

# Wall Shear Stress Distribution in Carotid Artery Stenosis: Changes Pre- and Post-Intervention by Carotid Endarterectomy

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**Introduction:** Wall shear stress (WSS) is the friction force of blood acting on the vessel endothelium [1]. Parameters such as low WSS magnitude and high oscillatory shear index (OSI) have been linked to the development of local atherosclerosis in the carotid arteries and aorta in animal models [2,3] and are, therefore, considered atherogenic wall parameters. Previous CFD and MRI studies demonstrated that critically low WSS and high OSI were concentrated at the physiologically dilated internal carotid artery (ICA) bulb, i.e. the posterior wall of the ICA opposite the bifurcation and a typical site of carotid plaque development [5,6]. These studies showed that the distribution of wall parameters is substantially altered in patients with moderate ICA stenosis. However, no previous study has investigated the in-vivo distribution of WSS and OSI in patients before and after intervention for high-grade ICA stenosis. It is known that stenosis treatment leads to a significant reduction of peak blood flow velocities but it is unclear how recanalization therapy by eversion carotid endarterectomy (CEA) affects carotid wall parameter distribution.

We therefore aimed to study the in-vivo WSS and OSI distribution along the carotid bifurcation by pre- and post-surgery carotid 4D flow MRI in a cohort of 20 patients with  $\geq 60\%$  ICA stenosis (defined by ECST criteria [6]) and undergoing eversion CEA. We hypothesized that plaque removal by recanalization and consecutive reduction of high intrastenotic velocity gradients and poststenotic complex flow would result in measurable alterations of the distribution of WSS and OSI in vivo.

**Methods:** The study cohort consisted of 20 prospectively and consequently included patients with  $\geq 60\%$  ICA stenosis (ECST criteria, age=69.4 $\pm$ 8.6 years, 5 female, stenosis grade = 80.8 $\pm$ 11.8%). All patients underwent CEA and received 4D flow MRI at 3T (Trio, Siemens, Germany) prior to and after the procedure to measure individual time-resolved 3D blood flow velocity.

MRI measurements included 3D time-of-flight MRA covering the left and right carotid bifurcation (spatial resolution=0.5 $\times$ 0.8 $\times$ 1.0mm<sup>3</sup>) and contrast enhanced (CE) MR angiography (figure 1, 0.1mmol/kg Gd contrast agent, Multihance, Bracco, Italy, spatial resolution=1.2 $\times$ 1.5 $\times$ 4.0mm<sup>3</sup>). ECG gated 4D flow MRI was acquired in an axial 3D imaging volume including the distal 2 centimeter of the common carotid artery (CCA), the carotid bifurcation, and the proximal 5 centimeter of the ICA and ECA ( $\alpha=15^\circ$ , velocity sensitivity=200cm/s, spatial resolution= 1.1 $\times$ 0.9 $\times$ 1.4mm<sup>3</sup>, temporal resolution=45.6ms). For follow-up 4D flow MRI after CEA, the velocity sensitivity was set to 120cm/s to account for the reduced flow velocities in the ICA after plaque removal. The distribution of WSS was evaluated in standardized analysis planes positioned along the CCA, ECA and ICA, and pre-/post-plaque location. For each analysis plane, systolic WSS and OSI using a 8-segment wall model (see figures 2) was calculated. In addition, global systolic WSS and OSI for the CCA, ICA and ECA were calculated as the mean over all segments.

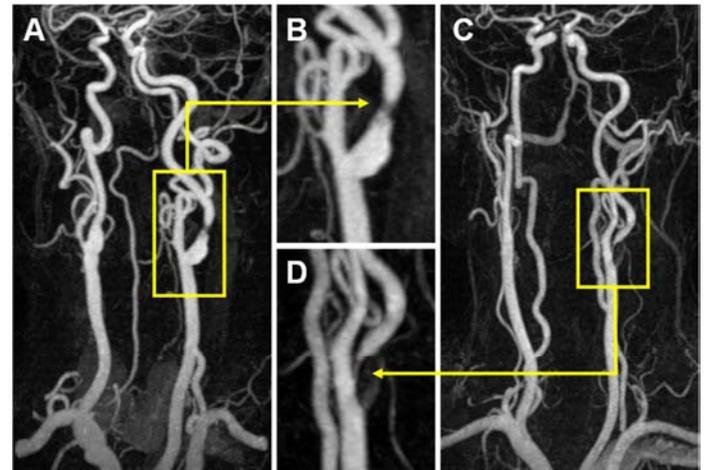
**Results:** CEA resulted in substantial alterations in wall parameters mostly confined to the ICA. Pre- and post-interventional global systolic WSS was similar for the CCA (0.49 $\pm$ 0.20N/m<sup>2</sup> vs. 0.47 $\pm$ 0.32N/m<sup>2</sup>, p=0.84) and the ECA (0.87 $\pm$ 0.45N/m<sup>2</sup> vs. 0.87 $\pm$ 0.73N/m<sup>2</sup>, p=0.95) but significantly lower (37% reduction) at the ICA after CEA (0.72 $\pm$ 0.30N/m<sup>2</sup> vs. 0.45 $\pm$ 0.21N/m<sup>2</sup>, p=0.0005). Pre- and post-interventional global OSI was reduced in the CCA (14.8 $\pm$ 9.1% vs. 10.8 $\pm$ 6.8%, p=0.03) similar in the ECA (10.4 $\pm$ 7.4% vs. 7.7 $\pm$ 7.1%, p=0.19) and significantly lower (25% reduction) for the ICA (12.6 $\pm$ 5.7% vs. 9.4 $\pm$ 4.8%, p=0.03).

The analysis planes closest to the in- and outlet of ICA stenosis were identified for each patient. The variability of stenosis morphology and position, i.e. length and extent of plaque tapering, resulted in variable pre-/post-plaque measurement positions between patients. As an example, figure 1 illustrates different distances of the stenosis maximum from the flow bifurcation for two patients with ICA stenosis. A comparison of the distribution of systolic WSS and OSI in locations directly proximal and distal to the ICA stenosis is shown in figure 2. CEA resulted in a significant decrease of systolic WSS in all 8 segments distal to the former ICA stenosis. In addition, significant post-treatment WSS reductions were found in 5/8 segments along the posterior ICA wall proximal to the stenosis. Segmental OSI decreased at the lateral wall proximal and distal to the former ICA plaque but not at the posterior wall. The segmental differences led to a significant reduction of mean post-interventional systolic WSS by 32% in locations proximal (0.37 $\pm$ 0.13N/m<sup>2</sup> vs. 0.25 $\pm$ 0.14N/m<sup>2</sup>, p=0.005) and by 52% in locations distal to the ICA stenosis (0.75 $\pm$ 0.46N/m<sup>2</sup> vs. 0.36 $\pm$ 0.19N/m<sup>2</sup>, p=0.0005). The relative reduction of OSI was 24% and 40% compared to preoperative values fproximal (14.8 $\pm$ 7.5% vs. 11.2 $\pm$ 5.2%, p=0.05) and distal (11.8 $\pm$ 8.7% vs. 7.1 $\pm$ 3.6%, p=0.01) to the stenosis, respectively

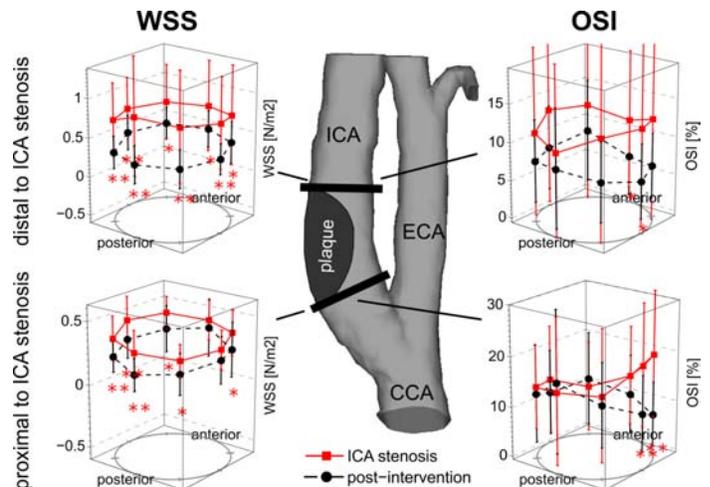
**Discussion:** 4D flow MRI allowed to selectively quantify regional 3D hemodynamics in patients before and after recanalisation of high-grade ICA stenosis. Plaque removal by surgery lead to significant reductions of systolic WSS and OSI in the ICA such while wall parameters in the CCA and ECA remained largely unchanged demonstrating the localized impact of CEA on carotid hemodynamics. Therefore, 4D flow MRI is a promising tool for longitudinal in vivo studies evaluating the influence of hemodynamics on plaque development and disease progression at the carotid bifurcation.

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**References:** 1. Malek AM, et al. *Jama* 1999;282:2035-2042. 2. Cheng C, et al. *Circulation* 2006;113:2744-2753. 3. Tomita H, et al. *Atherosclerosis*. 2012;220:78-85. 4. Lee SW, et al. *Stroke*. 2008;39:2341-7. 5. Markl M, et al. *Circ Cardiovasc Imaging*. 2010;3:647-55. 6. European Carotid Surgery Trialists' Collaborative Group. *Lancet*. 1991;337:1235-1243



**Figure 1:** CE MRA of two patients with high-grade ICA stenosis prior to carotid endarterectomy. **A and B:** ICA stenosis with 75% lumen narrowing: The physiologically dilated ICA bulb is preserved and the maximum of the stenosis is located 15 mm distal to the flow diverter. **C and D:** ICA stenosis with 65% lumen narrowing. In contrast to the other patient, the ICA bulb is not preserved and the maximum of the stenosis is located only 3 mm distal to the flow diverter indicating that the stenosis begins in the distal common carotid artery.



**Figure 2:** Distribution of average systolic WSS and OSI in 8 wall segments of the analysis planes before and after carotid endarterectomy in n=20 patients. \*indicates p < 0.05, \*\*indicates p < 0.01 in wall segments that show a significant change of values between pre- and postoperative measurements.