Clinical Neurology and Neurosurgery 146 (2016) 64–70

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Atherosclerotic carotid stenosis and cognitive function

Tao Wang, Bin Mei, Junjian Zhang*

Department of Neurology and Neuropsychological Research Center, Zhongnan Hospital, Wuhan University, Wuhan, China

ARTICLE INFO

Article history:
Received 5 January 2016
Received in revised form 23 February 2016
Accepted 29 March 2016
Available online 20 April 2016

Keywords:
Carotid stenosis
Cognitive function
Revascularization
Carotid endarterectomy
Carotid artery stenting

ABSTRACT

Atherosclerosis carotid stenosis is associated with stroke and cognitive impairment. Progressive cognitive decline may be an even greater problem than stroke, but it has not been widely recognized and therefore must be adequately addressed. Although both Carotid Endarterectomy (CEA) and Carotid Artery Stenting (CAS) have been proven can prevent future stroke in patients with atherosclerotic carotid stenosis, the influence of CEA and CAS on cognitive function is not clear. In the first part of this review, we evaluated the literature concerning carotid stenosis and the risk of cognitive impairment. Studies have suggested that both symptomatic and asymptomatic carotid stenosis are associated with cognitive impairment. In the second part, we reviewed the impact of CEA and CAS on cognitive function, some studies have shown benefits, but others have not.

Contents

1. Introduction

The prevalence of moderate (≥50%) asymptomatic carotid artery stenosis was 4.2% (95% CI, 3.1% to 5.7%) among people, while the prevalence of severe (≥70%) asymptomatic carotid artery stenosis was 1.7% (95% CI, 0.7% to 3.9%) [1]. The number of people with carotid stenosis will continue to increase in the future. Carotid stenosis is not only an independent risk factor of ischemic cerebrovascular diseases but is also a direct cause of reduced cognitive function. The ischemic damage of areas involved in mental performance can easily explain the cognitive problems in patients with symptomatic stenosis. However, whether patients with asymptomatic stenosis (conventionally defined as significant atherosclerosis without stroke or transient ischemic attack in the brain or eyes [2]) also suffer from cognitive dysfunction is still unclear. Although both CEA and CAS have been proven to prevent future stroke in patients with carotid stenosis [3,4], whether cognitive function can also benefit from carotid revascularization is unknown. Lastly, it is unclear whether any difference exists between CEA and CAS. In this review, we summarize the current available knowledge on the risk and possible pathomechanism of cognitive impairment in patients with carotid stenosis, including the influence of carotid revascularization on cognitive function.

2. Methods

A Medline/PubMed search of studies was conducted. A combination of carotid revascularization and neuropsychological key

* Corresponding author at: Department of Neurology and Neuropsychological Research Center, Zhongnan Hospital, Wuhan University, Donghu Road 169, Wuhan 430071, Hubei, China.
E-mail address: 851895243@qq.com (J. Zhang).

http://dx.doi.org/10.1016/j.clineuro.2016.03.027
0303-8467/

words was used to identify all relevant studies on cognitive testing in carotid revascularization. This search was restricted to English language papers published between January 2010 and July 2015. Carotid revascularization key words include "carotid endarterectomy"; "carotid angioplasty"; "carotid stenting" and "carotid revascularization". Neuropsychological key words include "cognitive function"; "neuropsychological outcome"; "cognitive disorders"; "cognition" and "dementia". Furthermore; relevant papers and books were checked for references. Studies that performed cognitive function evaluation before and after surgery were included. Studies were excluded when reporting: (1) cognitive changes after revascularization without description of preoperative findings; (2) cognitive function in nonsurgical patients; patients with intracranial stenosis or without postoperative assessment; (3) case reports and review articles without personal data and (4) findings reported by the same authors.

3. Carotid stenosis and the risk of cognitive impairment

Since conventional vascular risk factors (hypertension, diabetes, dyslipidemia and smoking) are risk conditions for carotid stenosis and dementia alike, carotid stenosis may be a direct cause of reduced cognitive function, or it may only serve as a marker of generalized atherosclerosis. The presence of ischemic brain injury in patients with symptomatic stenosis can easily explain the cognitive impairment observed in such cases. Whether patients with asymptomatic stenosis also suffer from cognitive dysfunction is unclear.

Three large population-based studies examined the relationship between asymptomatic carotid stenosis and cognitive function [5–7]. Johnston et al. [5] evaluated 4006 right-handed men and women ≥65 years who participated in the Cardiovascular Health Study. They found that high-grade (≥75%) stenosis of the left internal carotid artery was associated with cognitive impairment and cognitive decline during the follow-up, and no such correlation was observed for the right-sided stenosis patients. The Tromso study included a heterogeneous group of 189 stroke-free subjects with bilateral carotid stenosis and 201 controls. In this study, patients with carotid stenosis achieved significantly lower levels of performance in several subsets of cognitive tests, even after adjustment for relevant confounders (sex, age and length of education) [6]. In the Framingham Offspring Study, a subgroup of 1971 participants underwent cognitive testing and MRI of the brain 4 years later. Carotid stenosis was found to be associated with significantly poorer performance on cognitive tests in asymptomatic subjects [7]. Recent studies also indicate that asymptomatic carotid stenosis is an independent risk factor for cognitive decline [8–13].

4. Pathomechanism of cognitive impairment in patients with carotid stenosis

There is a prevalent opinion that cognitive problems in patients with symptomatic stenosis may be a consequence of the ischemic damage of areas involved in mental performance [14]. In patients with asymptomatic stenosis, chronic cerebral hypoperfusion has been established as an important causal factor leading to cognitive impairment [9,11]. Generally, there was a decrease of approximate 25% of cerebral blood flow in the side of stenosis with respect to the contralateral side, and the long-lasting insufficient perfusion may impair energy metabolism in neurons and cause cognitive impairment. In addition, investigations of cerebral imaging based on weighted diffusion and gradient echo techniques have suggested that both hemorrhagic and non-hemorrhagic microinfarcts are far more common than clinically recognized. Even in patients with asymptomatic stenosis, silent infarctions have been detected in 15–19% patients. These infarctions may be silent except for subtle effects on cognitive function [7]. Beyond hypoperfusion and silent infarction, studies have also demonstrated that altered cerebrovascular reactivity [11] and impaired regional functional connectivity [10,13] are associated with poorer cognitive performance in patients with asymptomatic stenosis.

5. Revascularization of carotid stenosis

The prevention of stroke in patients with high-grade carotid stenosis has been traditionally carried out with CEA [15]. However, with the development of the materials for interventional therapy and neuroimaging techniques, CAS is now being investigated as an alternative to CEA [4]. In trials with post-procedural stroke, myocardial infarction and mortality as primary end points, both CEA and CAS were proven to prevent future stroke [3,4]. However, studies have reported conflicting effects of CEA and CAS on cognitive function [16].

5.1. Impact of CEA on cognitive function

Studies that compared the pre- and postoperative cognitive function in patients who underwent CEA after 2010 are summarized below.

Study	Country	N	Patients	Follow up	Findings
Heyer et al. [17]	USA	53	Symptomatic	1 day	More patients with pulsatility index ≤0.80 exhibited cognitive improvement 1 day after CEA than those with pulsatility index >0.80. Patients with cognitive improvement had a significantly greater increase in cerebral blood flow than those without
Lefeng et al. [18]	China	40	Symptomatic	3 months	CEA improved the visual acuity, visual field, auditory acuity, general neurocognitive function and independent living ability of patients with minor stroke from severe carotid stenosis
Mracek et al. [19]	Czech Republic	60	Symptomatic	1 and 6 days	General anesthesia negatively influenced cognitive function on the first postoperative day. However, by the sixth postoperative day, this cognitive impairment no longer existed
Takaiwa et al. [20]	Japan	15	Asymptomatic	3 months	At 3 months after CEA, the rate of increase in the Repeatable Battery for the Assessment of Neuropsychological Status scores were 60.0% for immediate memory, 26.7% for visuospatial/constructional, 33.3% for language and attention, 26.7% for delayed memory, 47.7% for total scale and 26.7% for Wechsler Adult Intelligence Scale-Revised 2 subtests