The Impact of Carotid Artery Stenting on Cognitive Function in Patients with Extracranial Carotid Artery Stenosis

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Background: The effect of carotid artery stenting (CAS) on cognitive function in patients with extracranial carotid artery stenosis is equivocal. The aim of this study was to examine the impact of CAS on various domains of cognitive function.

Methods: We performed a meta-analysis of the studies evaluating various domains of cognitive function before and after CAS, namely, (1) global cognition using Mini-Mental State Examination (MMSE) and Rey Auditory Verbal Learning Test (RAVLT), (2) executive function using Trail Making Test (TMT) A or Color Trails Test (CTT) A and TMT B or CTT B, (3) language ability using Boston Naming Test (BNT), (4) memory, (5) attention/psychomotor speed, and (6) functional ability, using various cognitive tests. Pooled weighted mean differences (WMDs) and standardized mean differences (SMDs) with 95% confidence intervals (95% CIs) were appropriately calculated using fixed or random effects models after assessing between-study heterogeneity. Meta-regression analysis was performed with number of patients per study; mean age (years); follow-up (months); proportion of men; proportion of patients with hypertension, diabetes mellitus, hyperlipidemia, smoking, and coronary artery disease; proportion of symptomatic patients; and degree of ipsilateral and degree of contralateral carotid stenosis as covariates.

Results: Sixteen studies were eligible, including a total of 626 CAS patients. A statistically significant improvement of global cognition was detected with MMSE (WMD = 0.67, 95% CI = 0.29−1.05, $P < 0.001$; follow-up = 5.6 months), but not with RAVLT (SMD = 0.45, 95% CI = −0.03 to 0.93, $P = 0.07$; follow-up = 2.4 months). Significant improvement of memory (SMD = 0.33, 95% CI = 0.11−0.55, $P < 0.01$; follow-up = 4.1 months) and attention/psychomotor speed (SMD = 0.21, 95% CI = 0.04−0.39, $P = 0.02$; follow-up = 4 months) was also detected. No statistically significant effect on executive function (TMT A/CTT A and TMT B/CTT B; SMD = 0.08, 95% CI = −0.10 to 0.26, $P = 0.39$; follow-up = 3.9 months and SMD = −0.02, 95% CI = −0.20 to 0.16, $P = 0.82$, respectively; follow-up = 3.9 months), language ability (BNT; SMD = 0.24, 95% CI = −0.05 to 0.54, $P = 0.10$; follow-up = 4 months), and functional ability (SMD = −0.05, 95% CI = −0.25 to 0.15, $P = 0.63$; follow-up = 3.8 months) was observed. No significant effects of the examined covariates were demonstrated in the meta-regression analyses.

Conclusions: CAS may be associated with improvement in global cognition, memory, and attention/psychomotor speed. There was no positive effect on executive function, language, and functional ability, but CAS was not associated with a decline in any area of cognitive function. Future studies in larger groups of patients are probably needed to fully investigate the long-term effect of CAS on cognition in patients with carotid artery stenosis.

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INTRODUCTION

Carotid artery stenting (CAS) has been proposed as an alternative procedure to carotid endarterectomy (CEA) for reducing the risk of stroke, at least in some subgroups of patients with significant extracranial carotid stenosis. Cognitive function is being increasingly recognized as an important outcome measure that affects patient's well-being and functional status. However, the effect of CAS on neurocognitive functions in patients with extracranial carotid disease is still controversial. Several reports using transcranial Doppler have documented a significant number of microemboli during CAS,[1] whereas diffusion-weighted magnetic resonance imaging (MRI) has revealed that a large proportion of patients may develop new brain lesions.[2] Furthermore, studies have evidenced that the procedure-associated microembolization may be associated with poor cognitive function and memory decline after CAS.[1] On the other hand, cerebral blood flow is decreased in patients with severe carotid stenosis, especially in the elderly and normalized after CAS.[3] As a consequence, it is difficult to predict whether CAS will ultimately result in improvement or worsening of cognitive function.

The clinical assessment of cognitive function is usually difficult to perform. Many approaches regarding the timing of assessment after CAS and the type of tests have been used for that purpose. There are also various possible confounding factors such as age, symptomatic status, contralateral carotid or vertebral artery disease, severity of carotid stenosis, the use of protection devices, and others. As a result, several attempts to assess the effect of CAS on cognitive function have yielded conflicting conclusions. Given this background, we performed a meta-analysis to clarify the impact of CAS on various domains of cognitive function.

METHODS

Data Collection, Types of Studies, Search Terms, Eligibility, and Exclusion Criteria

The ''Preferred Reporting Items for Systematic Reviews and Meta-Analyses'' guidelines were used for the current meta-analysis.[4] We performed a combined computerized and manual systematic literature search in MEDLINE, EMBASE, Scopus, Google Scholar, Ovid, and the Cochrane Library, and reference lists were thereafter manually searched for relevant articles.

Publications of interest included any type of study (randomized and nonrandomized), systematic reviews, meta-analyses, short papers, and case series. Mesh terminology used was as follows: ''cognitive function'' [All Fields] OR ''cognition'' [All Fields] AND ''carotid angioplasty'' [All Fields] OR ''carotid stenting'' [All Fields] OR ''carotid revascularization'' [All Fields]. We identified all studies that reported on cognitive tests comparing pre- and postoperative performance (before versus after comparison) of CAS and included both numbers of examined study groups and quantitative measures of cognitive evaluation in symptomatic and asymptomatic patients. Scientific papers published up to February 2014 were included without applying any language or other restrictions. The studies that did not refer to patients treated with CAS or did not report measures of cognitive performance before and after CAS were excluded. Two researchers (C.N.A. and J.D.K.) independently extracted and analyzed the results of systematic literature search. In case of disagreements, the final decision was reached by consensus.

Data Extraction

Data extracted from eligible studies included first author's name; country of origin; study period; number of patients before and after CAS; proportion of men; mean age; proportion of patients with hypertension, diabetes mellitus (DM), hyperlipidemia, smoking, coronary artery disease (CAD); proportion of symptomatic patients; degree of ipsilateral and contralateral carotid stenosis, use of protection device, as well as inclusion criteria, follow-up (months), and results of cognitive tests for each study.

Statistical Analyses

Six separate meta-analyses were performed to evaluate different aspects of cognitive function, pre- and post CAS. More specifically, the effect of CAS was tested among studies evaluating the following: (1) ''global cognition,'' using Mini-Mental State Examination (MMSE) and Rey Auditory Verbal Learning Test (RAVLT); (2) ''executive function,'' using Trail Making Test (TMT) A or Color Trails Test (CTT) A and TMT B or CTT B; (3) ''language ability,'' using Boston Naming Test (BNT); (4) ''memory,'' using Verbal Fluency, Babcock Story Recall, Hopkins Verbal Learning Test, Rey–Osterrieth Complex Figure, Rivermead Behavioral Memory Test, and Fuld Object Memory Evaluation; (5) ''attention/psychomotor speed,'' using Digital Symbol - Wechsler Adult Intelligence Scale, mental speed, and Paced Visual Serial Addition Test; and (6) ''functional ability'' using National Institutes of Health Stroke Scale and Instrumental Activities of Daily Living. A