Low cerebral blood flow can affect cognition in patients with high-grade asymptomatic internal carotid artery (ICA) stenosis, but the relationship between blood flow and cognition has not been well quantified. We hypothesized a threshold value below which hemodynamic impairment affected cognition.

**METHODS**

**Subjects.**
Inclusion criteria: age 18-85, ≥80% carotid stenosis or complete occlusion by Doppler, MRA, or CTA, asymptomatic status or TIA only. Exclusion criteria: prior clinical stroke, dementia, head trauma with LOC, CHF. All patients signed informed consent approved by the Columbia Institutional Review Board.

**Measurement of blood flow.**
Middle cerebral arteries (MCAs) were imaged on a depth of 50-58 mm using 2 MHz probes (Terumo Trifid PDM150B, Spencer Technologies Seattle WA, USA) attached to a standard headframe. Peak systolic velocity (PSV), end diastolic velocity (EDV), and mean flow velocity (MFV) were recorded for 10 minutes with the patient lying supine.

**RESULTS**

Forty-two patients with unilateral high grade carotid artery stenosis without stroke were enrolled in the study (27M, mean age=74±9, mean EDUC =16±3 yrs). Average Z-score was -0.31SD. In univariate analysis, MFV correlated with composite Z-score but did not reach statistical significance (R=.294, p=0.059); EDUC was significant (R =.345, p=0.022). In linear regression, MFV was a significant predictor of cognitive Z-score (β =3.08, p=0.043); EDUC was not (β=.267, p=.077). A single breakpoint was identified at 45cm/sec by the Davies test (p=0.061). (See Figure 1.) For MFV<45cm/sec, Z-score increased significantly 0.05 SD (95% CI:0.01 to 0.10) per cm/sec MFV. For MFV>45cm/sec, the Z-score decreased 0.01 SD (95% CI:-0.07 to 0.05, NS).

**Figure 1: TCD mean flow velocity vs cognitive Z-score**

**Statistical analysis.**
Pearson correlations and multivariable linear regression were used to look for associations between MFV and Composite Z-score, adjusting for age, education (EDUC) and depression, entering variables stepwise with p≤0.10 (SPSS v.22). The Davies test was used to identify a single breakpoint for non-zero difference-in-slope of a segmented relationship between the main variables of interest: MFV and composite Z-score. Subsequently, a piecewise linear model was fitted, assuming one (unknown) breakpoint.

**CONCLUSION**

In high grade, asymptomatic carotid artery stenosis, cognitive impairment correlated linearly with lower flow in the hemisphere fed by the occluded ICA, but the relationship held only below a threshold of MFV=45cm/sec. Such a finding has implications for management of what would otherwise be considered “asymptomatic” carotid artery disease, and prompts further investigation as to whether revascularization can reverse cognitive impairment or prevent further decline. The question of reversibility of hemodynamically induced cognitive decline is currently being tested in the ongoing CREST-H study.

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1Haybach, Kuechenhoff: Testing for a Breakpoint in Two-Phase Linear and Logistic Regression Models Sonderforschungsbereich 386, Paper 77 (1997)