factors presented in Table 1 among patient with and without atherosclerotic plaque at any side. This was also the case of hemoglobin and fibrinogen levels – two main determinants of blood viscosity. Diabetics did not have significantly lower WSR than non-diabetics (p-value reached 0.5).

CIMT was inversely correlated to WSRmean (r = -0.3, p = 0.04). WSRmax was inversely related to the activity of vWf (r = -0.65, p = 0.016).

Discussion

This study has shown that lower common carotid WSR is associated with the presence of carotid bifurcation plaques in ESRD patients. This pro-atherogenic local hemodynamic profile could not be explained by traditional risk factors of atherosclerosis. Common carotid WSR is inversely related to CIMT and to the activity of von Willebrand factor, a marker of endothelial function.

Carotid arteries with bifurcation plaques were significantly larger and had slower blood flow than plaque-free arteries. This relation between diameter and velocity keeps maintaining the brain perfusion unchanged. However, the opposing changes of these two WSR determinants lead to its deeper decrease. Arterial dilatation is believed to be the primary change. Samijo et al.(2002) documented that ESRD patients have larger arteries than healthy subjects. Earlier, London et al. (1990) observed larger aortic roots and aortic bifurcations, probably due to higher pulse pressure in ESRD patients. The increase of pulse pressure occurs in subjects with faster pulse wave velocity due to stiffed aortas and arteries – the reflected pulse wave reach the aortic valve still open (Malik *et al.* 2009). Repetitive volume retention between hemodialyses and increased

collagen turnover probably also plays a role (Dellegrottaglie *et al.* 2011). One would expect that the WSS changes with the fluid status (and thus blood viscosity) between hemodialyses and with the hemoconcentration after the procedure. However, Samijo et al.(2002) found that the increased viscosity due to hemoconcentration after hemodialysis is "compensated" by the decrease of blood velocity due to decreased cardiac output and WSS remains practically unchanged.

Carotid intima-media thickness has been accepted as a surrogate of premature atherosclerosis and has been used as it in various studies with coronary artery disease (Holaj *et al.* 2003), hypertension (Bots *et al.* 1993), dyslipidemia (Fisicaro *et al.* 1994) etc. However, some authors (Bots *et al.* 1997) concluded that at lower degrees of CIMT (below 1.1 mm) , the intima/media thickening appeared to reflect an equilibrium state in which the effects of pressure and flow on the arteries are in balance, given a characteristic relation between shear stress and local transmural pressure. The latter could represent the effect of Laplace law at arteries, similarly to the left ventricular hypertrophy in hypertensive subjects. A synthetic approach was presented in the study by Vaudo et al.(2000): in a group of subjects with untreated newly diagnosed essential hypertension, CIMT was related to both left ventricular mass, but also to age and triglycerides and inversely to HDL-cholesterol, factors associated with atherosclerosis. In our study, CIMT was significantly related to the WSR, but not to the carotid internal diameter, suggesting that it was rather linked to atherosclerosis.

Von Willebrand factor is produced by both endothelium and platelets. The use of vWf as a marker of endothelial function is therefore not advocated by all researchers. Asberg et al.(2001), for example, tested vWf before and after atorvastatin therapy in renal transplant recipient – while the vasomotor endothelial function improved, the vWf

levels did not change. On the contrary, we observed significant decrease of vWf after lipid-lowering therapy as well as improvement in vasomotor function (Malik *et al.* 2002). The release of vWf from endothelium and its activation is increased in subjects with endothelial dysfunction and low WSS (as in this study), but also in states with very high WSS (Malek *et al.* 1999). A recent study by Pequeriaux et al. (2011) measured vWf in a large group of 671 hemodialysis patients. Higher vWf levels (upper quartile) were significantly associated with higher mortality with a hazard ratio of 1.8 after adjustment for traditional risk factors. Our data could explain the effect of higher vWf levels by the lower WSS and thus atherogenic profile. Suprisingly, there was no association of vWf and mortality in peritoneal dialysis patients in the study by Pequeriaux.

The outer walls of carotid bifurcations represent a typical site of atherosclerotic plaques development due to the local WSS decrease. However, it is technically complicated to measure the local WSS at bifurcations. It is far easier to estimate WSR in a straight segment, where the flow is more laminar. Furthermore, the common carotid flow characteristics influence the flow pattern in the bifurcation. The relation between common carotid WSR and bifurcation plaques can be explained by fluid dynamics in bifurcations (Asberg *et al.* 2001). Internal carotid artery is wider at the site of its origin in the majority of patients – internal carotid sinus or bulb. This site is responsible for the flow separation from the arterial wall. Recirculation and stagnation area develops and narrows the axial flow. When the flow velocity decreases, the recirculation area becomes larger. Recirculation areas are characterized by low WSS with changing vector during the cardiac cycle, i.e. pro-atherogenic hemodynamic profile (Grus *et al.* 2007). Furthermore, carotid bifurcations change during the life – they become wider and the

angle between common and internal carotid arteries is more perpendicular (Thomas *et al.* 2005). This is another reason, why the recirculation areas grow with ageing.

The limitation of this study is in its size and in the use of WSR as the surrogate of WSS. The former is surmounted by the statistically significant differences in WSR in plaque and plaque-free bifurcations. Larger studies can bring a more detailed understanding of WSS relation to various laboratory data. Technical limitations of real dynamic viscosity measurements could bring more impreciseness than using only WSR. Another problem is that poiseuillean flow was assumed, while unsteady pulsatile flow is present in the carotid arteries – the latter is, however, much more complicated not only in terms of data calculation, but also in data acquisition.

We think that this study helps us to better understand some aspects of ESRD vascular complications development. It seems that the accelerated arterial dilatation is responsible for the decrease of WSS, which, in turn, leads to endothelial dysfunction and to both CIMT and atherosclerotic plaque growth. Adequate blood pressure and water overload control could theoretically slower this process in concert with other traditional risk factors management.

References:

ASBERG A, HARTMANN A, FJEDSA E, HOLDAAS H. Atorvastatin improves endothelial function in renal-transplant recipients. *Nephrol Dial Transplant* **16(9)**: 1920-1924, 2001.

BALLANTI P, SILVESTRINI G, PISANÒ S, DE PAOLIS P, DI GIULIO S, MANTELLA D, IAPPELLI M, FAVARÒ A, BONUCCI E, COEN G. Medial artery calcification of uremic patients: a histological, histochemical and ultrastructural study. *Nephrol Dial Transplant* **26(10)**: 349-57, 2011.

BOTS ML, HOFMAN A, DE BRUYN AM, DE JONG PT, GROBBEE DE. Isolated systolic hypertension and vessel wall thickness of the carotid artery. The Rotterdam Elderly Study. *Arterioscler Thromb* **13(1)**: 64-69, 1993.

BOTS ML, HOFMAN A, GROBBEE DE. Increased common carotid intima-media thickness. Adaptive response or a reflection of atherosclerosis? Findings from the Rotterdam Study. *Stroke* **28(12)**: 2442-2447, 1997.

CARALLO, C., LUCCA LF, CIAMEI M, TUCCI S, DE FRANCESCHI MS. Wall shear stress is lower in the carotid artery responsible for a unilateral ischemic stroke. *Atherosclerosis* **185(1):** 108-113, 2006.

COLL B, BETRIU A, MARTINEZ-ALONSO M, AMOEDO ML, ARCIDIACONO MV, BORRAS M, VALDIVIELSO JM, FERNANDEZ E. Large artery calcification on dialysis patients is located in the intima and related to atherosclerosis. *Clin J Am Soc Nephrol* **6(2)**: 303-310, 2011

COLL B, BETRIU A, MARTINEZ-ALONSO M, BORRAS M, CRAVER L, AMOEDO ML, MARCO M, SARRO F, JUNYENT M, VALDIVIELSO JM, FERNANDEZ E. Cardiovascular risk factors underestimate atherosclerotic burden in chronic kidney

disease: usefulness of non-invasive tests in cardiovascular assessment. *Nephrol Dial Transplant* **25(9)**: 3017-3025, 2010.

COLLINS AJ: Cardiovascular mortality in end-stage renal disease. *Am J Med Sci* **325**: 163-167, 2003.

CHYTILOVA E, MALIK J, KASALOVA Z, DOLEZALOVA R, STULC T, CESKA R. Lower wall shear rate of the common carotid artery in treated type 2 diabetes mellitus with metabolic syndrome. *Physiol Res* **58(2)**: 185-191, 2009.

DELLEGROTTAGLIE S, SANDS RL, GILLESPIE BW, GNANASEKARAN G, ZANNAD F, SENGSTOCK D, FINKELSTEIN F, KISER M, EISELE G, HINDERLITER AL, LEVIN NW, CATTAN V, SARAN R, RAJAGOPALAN S. Association between markers of collagen turnover, arterial stiffness and left ventricular hypertrophy in chronic kidney disease (CKD): the Renal Research Institute (RRI)-CKD Study. *Nephrol Dial Transplant* 2011 May 11. [Epub ahead of print]

FISICARO M, DA COL PG, TONIZZO M, FONDA M, BOLLINI M, CATTIN L. Early carotid atherosclerosis in asymptomatic adults with primary moderate hypercholesterolemia: a case-control study. *Atherosclerosis* **106(2)**: 255-261, 1994;.

GNASSO A, IRACE C, CARALLO C, DE FRANCESCHI MS, MOTTI C, MATTIOLI PL, PUJIA A. In vivo association between low wall shear stress and plaque in subjects with asymmetrical carotid atherosclerosis. *Stroke* **28(5)**: 993-998, 1997.

GRUS T, LINDNER J, VIK K, TOSOVSKY J, MATECHA J, NETREBSKA H, TUMA J, ADAMEC J. Particle image velocimetry measurement in the model of vascular anastomosis. *Prague Med Rep* **108(1)**: 75-86, 2007.

HOLAJ R, SPACIL J, PETRASEK J, MALIK J, HAAS T, ASCHERMANN M. Intima-media thickness of the common carotid artery is the significant predictor of angiographically proven coronary artery disease. *Can J Cardiol* **19(6)**: 670-676, 2003.

IRACE C, CARALLO C, CRESCENZO A, MOTTI C, DE FRANCESCHI MS, MATTIOLI PL, GNASSO A. NIDDM is associated with lower wall shear stress of the common carotid artery. *Diabetes* **48(1)**: 193-197, 1999.

IRACE C, CARALLO C, DE FRANCESCHI MS, SCICCHITANO F, MILANO M, TRIPOLINO C, SCAVELLI F, GNASSO A. Human common carotid wall shear stress as a function of age and gender: a 12-year follow up study. *Age (Dordr).* 2011 Oct 12. Epub ahead of print.

JIANG, Y., K. KOHARA, K. HIWADA, Association between risk factors for atherosclerosis and mechanical forces in carotid artery. *Stroke* **31(10)**: 2319-2324, 2000.

KONO K, FUJII H, MIYOSHI N, KAWAMORI H, SHITE J, HIRATA K, FUKAGAWA M. Coronary plaque morphology using virtual histology-intravascular ultrasound analysis in hemodialysis patients. *Ther Apher Dial.***15(1)**: 44-50, 2011.

LONDON GM, MARCHAIS SJ, SAFAR ME, GENEST AF, GUERIN AP, METIVIER F, CHEDID K, LONDON AM. Aortic and large artery compliance in end-stage renal failure. *Kidney Int* **37(1)**: 137-142, 1990.

MALIK J, WICHTERLE D, MELENOVSKY V, SIMEK J. Von Willebrand factor and assessment of endothelial function. *Cardiovasc Res* **54**: 193-194, 2002.

MALIK J, TUKA V, MOKREJSOVA M, HOLAJ R, TESAR V. Mechanisms of chronic heart failure development in end-stage renal disease patients on chronic hemodialysis. *Physiol Res* **58(5)**: 613-621, 2009.

MALEK AM, ALPER SL, IZUMO S. Hemodynamic shear stress and its role in atherosclerosis. *JAMA* **282**: 2035-2042, 1999.

PÉQUÉRIAUX NC, FIJNHEER R, GEMEN EF, BARENDRECHT AD, DEKKER FW, KREDIET RT, BEUTLER JJ, BOESCHOTEN EW, ROEST M. Plasma concentration of von Willebrand factor predicts mortality in patients on chronic renal replacement therapy. *Nephrol Dial Transplant* 2011 Epub ahead of print.

SAMIJO SK, BARKHUYSEN R, WILLIGERS JM, LEUNISSEN KML, LEDOUX LAF, KITSLAAR JEHM, HOEKS AG. Wall shear stress assessment in the common carotid artery of end-stage renal failure patients. *Nephron* **92**: 557-563, 2002.

SCHIRMER CM, MALEK AM. Wall shear stress gradient analysis within an idealized stenosis using a non-Newtonian flow. *Neurosurgery.* **61(4):**853-63, 2007.

THOMAS JB, ANTIGA L, CHE SL, MILNER JS, STEINMAN DA, SPENCE JD, RUTT BK, STEINMAN DA. Variation in the carotid bifurcation geometry of young versus older adults: implications for geometric risk of atherosclerosis. *Stroke* **36(11)**: 2450-2456, 2005.

TOUBOUL PL, HENNERICI MG, MEAIRS S, ADAMS H, AMARENCO P, DESVARIEUX M, EBRAHIM S, FATAR M, HERNANDEZ HERNANDEZ R, KOWNATOR S, PRATI P, RUNDEK T, TAYLOR A, BORNSTEIN N, CSIBA L, VICAUT E, WOO KS, ZANNAD F. Mannheim intima-media thickness consensus. *Cerebrovasc Dis.* **18(4)**: 346-349, 2004.

VAUDO G, SCHILLACI G, EVANGELISTA F, PASQUALINI L, VERDECCHIA P, MANNARINO E. Arterial wall thickening at different sites and its association with left ventricular hypertrophy in newly diagnosed essential hypertension. *Am J Hypertens* **13**: 324-331, 2000.

Table 1: Group characteristics

	Mean	SD
Age (years)	61.3	13.1
Females	55%	-
Diabetes mellitus	49%	-
Height (cm)	169.7	9.6
Weight (kg)	75.3	13.7
Systolic blood pressure (mmHg)	143.7	18.4
Diastolic blood pressure (mmHg)	84.7	11.2
Calcium (mmol/l)	2.3	0.2
Phosphorus (mmol/l)	1.56	0.37
Osmolarity mmol/kg	311.5	13.03
Ferritine (µg/l)	447	471
Uric acid (µmol/l)	358	140
Total cholesterol (mmol/l)	4.68	0.98
HDL-cholesterol (mmol/l)	1.14	0.32
LDL-cholesterol (mmol/l)	2.66	0.84
Triglycerides (mmol/l)	2.03	1.12
Total protein (g/l)	68.2	7.18
Albumin (g/l)	39.6	4.5
Hemoglobin (g/l)	110.0	20.4
Fibrinogen (g/l)	5.12	1.25
Von Willebrand factor (%)	153.0	47.2

Table 2: Carotid plaques – the effect of hemodynamic and structural variables

	Bifurcation plaque		p-value
	Yes n = 36	No n = 32	
Internal diameter (mm)	**6.98 ± 1.23**	**6.10 ± 0.75**	**0.01**
CIMTmean (mm)	**0.86 ± 0.27**	**0.69 ± 0.14**	**0.02**
CIMTmax (mm)	1.05 ± 0.40	0.87 ± 0.25	0.09
Vmax (cm/sec)	**58.3 ± 16.3**	**73.4 ± 22.8**	**0.01**
Vmean (cm/sec)	**29.2 ± 9.8**	**37.9 ± 11.9**	**0.01**
WSRmax (s^{-1})	**349 ± 148**	**506 ± 206**	**0.005**
WSRmean (s^{-1})	**175 ± 85**	**259 ± 108**	**0.006**

CIMT = carotid intima-media thickness; V = velocity (maximal and minimal – end-diastolic); WSR = wall shear rate