REVIEW

Comparison of Cognitive Function after Carotid Artery Stenting versus Carotid Endarterectomy

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WHAT THIS PAPER ADDS

This article has reviewed the literature for studies evaluating the changes in cognitive function after carotid artery stenting (CAS) versus carotid endarterectomy (CEA). The majority of the 13 studies that were identified did not demonstrate a significant difference between the two procedures with regard to an effect on cognitive function. However, the lack of standardization of specific cognitive tests and timing of assessment of cognitive function after CAS and CEA do not allow for definite conclusions to be drawn. Future studies should address the limitations of the previous studies and systematically evaluate the effect of CAS and CEA on cognitive function.

The effect of carotid artery stenting (CAS) and carotid endarterectomy (CEA) on cognitive function is unclear. Both cognitive improvement and decline have been reported after CAS and CEA. We aimed to compare the changes in postprocedural cognitive function after CAS versus CEA. A systematic qualitative review of the literature was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement for studies evaluating the changes in cognitive function after CAS compared with CEA. Thirteen studies (403 CEAs; 368 CAS procedures) comparing the changes in cognitive function after CEA versus CAS were identified. Most studies did not show significant differences in overall cognitive function or only showed a difference in a single cognitive test between the two procedures. A definitive conclusion regarding the effect of CAS versus CEA on cognitive function was not possible owing to heterogeneity in definition, method, timing of assessment, and type of cognitive tests. For the same reasons, performing a meta-analysis was not feasible. The lack of standardization of specific cognitive tests and timing of assessment of cognitive function after CAS and CEA do not allow for definite conclusions to be drawn. Larger, adequately-powered and appropriately designed studies are required to accurately evaluate the effect of CAS versus CEA on postprocedural cognitive function.

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INTRODUCTION

It has previously been reported that carotid endarterectomy (CEA) and carotid artery stenting (CAS) are effective procedures for the prevention of stroke in patients with carotid artery stenosis.[1,2] The effect of CAS and CEA on cognitive function, however, is controversial. The term "cognitive function" includes a variety of functions, such as verbal and non-verbal memory, attention, executive function, mood, language, and motor skills. A cross-sectional, cohort study on 4,006 patients without a history of a cerebrovascular event reported that a $\geq$75% internal carotid artery stenosis is associated with an almost sevenfold increased risk of cognitive impairment and an almost threefold increased risk of cognitive decline.[3] These results suggest that even asymptomatic carotid artery stenosis is strongly associated with cognitive impairment and decline.[3] Some studies have demonstrated cognitive improvement after both CEA[4] and CAS,[5,6] whereas others have shown no change[7,8] or even cognitive decline.[9,10]

A systematic review on the effects of CAS and CEA on cognitive function, a few years ago, concluded that neither procedure clearly affected cognition.[11] This systematic review included 25 articles evaluating cognitive function after CEA, four after CAS, and only three studies comparing the effects of CAS versus CEA on cognitive performance (113 CEAs vs. 94 angioplasty/CAS procedures).[11] The

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	PICOS Appendix
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Not registered
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	6 and PICOS Appendix
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Figure 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6 PICOS Appendix
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Cochrane check list (Table 3)
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	No quantitative synthesis undertaken
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	No quantitative synthesis undertaken
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Cochrane check list (Table 3)
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Not applicable
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7 and Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 1, Cochrane check list (Table 3)
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	No quantitative synthesis undertaken
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Cochrane check list (Table 3)
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Not applicable

Figure 1. Checklist with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) Statement.[16] For more information, visit www.prisma-statement.org.

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	8-10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10-11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	11
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	11

PICOS Appendix:

PICOS Statement

Population: The patient population is comprised of patients subjected to a carotid revascularization procedure (CAS vs. CEA) for symptomatic or asymptomatic carotid stenosis. All patients meeting the intervention criteria were considered eligible.

Intervention: Carotid endarterectomy vs. carotid angioplasty with or without stenting

Comparator: Objective of the present systematic review is to compare cognitive outcomes in the two groups. Cognitive outcomes include verbal and non-verbal memory, attention, executive function, mood, language and motor skills.

Outcome: A formal meta-analysis was not possible due to heterogeneity in study populations, study designs and outcome definitions. Methodological quality of included observational studies was assessed with the Newcastle-Ottawa Scale; quality of randomized controlled trials (RCTs) was assessed via the Cochrane checklist for the assessment of bias in RCTs.

Study Design: Case series, case control studies, cohort studies and randomized controlled trials were considered eligible.

Figure 1. (*continued*).

results of the studies evaluating cognitive function after CEA or CAS were inconsistent. Some reports showed improvement, others did not show any substantial change, while others reported deterioration in cognitive function after either procedure.[11] The three studies directly comparing CAS and CEA were all performed within two randomized, controlled trials, that is, two within the Carotid And Vertebral Artery Transluminal Angioplasty Study (CAVATAS)[12,13] and the third within the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE)[14] study.

The studies included in this early systematic review[11] had several limitations. One limitation of the first two reports from CAVATAS[12,13] was that all endovascular procedures but one were performed by angioplasty alone (i.e., without the use of a stent). Another limitation of all three studies[12—14] was that an embolic protection device (EPD) was not used routinely. CAS is associated with higher microembolic event rates than CEA.[10,15] EPDs successfully reduce the number of microembolic events after CAS.[15] An EPD was only used in 151 of the 567 patients (27%) in SPACE[14] and in none of the patients participating in CAVATAS.[12,13] Finally, the number of patients included in these three substudies[12—14] was small because only a small subgroup of the overall randomized population in CAVATAS (46/504 patients)[13] and SPACE (45/1,183 patients)[14] was analyzed for cognitive performance. The results of this early systematic review[11] regarding the possible effects of CAS versus CEA on cognitive function may therefore be inaccurate and not up-to-date. Since the publication of the previous systematic review,[11] several more recent studies have compared the effects of CAS versus CEA on cognitive function. We therefore updated this early systematic review[11] to investigate the current status regarding the effects of CAS versus CEA on cognitive function.

METHODS

This systematic review was conducted according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement.[16] The PRISMA checklist with a related appendix (participants, interventions, comparisons, outcomes, and study design) are shown in Fig. 1. We sought to identify all studies comparing the pre- and postoperative cognitive performance and cognitive function after CAS versus CEA that were published up to 15 August 2013. The PubMed/Medline, Cochrane and Embase (1974—present) databases were searched using the following terms: “carotid artery stenting”, “carotid endarterectomy”, “carotid revascularization”, “cognitive function”, and “cognitive test” in various combinations. The reference lists of the gathered reports were manually searched. This produced additional studies, which were also considered.

Studies were included if they compared the cognitive function pre- and postoperatively after CAS versus CEA, and included at least 10 patients in each group. Studies assessing the cognitive function after CAS or CEA alone were excluded. Case reports, review articles, and letters were also excluded from analysis. Articles from the same authors were included when they reported additional information that was not included in the previous report, such as different tests, measurements, and different patients.

The search was independently performed by two investigators (K.I.P. and C.L.) and was completed on 15 August 2013. The data were checked independently for quality. The methodological quality of individual observational studies was assessed with the Newcastle—Ottawa Scale (NOS),[17] a validated instrument specifically designed to evaluate the quality of observational studies in systematic reviews and meta-analyses.[18,19] The NOS evaluates three domains of

study methodology: the selection of study groups (score range: 0—4), the comparability of groups (score range: 0—1), and the quality of ascertainment of either the exposures (for case-control studies) or of the outcomes of interest (for cohort studies; score range: 0—3). The composite NOS score ranges from 0 to 8, with a NOS score >5 indicating an acceptable methodological design. For the randomized controlled trials included in this review, the methodological quality was assessed using the Cochrane Collaborations risk of bias assessment tool.[20]

RESULTS

A total of 37 reports were identified using the mesh terms "carotid artery stenting AND cognitive function". Another 104 articles were identified when the mesh terms "carotid endarterectomy AND cognitive function" were used. The combinations "carotid revascularization AND cognitive function" and "carotid revascularization AND cognitive test" produced 31 and 16 articles, respectively. These last two searches did not produce any additional articles relevant to the topic beyond the results of the first two searches, and

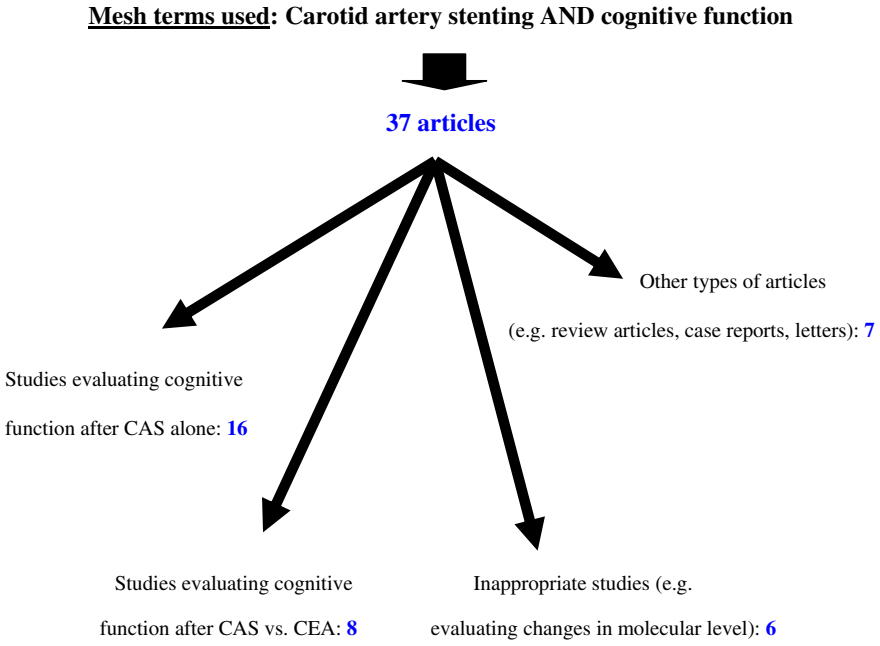

Figure 2. Flow chart of search results.

Table 1. Studies comparing cognitive outcomes after carotid artery stenting (CAS) versus carotid endarterectomy (CEA).

Study (year)	Patient groups	Timing of assessment	Outcome
Sivaguru et al. (1999)[12,a]	63 symptomatic CEA vs. 53 PTA patients	Before and 6 mo after the procedure	No significant difference in the overall score between PTA and CEA
Crawley et al. (2000)[13,a]	26 symptomatic CEA vs. 20 PTA patients	Before, 6 wks after and 6 mo after the procedure	No significant differences between the two groups on any test at any of the assessment times. The only significant difference was found with the Grooved Pegboard (dominant hand), with CEA patients performing better at the 6-mo assessment compared with PTA (0.45 vs. −0.06, respectively; $p = 0.047$)
Witt et al. (2007)[14,b]	21 symptomatic CAS vs. 24 CEA patients	Before, 6 d after and 1 mo after the procedure	There were no differences between CAS and CEA in any neuropsychological outcome
Gossetti et al. (2007)[10,b]	50 CEA vs. 50 CAS patients (mixed population)	Before, at discharge and 2 mo after the procedure	• Microemboli were detected in 37 CEA (74%) and all 50 (100%) CAS procedures • Cognitive capability worsened in 18 patients after CAS (36%) and 2 after CEA (4%)
Jansen et al. (2008)[27,a]	17 symptomatic CAS patients vs. 10 CEA patients vs. 13 healthy controls	Before, 1 mo, and 6 mo after the procedure	• No difference in memory function ($p = 0.241$) and alertness ($p = 0.220$) between patients undergoing CAS vs. CEA • Memory function and alertness at 6 mo deteriorated in both groups compared with healthy controls (for CEA vs. controls: $p = 0.041$; for CAS vs. controls: $p = 0.003$)
Takaiwa et al. (2009)[25,a]	11 CEA vs. 15 CAS patients (mixed population)	Preoperatively, 1 wk, 3 mo, 6 mo, and 1 y postoperatively	• Both CEA and CAS demonstrated improved RBANS scores 3 mo postoperatively (for CAS: from 86.3 ± 11.0 to 100.3 ± 10.8; $p < 0.01$; for CEA: from 93.4 ± 12.5 to 106.8 ± 15.3; $p < 0.01$) which persisted at 1 y • CAS patients showed improved MMSE scores 1 wk postoperatively (from 27.7 ± 1.3 to 28.5 ± 1.6; $p < 0.01$), whereas CEA patients showed improved MMSE scores 6 mo postoperatively (from 28.0 ± 1.5 to 28.9 ± 0.7; $p < 0.01$)
Capoccia et al. (2010)[28,b]	20 asymptomatic CEA vs. 23 CAS patients	Preoperatively, ≤24 h postoperatively, and 6 mo after the procedure	• For CEA patients, the mean MMSE scores decreased non-significantly (from 26.1 ± 3.46 to 25.6 ± 3.27; $p = 0.67$) • For CAS patients, the mean MMSE scores decreased significantly (from 25.6 ± 4.46 to 22.9 ± 4.54; $p = 0.045$) • Between-group analysis showed a significant decrease in the postoperative score of CAS vs. CEA patients ($p = 0.03$) • At the 6-mo follow-up, the MMSE score showed an improvement in CAS patients (23.7 ± 4.58), while it was stable in the CEA group (25.9 ± 3.43; within- and between-group analysis $p =$ NS)

Continued

Table 1-*continued*

Study (year)	Patient groups	Timing of assessment	Outcome
Feliziani et al. (2010)[21,b]	22 asymptomatic CEA vs. 24 CAS patients	Preoperatively (T0), at 3 (T3) and 12 (T12) mo postoperatively	• No significant differences were observed at T0, T3, and T12 between CEA and CAS patients (for CEA: from 27.8 ± 2.3 to 27.4 ± 2.4 and 27.6 ± 3.0; for CAS: from 27.2 ± 1.9 to 26.5 ± 2.8 and 27.7 ± 2.1) • CAS showed worse outcomes in the trail-making test part A compared with CEA (preoperatively: 52.9 ± 24.4 vs. 74.1 ± 37.7, for CEA vs. CAS, respectively; $p = 0.058$; at 3 mo: 63.2 ± 50 vs. 109.2 ± 74.4, for CEA vs. CAS, respectively; $p < 0.05$; at 12 mo: 55.6 ± 22.5 vs. 97.2 ± 51.0, for CEA vs. CAS, respectively; $p < 0.01$)
Lal et al. (2011)[22,b]	25 asymptomatic CEA vs. 21 CAS patients	1–3 d before and 4–6 mo after CEA/CAS	• The composite change score for the entire test battery improved in patients both after CEA and after CAS compared with their baseline values (+0.51 for CEA vs.+0.47 for CAS, respectively; $p =$ NS) • CEA resulted in a deterioration of working memory index (a measurement of memory/concentration), while CAS improved it (change score: −0.41 vs. 0.46, for CEA vs. CAS, respectively; $p = 0.001$) • CAS resulted in a deterioration of the Processing Speed Index (a measurement of psychomotor speed), while CEA improved it (change score: −0.32 vs. 0.58, respectively; $p = 0.001$)
Altinbas et al. (2011)[23,a]	61 symptomatic CAS vs. 58 CEA patients	1 wk before and 6 mo after the procedure	• From baseline to 6-mo follow-up there was a significant decrease in the cognitive sumscore after CAS of 0.19 (95% CI: 0.10–0.29; $p < 0.0001$) and a non-significant decrease after CEA of 0.02 (95% CI: −0.16 to 0.21; $p = 0.825$) • Mean difference: −0.17 (95% CI: −0.38 to 0.03; $p = 0.092$) • Within the individual domains, the unadjusted change in the cognitive domain abstract reasoning was significantly worse after CAS (difference between changes: −0.22; 95% CI: −0.44 to 0.00; $p = 0.046$), but after adjustment for age, sex, and education this did not stay statistically significant. The lack of a difference in cognition between CAS with CEA may be explained by insufficient statistical power
Wasser et al. (2012)[29,b]		1 d before, 1–4 d after, and 3 mo after the procedure	• Patients < 68 y did not show any significant cognitive alteration after either CEA or CAS

	19 CAS vs. 27 CEA patients (mixed population)		• Patients $\geq$ 68 y treated by CAS demonstrated a significant deterioration in post- vs. pre-procedural scores ($p = 0.01$), but then their cognitive performance improved by 3 months ($p = 0.017$) • Patients $\geq$ 68 y treated by CEA demonstrated a significant deterioration in post- vs. pre-procedural scores ($p = 0.022$), which persisted at 6 mo ($p = 0.002$)
Zhou et al. (2012)[24,b]	16 CAS and 35 CEA patients (mixed population)	1–2 wks before and 1 mo after the procedure	• Microemboli after the procedure were found in 8 CAS (50%) and 3 CEA (8.6%) patients • There was a trend for a decrease in mean RAVLT scores for patients with procedure-related microemboli (from 37.2 $\pm$ 12 to 29.7 $\pm$ 9.3; $p = 0.0525$), whereas those without microemboli had a slightly increased RAVLT mean score (from 33.3 $\pm$ 8.8 to 34.2 $\pm$ 9.4; $p =$ NS)
Capoccia et al. (2012)[26,b]	32 asymptomatic CEA vs. 28 CAS patients	Preoperatively, 1 d, 6 mo and 12 mo postoperatively	• New ischemic lesions were detected in 6 CAS vs. 1 CEA patients (21.4% vs. 3%, respectively; $p = 0.03$) • In CAS patients, new DW-MRI lesions were associated with MMSE score decline ($p = 0.001$) • At 12 months, patients presenting with new lesions showed lower MMSE scores ($p = 0.08$)

Note. PTA = percutaneous transluminal angioplasty; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; MMSE = Mini-Mental State Examination; NS = non-significant; CI = confidence interval; RAVLT = Rey Auditory Verbal Learning Curve; DW-MRI = diffusion-weighted magnetic resonance imaging.

[a] Randomized controlled trial.

[b] Non-randomized trial.

Table 2. Quality of observational studies (Newcastle–Ottawa Scale).[17]

Study	Selection (0–4)[a]	Comparability (0–1)[b]	Outcome/ exposure (0–3)[c]	Total
Gossetti et al.[10]	4	0	1	5
Takaiwa et al.[25]	4	0	2	6
Capoccia et al.[28]	4	1	3	8
Feliziani et al.[21]	4	1	3	8
Lal et al.[22]	3	1	2	6
Wasser et al.[29]	4	1	2	7
Zhou et al.[24]	4	1	0	5
Capoccia et al.[26]	4	0	2	6

Note. Maximum score = 8, minimum = 0.

[a] For cohort studies, "selection" refers to the representativeness of the exposed cohort (yes = 1, no = 0), selection of the non-exposed cohort (adequate = 1, inadequate = 0), ascertainment of exposure (clear = 1, unclear = 0), and demonstration that the outcome of interest was not present at the beginning of the study (yes = 1, no = 0). For case-control studies, "selection" refers to the case definition (adequate = 1, inadequate = 0), representativeness of the cases (yes = 1, no = 0), selection of controls (adequate = 1, inadequate = 0), and definition of controls (adequate = 1, inadequate = 0).

[b] For cohort studies, "comparability" refers to adjustment for bias/confounding (yes = 1, no = 0). For case-control studies, "comparability" refers to adjustment for bias/confounding (yes = 1, no = 0).

[c] "Outcome" refers to outcome assessment, i.e., independent blind assessment (yes = 1, no = 0), appropriate duration of follow up (yes = 1, no = 0), and adequacy of follow-up (>90% = 1, ≤ 90% = 0). "Exposure" assessment refers to ascertainment of exposure (adequate = 1, inadequate = 0); identical method of ascertainment for cases and controls (yes = 1, no = 0), and non-response rate (same rate for both groups = 1, other = 0).

were therefore ignored. The search of the Cochrane and Embase databases did not produce any additional studies.

The flow chart of the first two search results is presented in Fig. 2. Eight articles comparing cognitive functions after CAS versus CEA were identified.[10,14,21–26] Another five articles were retrieved[12,13,27–29] by searching the reference lists of these full-text articles,[10,14,21–26] as well as by including the studies of the earlier published systematic review.[11]

The findings of these 13 studies[10,12–14,21–29] (403 CEAs; 368 CAS procedures) are presented in Table 1. Six studies failed to show a significant overall difference in cognitive functions between CAS and CEA.[12–14,21–23] Some of these studies demonstrated a difference in only one of the specific cognitive function tests between the two procedures (e.g., the Trail Making Test,[21] the Processing Speed Index,[22] or the Grooved Pegboard).[13] Other studies showed a significant deterioration in cognitive functions after CAS, but not after CEA.[23,26,28] One study showed a deterioration in one cognitive domain (working memory index) after CEA, but not after CAS.[22] Another study suggested that patients aged ≥68 years (but not younger individuals) may demonstrate differences in cognitive functions when undergoing CAS or CEA.[29] In this study, patients undergoing both CEA and CAS demonstrated postoperative deterioration in cognitive function. While this decline in cognitive function improved 3 months after CAS, it persisted 6 months after CEA.[29]

The methodological quality of the observational studies included, was acceptable, with all studies achieving a NOS score >5 (Table 2). Among randomized controlled trials, two studies had an overall low risk of bias,[13,23] whereas the study by Sivaguru et al.[12] has only been available in abstract form (Table 3).

Unfortunately, there was considerable heterogeneity in the 13 studies[10,12–14,21–29] identified. For instance, in one study,[12] assessment of cognitive functions was performed before and 6 months after the procedure; in another[13] before, 6 weeks, and 6 months after the procedure; while in a third study,[14] this was performed before, 6 days after, and then at 1 month after the procedure. A fourth study assessed the cognitive function preoperatively, and 1 week, 3 months, 6 months, and 1 year postoperatively,[25] while a fifth study assessed cognition preoperatively, ≤24 hours postoperatively, and 6 months after carotid revascularization.[28] There was also considerable heterogeneity regarding the types of test used to assess cognitive function (e.g., the Mini-Mental State Examination,[21,24–26,28] the Repeatable Battery for the Assessment of Neuropsychological Status,[25] or the Rey Auditory Verbal Learning Curve[24]). Furthermore, some studies included only symptomatic patients,[12–14,23,27] some other studies included only asymptomatic individuals,[21,22,26,28] and others included both symptomatic and asymptomatic carotid patients.[10,24,25,29] Finally, the studies range over a relatively long period (from 1999[11] to 2012[24,26]), and most of them include few (<50) patients.[13,14,21,22,25,27–29]

Table 3. Cochrane Collaborations' tool[20] for assessing risk of bias in randomized controlled trials.

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Sivaguru et al.[12]	?	?	?	?	?	?	–
Crawley et al.[13]	+	+	–	+	+	+	?
Witt et al.[14]	+	?	–	?	+	+	?
Altinbas et al.[23]	+	+	–	+	+	+	+
Jansen et al.[27]	+	?	–	?	+	?	?

Note. (+) = low risk of bias; (–) high risk of bias; (?) = unclear risk of bias.

DISCUSSION

Our literature search revealed five randomized controlled trials[12–14,23,27] and eight non-randomized trials[10,21,22,24–26,28,29] comparing cognitive function changes after CAS versus CEA. Owing to the heterogeneity in definition, methods, type of tests, and time of assessment of cognitive function, the data from this systematic review could not be combined in a formal meta-analysis. This was in accordance with the PRISMA statement.[16] Overall, a clear difference in postprocedural cognitive function after CAS compared with CEA could not be demonstrated.

Several mechanisms have been postulated to explain the changes in cognitive function after CAS or CEA. Some studies[4–6] support that the improvement in cognitive function after CAS or CEA is owing to the fact that carotid revascularization procedures correct the cerebral hypoperfusion resulting from carotid artery stenosis. In contrast, the mechanisms providing possible explanations for the cognitive decline after carotid revascularization include cerebral emboli and hypoperfusion generated during the procedure.[10,15] CAS is associated with a higher incidence of embolization[10,15] and stroke[30] rates compared with surgery. It was suggested that the difference in embolization rates between the two procedures may account for the difference in cognitive function.[10,24] However, if this mechanism could explain the postprocedural differences in cognitive function between CAS and CEA, all studies would produce similar results in favor of CEA. Thus, this mechanism may account for the difference in cognitive function in certain cases, but not in others.

Whether or not the higher embolization rates after CAS compared with CEA are responsible for a greater cognitive decline is a subject for debate. The arguments supporting this theory derive from studies on patients undergoing coronary artery bypass grafting (CABG).[31,32] Cerebral emboli generated during CABG are responsible for postoperative cognitive deficits in these patients.[31,32] A similar mechanism has thus been postulated for patients undergoing CAS.[10,15] In contrast, others have claimed that the higher incidence of microemboli after CAS compared with CEA is not associated with a greater cognitive decline.[33]

A recent study evaluated the association between asymptomatic cerebral lesions on diffusion-weighted magnetic resonance imaging (DW-MRI) after CAS with postoperative cognitive function in 37 patients.[34] This study demonstrated that CAS-induced new postprocedural asymptomatic cerebral ischemic lesions on DW-MRI had a negative impact on cognitive functions.[34] This report confirmed the results of an earlier study[10] demonstrating an increased rate of cognitive dysfunction in patients with higher microemboli rates after CAS compared with CEA. Therefore, preliminary evidence suggests that the higher embolization rates after CAS compared with CEA may predispose patients to higher post-procedural cognitive dysfunction.[34] This association should be verified in larger studies in the future before a definitive conclusion can be drawn.

This review has several limitations. A major limitation is that the studies included may not be adequately powered to assess with certainty the effects of CAS and CEA on cognitive function. A second limitation is that current guidelines recommend the performance of both CEA and CAS within 2 weeks of the development of cerebrovascular symptoms.[2,35] Future studies should assess changes in cognitive function when the carotid revascularization procedure is performed within 2 weeks of the index symptom. Another limitation is that the cognitive tests employed, the duration of follow-up, and the time intervals between the assessment points vary considerably between studies. Consequently, at this time, it is not possible to reach a definite conclusion regarding the effects of carotid revascularization on cognitive function. Future studies should address these limitations and should systematically evaluate the changes in cognitive functions after CAS and CEA.

CONCLUSIONS

The studies comparing the outcomes after CEA and CAS always report stroke and death rates, but rarely measure the effects of these procedures on cognitive functions. This systematic review aimed to compare cognition before and after CAS versus CEA. There is marked inconsistency in the literature regarding the effect of CAS and CEA on cognitive function. The studies so far produce mixed and heterogeneous results, and thus do not allow for accurate conclusions to be drawn. Standardization of neuropsychological testing, follow-up timing, and incorporation of neuroimaging could all enhance the ability of further clinical studies to investigate the effect of carotid interventions on cognitive function and to elucidate the underlying pathophysiology. Besides stroke and death rates, CAS and CEA should also be compared with regard to their effect on postprocedural cognitive function.

CONFLICT OF INTEREST

None.

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