OPINION ARTICLE

CAROTID REVASCULARIZATION FOR NEUROCOGNITIVE BENEFIT: MYTH OR REALITY?

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While stroke is a well-known cause of cognitive impairment, the relationship between carotid artery stenosis and cognitive function in individuals remains highly unclear due to methodological heterogeneity across studies evaluating cognitive benefit following carotid revascularization.

Indeed, when carotid stenosis is classified as symptomatic or asymptomatic, the patient's cognitive status is usually not taken into account. In this context, the impairment may be either pre-existing or progressive and will be closely linked to declines in cerebral perfusion and function.[1] On the other hand, the cognitive issues experienced by patients are sometimes subtle and not severe enough to interfere with their daily activities; consequently, they go unnoticed and are underestimated even by their closest family and friends. The use of revascularization to improve function remains a subject of debate due to the lack of standardization in research protocols and the diversity of assessment tests employed. Therefore, if this relationship is not clear to us, the question arises: could we expect any change after surgery? Or, more importantly, is it worth performing in terms of neurocognitive outcomes?

The pathophysiology of cognitive dysfunction is quite complex, as multiple factors can influence it. Vascular mechanisms (cerebral hypoperfusion, silent cerebral infarction, or silent embolization) could be involved; accordingly, we could assume that the revascularization procedure might improve cognitive function primarily by restoring cerebral blood flow, correcting chronic cerebral hypoperfusion, and ultimately reducing microemboli formation.[2,3] However, findings regarding changes in cognitive function post-surgery are remarkably contradictory. Some trials report improvement, whereas others report no changes or even subsequent functional decline.[4-6] Differences in study design, small sample sizes, and inconsistent selection of cognitive tests could account for these significant discrepancies and the lack of a definitive conclusion. Furthermore, more recent studies focus solely on the cognitive deficit attributable to carotid stenosis, overlooking the scope of all other mental and cognitive correlations that might be involved. Evidently, other aspects would seem to be of interest when indicating revascularization.

Neurocognitive impairment or dementia entails a reduction in mental activities, memory, judgment, and problem-solving capacity. Its association with decreased cerebral perfusion is evident, as are the hemodynamic consequences of carotid stenosis and its subsequent resolution. Critical

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brain regions (adjacent to the middle cerebral artery) are compromised, reflecting delayed blood flow to vulnerable areas and correlating the cognitive deficit with reduced oxygen and nutrients delivered to the neural network (memory, attention, and processing speed).[2] Following revascularization, better-perfused brain areas have been documented. Pre-existing lesions, such as white matter hyperintensities, cortical atrophy, and lacunar infarcts, have become negative predictors of postoperative clinical improvement.[7,8] However, the clinical benefit in this group of patients remains unclear, as does the extent to which pre-existing lesions may influence more or less favorable outcomes. Despite the acknowledged limitations regarding heterogeneity in non-randomized studies, carotid endarterectomy / carotid artery stenting (CEA/CAS) rarely improves overall late cognitive function in asymptomatic patients (< 2%).[1]

Although the significant association between cognitive impairment and carotid stenosis in asymptomatic patients is widely reported, it does not establish into a proven causal relationship and does not automatically imply an etiological link, since, to date, there is still no clear evidence that such stenosis causes cognitive decline. However, patients with severe carotid lesions and impaired cerebrovascular reserve might be more likely to present cognitive impairment, even in the long term. This raises the need to evaluate vulnerable patient subgroups that might benefit most from interventions to prevent or reverse cognitive decline.[9]

The assessment of cognitive impairment in the context of cerebrovascular disease remains a source of controversy, due to the lack of tools specifically designed and validated for this population. The Mini-Mental State Examination (MMSE), developed by Marshall Folstein and colleagues in 1975, has historically been one of the most widely used tests for global cognitive assessment in clinical practice. Its widespread dissemination is due to its brevity, ease of administration, and utility as a screening instrument. However, it presents significant limitations, particularly in detecting mild cognitive impairment, due to its lower sensitivity in assessing executive functions, complex attention, and other higher-order domains.[10] On the other hand, the Montreal Cognitive Assessment (MoCA), developed by Ziad Nasreddine in 2005, was designed to improve the early detection of mild cognitive impairment. This tool explores multiple cognitive domains more comprehensively—including memory, attention, executive functions, visuospatial skills, language, and orientation—which grants it greater sensitivity, especially in early stages and in domains frequently compromised in vascular disease.[11] Although both tests are widely used, their diagnostic performance varies with the assessed domain and the patient's clinical characteristics. In the context of post-stroke cognitive impairment, some studies have shown comparable performance between the two tools; nevertheless, accumulated evidence suggests that the MoCA exhibits greater sensitivity for detecting subtle deficits, particularly in executive functions, attention, and visuospatial skills.[12] In contrast, the MMSE tends to underestimate cognitive compromise in early stages. These aspects acquire special relevance in patients with transient ischemic attack and stroke, in whom early detection of cognitive impairment has prognostic and therapeutic implications. In this group, the MoCA has demonstrated greater discriminative capacity, identifying alterations that the MMSE fails to detect.[12-15] Similarly, in vascular dementia, the MoCA has evidenced better diagnostic parameters.[14] Nonetheless, both tools present limitations, including the influence of educational level and sociocultural factors on the results. Furthermore, neither test alone allows for a comprehensive assessment of the complexity of vascular cognitive impairment, which is characterized by a heterogeneous compromise across multiple domains. In this context, although the MoCA could be considered more suitable for initial screening, its use should be integrated into a multimodal approach that includes more comprehensive neuropsychological evaluations.[16,17] Combining both tools can improve diagnostic accuracy and provide a more comprehensive assessment of cognitive function. Future studies should focus on standardizing specific protocols and validating instruments with greater diagnostic precision and long-term prognostic value.

Regarding medical treatments with neuroprotective effects, aggressive medical therapy has been linked to a beneficial effect by reducing the incidence of stroke/TIA in patient populations with asymptomatic carotid stenosis.[18,19] However, standardized therapeutic regimens are lacking, both in dosing and in the populations under study. Some studies indicate that combining statin therapy with surgery could improve cognitive outcomes, while others report no significant effects. Preoperative use has been associated with a lower incidence of postoperative cognitive dysfunction (POCD), probably due to its neuroprotective effect, and its utilization could be justified by its direct impact on the pathophysiological processes of cognitive impairment in carotid stenosis,

chronic cerebral hypoperfusion, and the effects of microembolization originating from unstable plaques. Its efficacy and use in reducing major adverse cardiovascular events are well established, making statins indispensable in both primary and secondary prevention strategies. However, variability in the findings highlights the need for standardized tests and long-term follow-up to accurately assess the cognitive impact of revascularization accurately. Dexmedetomidine (DEX), an alpha-2 adrenergic agonist, is used in anesthesia for better sedation and for the management of postoperative delirium and chronic nerve compression pain. A randomized study demonstrated improvements in MMSE and MoCA scores following carotid endarterectomy and DEX use, primarily related to brain-derived neurotrophic factor (BDNF) and lactate levels.[20] The use of nimodipine, a calcium channel blocker and cerebral vasodilator, was promoted to improve memory and sensorimotor function associated with aging, as well as neurological deficits following ischemic stroke and subarachnoid hemorrhage.[21] Its neuroprotective effect likely contributes to combined perioperative strategies alongside carotid revascularization. Further clinical trials with larger sample sizes will be required to optimize dosage and administration strategies.

But the final question, from my perspective and within this context of uncertainty, is: carotid endarterectomy or endovascular treatment (carotid stenting) to improve neurocognitive impairment? Certain considerations must be clarified.

Based on current evidence, revascularization could benefit patient subgroups with high-risk characteristics (ulcerated and unstable plaques, microembolism, silent infarcts). Individual selection would seem to be the most recommended approach. Indiscriminate use in asymptomatic patients remains highly controversial, as the risks of the procedure and subsequent restenosis must be weighed.[22] First, the neurocognitive benefit of carotid endarterectomy is related to the improvement of chronic hypoperfusion, especially in patients with mild cognitive impairment, particularly in the areas of attention and memory.[23] Very elderly patients (>80 years old) would not benefit significantly, likely due to their limited vascular plasticity and prior decline.[24] However, the benefit of their treatment should be weighed against postoperative cognitive decline and a probable cerebral hyperperfusion syndrome, which has an observed incidence between 6% and 30% of cases, where the resulting edema and cortical brain damage could determine even greater cognitive impairment.[19] Factors such as prolonged carotid clamping, diabetes, or the degree of previous carotid stenosis have been linked to this condition.[25]

Regarding endovascular treatment, carotid artery stenting has demonstrated greater benefits in visual, spatial, executive, and motor functions. This difference compared to endarterectomy is not entirely clear, though it is probably related to the type of flow restoration.

The truth is that both procedures appear to be safe. Yet, they are dependent on factors such as age, comorbid conditions (hypertension, diabetes, prior cognitive deficit, psychiatric disorders), prior microvascular disease, lesion laterality, and the complications inherent to each procedure, which affect the rehabilitation of each patient.

In our experience, we recently and prospectively estimated cognitive performance in asymptomatic and symptomatic patients using two versions of neurological tests.[26] We used both the MoCA and the MMSE to assess cognitive function in relation to the performed carotid endarterectomy. Although a larger sample size and a longer follow-up period are required, our main finding was that carotid revascularization may improve language function in asymptomatic patients with severe carotid disease, as assessed by the MoCA test. This finding could not be corroborated with the MMSE. This result probably aligns with the original MoCA study and other studies, which showed that the MoCA has higher sensitivity than the MMSE for detecting subtle cognitive impairment.[11,12] Furthermore, we must consider that language assessment with the MMSE is more superficial, which could explain the lack of improvement on that test. This promising finding could spur additional studies to evaluate language and other cognitive domains in this group of patients.

CONCLUSION

Given the current information, it is difficult to recognize the neurocognitive impact of carotid revascularization. Highly heterogeneous populations and treatments suggest that the effectiveness of these interventions would depend on proper patient selection and on individual factors such as age, vascularization, or prior cognitive status. Certain types of lesions may predict more favorable or adverse outcomes, as underlying brain pathology can influence the treatment response.

On the other hand, many tools for assessing cognitive status seem insufficient for evaluating specific, significant impairment in each domain. Future research could identify vulnerable subgroups (for example, those with impaired cerebrovascular

reserve) or provide stronger evidence that silent embolization in patients with carotid stenosis causes cognitive impairment. To date, there is no conclusive evidence supporting that interventions in patients with severe carotid stenosis can prevent or reverse cognitive impairment.

Declaration

The author declares no conflicts of interest.

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