The effect of Pravastatine on the Wall Shear Stress in the internal carotid artery; results from the PROSPER study

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Introduction: Wall Shear Stress (WSS) is considered to be related to atherosclerosis. Wall Shear Stress (WSS) in small vessels can be assessed by fitting a parabolic velocity profile on blood flow measurements obtained from velocity encoded MRI. In this study a method for automatic blood flow quantification was extended to automatic WSS determination in the internal carotid artery [1]. Decreased WSS is associated with the development of atherosclerosis via the NO pathway and there is some experimental evidence that the class of pharmaceutical agents known as statins increase NO synthesis [2]. To assess the influence of statins on WSS in vivo, we assessed WSS in 206 participants of a placebo-controlled longitudinal study in elderly patients.

Materials and Methods: We studied 206 elderly patients (age 70-86 y, enrolled in the PROSPER trial [3]. The study population consisted of a Pravastatin treated group of N=100 patients (48 men, 52 women) and a placebo group of N=106 patients (33 men, 73 women) who had at least one risk factor for developing atherosclerotic disease. A total of 409 internal carotid arteries were scanned and analyzed at baseline, and these were repeated after a treatment period of 3 years. Velocity encoded Phase Contrast cine MRI was performed on a 1.5 T MR system (Philips Medical Systems, the Netherlands) using a standard head coil. Retrospective cardiac triggering by means of a peripheral pulse unit was applied to obtain 16 phases over the cardiac cycle. The imaging parameters were: TE/TR 9/16 ms, flip angle 7.5°, slice thickness 5 mm, FOV 150 mm, scan matrix 256 x 256 and velocity sensitivity 100 cm/s. Velocity profiles were assessed in a plane perpendicular to the internal carotid artery 2 cm distal from the bifurcation. The flow was determined by fitting of a parabolic velocity profile to the actual measured velocity profile in this internal carotid artery. Velocity profiles in small arteries can be approximated by a 3D paraboloid. This model assumes no slip at the vessel wall. A Levenberg-Marquard algorithm which minimized chi-squared error for non-linear functions was used. The diameter was calculated by using the Hagen-Poiseuille formula:

$$D=\mathrm{sqrt}(8Q/ v_{max}\pi) \text{ and } v_{max}=0.5\, v_{mean,} \quad (1)$$

with Q the blood flow and D the diameter of the lumen. Finally, the WSS was assessed from [4] as follows:

$$WSS=4\mu v_{max}/D \quad (2)$$

with μ being the blood viscosity. Blood is assumed to be a Newtonian fluid and the viscosity is taken as 5.5 mPas. A quality parameter was used to examine the difference between the fitted paraboloid and the velocity profile. When the fit was of poor quality the scan was excluded.

Results: In the following tables the WSS is given in Pa, MWSS is the mean WSS over the cardiac cycle, DWSS is the diastolic WSS, PWSS is the WSS during peak systole. The presented data are means and the standard error is given between brackets.

	Pravastatin			Placebo		
	Baseline	Follow up	decline	Baseline	Follow up	decline
MWSS	1.03 (0.019)	0.97 (0.016)	0.066 (0.018)	1.08 (0.017)	1.04 (0.019)	0.045 (0.017)
DWSS	0.74 (0.014)	0.70 (0.012)	0.034 (0.014)	0.79 (0.012)	0.77 (0.015)	0.045 (0.015)
PWSS	1.52 (0.032)	1.40 (0.029)	0.106 (0.032)	1.56 (0.029)	1.52 (0.030)	0.013 (0.030)

An independent samples T test was performed to examine whether the difference in decline of WSS between both groups, Pravastatin vs. placebo, was statistically significant. This was not significant for mean, diastolic or peak WSS (MWSS p=0.284; DWSS p=0.326; PWSS p=0.120).

Conclusion: The decline in WSS over time is significant in both groups for all measured WSS parameters. However, we found no in vivo evidence for an effect of Pravastatin on WSS.

References: [1] Box FMA et al, Invest Radiol. 38 (2003) 567-77; [2] Rosati E et al, Minerva Cardioangiol. 50(1) (2002) 63-8; [3] Shepherd J et al, Lancet 360 (9346) (2002) 1623-1630; [4] Gnasso A et al: Circulation 94 (1996) 3257-62

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