Elevations in Preoperative Monocyte Count Predispose to Acute Neurocognitive Decline After Carotid Endarterectomy for Asymptomatic Carotid Artery Stenosis

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Background and Purpose—Although the incidence of major stroke attributable to carotid endarterectomy (CEA) is low (1% to 2%), ≈25% of patients experience subtle postoperative neurocognitive dysfunction. This study examines whether preoperative leukocyte profiles predict cognitive outcome in asymptomatic CEA patients.

Methods—Sixty-nine asymptomatic CEA patients underwent neuropsychometric testing preoperatively and on postoperative day 1 (POD1). Preoperative white blood cell counts and differentials were obtained. Logistic regression was performed for risk factors for neurocognitive decline. Variables achieving univariate \( P < 0.10 \) were included in multivariate analysis.

Results—Eighteen (26%) patients experienced neurocognitive decline on POD1; multivariate analysis demonstrated that preoperative monocyte count (\( P = 0.011 \)) and age (\( P = 0.02 \)) independently predicted outcome.

Conclusions—Preoperative monocyte count and age are independently associated with acute neurocognitive decline after CEA for asymptomatic stenosis. (Stroke. 2006;37:240-242.)

Key Words: carotid endarterectomy ■ ischemia ■ neuropsychology
expressed as mean±SD (odds ratio, 95% CI, P value) or with P<0.05 considered significant.

## Results

### Cohort Characteristics

Demographic/intraoperative variables for CEA and control patients are presented in Table 2. Eighteen (26%) patients experienced neurocognitive decline on POD1. There was no significant difference in age or anesthesia between the experimental/control groups or percent ipsilateral carotid stenosis between the injured/uninjured cohorts. No patients experienced radiographically/clinically apparent major postoperative stroke.

### Statistics

Leukocyte analysis demonstrated no statistically significant differences between injured/uninjured groups, with the exception of monocytes. Mean preoperative monocyte counts were 0.70±0.19 cells/nL in the injured and 0.52±0.18 cells/nL in the uninjured group (P<0.001).

Univariate analysis demonstrated a 12% increased risk of neurocognitive injury (1.12, 1.02 to 1.22, 0.02) for each year age increase. Each SD increase in monocyte count (SD=0.20 cells/nL) resulted in a 179% increase risk of neurocognitive injury (2.79, 1.46 to 5.35, 0.002). Neutrophil count trended toward significance in univariate analysis (1.64, 0.96 to 2.80, 0.07). Lymphocyte count and other stroke risk factors did not reach significance (P<0.10). Total WBC count was not included in the multivariate analysis because of high correlation with neutrophil count (Pearson correlation r=0.89; P<0.0001).

Multivariate analysis included age, monocyte, and neutrophil count (Table 1). Age was predictive of outcome (1.12, 1.02 to 1.24, 0.02). Monocyte count remained highly significant (2.37, 1.21 to 4.62, 0.01), and neutrophil count a borderline predictor (1.78, 0.97 to 3.27, 0.06).
Discussion

Preoperative monocyte count and age independently predict acute neurocognitive outcome after CEA for asymptomatic stenosis. These associations persist when accounting for conventional stroke risk factors, including smoking, which is known to elevate WBC counts.

Acute post-CEA neurocognitive dysfunction is believed to be ischemic in nature attributable to cerebral hypoperfusion or microembolization of plaque. Previous work demonstrates an association between impaired post-CEA NPMT performance and elevated serum levels of S100b, a marker of glial cell death, supporting this hypothesis. NPMT testing offers a more detailed assessment of higher cortical functioning than traditional neurological examination. Thus, patients may experience cognitive decline attributable to subtle ischemia without the traditional radiographic or clinical characteristics of major stroke.

Our findings suggest an inflammatory component to acute post-CEA cognitive dysfunction. Atherosclerosis is viewed as a chronic inflammatory condition, with monocyte activation and infiltration implicated as initiating events, and plaque macrophage content independently associated with instability. Elevated preoperative monocyte counts may therefore indicate the presence of unstable plaque more prone to microembolize during CEA. Furthermore, a role for monocytes in stroke, independent of atherosclerosis, has been suggested. Interleukin-8, a monocyte release product, is elevated after stroke and serves as a strong neutrophil chemoattractant. This may “prime” patients for acute ischemic post-CEA neurocognitive decline by creating a favorable environment for neutrophil recruitment after disrupted cerebral blood flow during surgery.

Further investigation is necessary to elucidate the mechanisms linking elevated monocyte counts with acute post-CEA cognitive dysfunction. Although previous data suggest that the majority of these patients will continue to experience impaired NPMT performance at 1 month, additional investigations assessing the association of monocyte counts and delayed post-CEA cognitive decline are warranted.

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References

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