#245: Cognitive Impairment Correlates Linearly With Mean Flow Velocity by Transcranial Doppler Below a Definable Threshold

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BACKGROUND

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 insonated at a depth of 50-58 mm using 2 MHz probes (Terumo Trifid PMD150B, 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 =.308, p=0.043); EDUC was not (β=.267, p=0.77). 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).

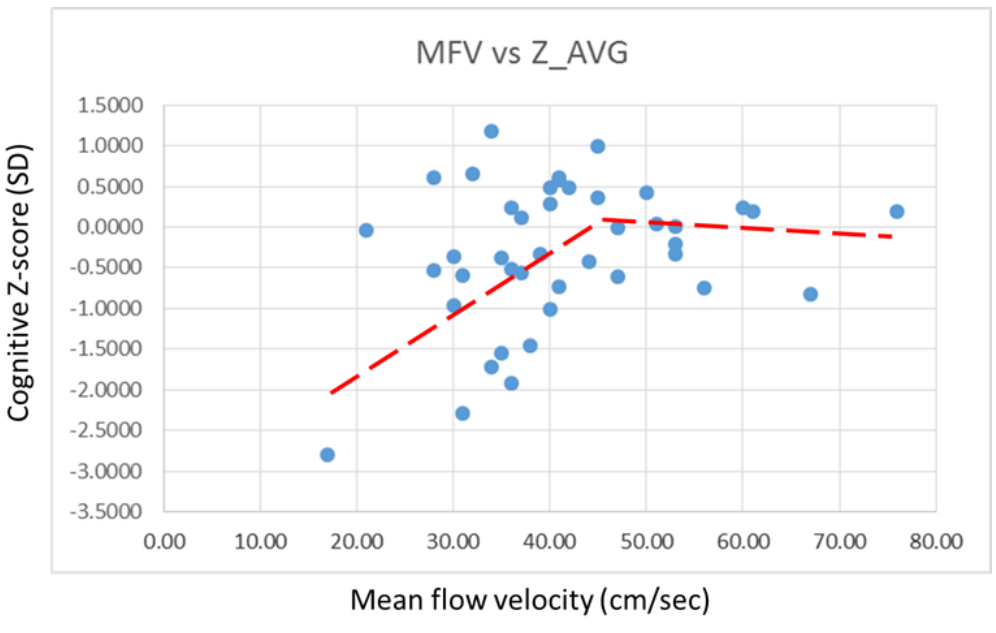

Figure 1: TCD mean flow velocity vs cognitive Z-score

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METHODS, cont'd

Neurocognitive testing.

Patients underwent a 1-hour neurocognitive battery, administered by a trained tester consisting of 14 standardized neuropsychological tests, designed to assess left hemisphere function, right hemisphere function, and global (bilateral) function. (Table) Raw test scores were transformed into age-adjusted Z-scores derived from published norms. Z-scores were summed and divided by the number of tests completed to calculate a composite Z-score for each patient.

Neurocognitive test	Hemisphere specificity	Outcome Variable
Trails A	global	Time (sec)
Trails B	global	Time (sec)
Digit Span	global	Digits forward + backward
Digit Symbol	global	Correct Number of symbols
Boston Naming	left	Number Correct
BDAE Repetition	left	Number Correct
Hopkins Verb mem	left	Total (3 trials+delayed recall)
COWA word fluency	left	Total Number words (F/ A/S)
Rey Figure copy	right	Score
Rey Figure recall	right	Score
†Line bisection	right	Percent Deviation
‡Target cancellation	right	No. Correct+Search Pattern
*Grooved pegboard ("affected" hand)	Left / right	Time (Sec)
*Grooved pegboard ("unaffected" hand)	global	Time (Sec)

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[1] 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.[2]

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

[2]Marshall RS, Lazar RM, et al, CREST-H: Study design and rationale *Int J Stroke* 2018