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REVIEW

Safety of Stenting and Endarterectomy for Asymptomatic Carotid Artery Stenosis: A Meta-Analysis of Randomised Controlled Trials

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WHAT THIS PAPER ADDS

The results of this study indicate that carotid endarterectomy (CEA) has a lower rate of peri-procedural stroke than carotid artery stenting (CAS) in patients with asymptomatic carotid stenosis. Numerous investigations comparing CAS and CEA cover symptomatic patients. Although a few recently published studies have reported asymptomatic cases separately, because of the limited sample size and ambiguous inclusion criteria, these studies are not powered to validate any generalisability. The present meta-analysis strictly covered two arm randomised controlled trials comparing CEA and CAS with pre-specified criteria. It was found that CEA remains a reliable approach to asymptomatic carotid stenosis when performed in combination with best medical treatment. The risks of mid- to long-term complications and post-procedural health related quality of life should be emphasised in further clinical practice.

Objective/Background: A meta-analysis of recently published randomised controlled trials (RCTs) was performed to evaluate the safety of carotid artery stenting (CAS) versus carotid endarterectomy (CEA) for asymptomatic carotid stenosis with average risk.

Methods: The MEDLINE, Embase, and Cochrane Library databases were systematically searched for RCTs that compared CAS with CEA for asymptomatic carotid stenosis. These publications reported clinical outcomes after revascularisation in patients with asymptomatic carotid stenosis during their primary intervention. Trials published in English were searched for on 31 May 2017. End points (composite of ipsilateral stroke, any stroke, major stroke, minor stroke, myocardial infarction [MI], and death during the post-procedural period) were extracted from the publications by two reviewers. The pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for peri-operative outcomes following CAS and CEA using a fixed effects model.

Results: Five studies involving 3901 patients (1585 with CEA; 2316 with CAS) were included in the meta-analysis. The risk of any stroke during the peri-procedural period was significantly lower in patients who underwent CEA than CAS (OR 0.53; 95% CI 0.29—0.96). The difference between CAS and CEA in the rate of stroke could be driven by minor stroke (OR 0.50; 95% CI 0.25—1.00). The risk of death, major stroke, ipsilateral stroke, and MI were not significantly different between the two interventions (peri-procedural death: OR 1.49 [95% CI 0.26—8.68]; peri-procedural major stroke: OR 0.69 [95% CI 0.20—2.35]; peri-procedural ipsilateral stroke: OR 0.63 [95% CI 0.27—1.47]; peri-procedural MI: OR 1.75 [95% CI 0.84—3.65]). No robust conclusion could be drawn regarding mid to long-term complications because of the heterogeneity of the reported data. The different outcomes precluded any further analysis being conducted.

Conclusion: Among patients with asymptomatic carotid stenosis, stenting has a significantly higher rate of any peri-procedural stroke and peri-procedural minor stroke than CEA, and similar risk of peri-procedural major stroke, peri-procedural ipsilateral stroke, or MI.

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INTRODUCTION

Moderate and severe carotid stenosis (≥50%) accounts for 10−15% of all strokes,[1,2] leading to a non-negligible public health burden each year. Asymptomatic carotid artery stenosis affects 7% of women and 12% of men, and is especially prevalent among patients aged >70 years.[3,4] Patients with severe asymptomatic carotid stenosis have an increased risk of further stroke related complications. Besides medical management alone (life expectancy > 5 years; favourable anatomy; one or more feature suggesting higher stroke risk on best medical treatment [BMT], Class IA), carotid revascularisation has been recommended as a therapeutic option. This raises the question regarding whether stenting is more effective than endarterectomy for patients with asymptomatic stenosis when performed in combination with BMT.

The first successful carotid endarterectomy (CEA) was performed in 1951.[5] Carotid artery stenting (CAS) became an alternative to CEA in the 1990s. Clinical data and meta-analysis findings have been used to compare the safety and non-inferiority between CAS and CEA, regardless of patients' symptomatic status.[3,6−9] However, no data restricted to randomised controlled trials (RCTs) of asymptomatic patients are currently available. A meta-analysis of RCTs was performed that compared the safety (risk of stroke, death, and myocardial infarction [MI]) between CAS and CEA.

METHODS

Search strategy

The online MEDLINE, Embase, and Cochrane Central Register of Controlled Trials databases was searched from 1994 (when Morris et al.[10] first deployed metal stents in two patients with carotid artery stenosis) to May 2017 for all RCTs that compared CAS with CEA for asymptomatic carotid stenosis. The following medical subject heading terms were used in Medline, and Emtree terms in Embase: carotid stenosis, stents, and carotid endarterectomy. The following keyword search terms were also used in the three databases: carotid stenosis, asymptomatic, stenting, and endarterectomy. The references of previous reviews and related original studies were searched to retrieve potential RCTs that were not included in the electronic search.

Inclusion criteria

Eligible studies were restricted to the following pre-defined criteria: (i) the study compared any peri- or post-procedural outcomes between CAS and CEA; (ii) both CAS and CEA should be restricted as the primary intervention; (iii) the study involved adults (aged ≥ 18 years) with asymptomatic extracranial carotid stenosis. However, trials with mixed groups (symptomatic and asymptomatic participants) were also included. The definitions of asymptomatic carotid stenosis mentioned in each study were accepted.

Exclusion criteria

Observational or retrospective studies (e.g., case control studies, cohort studies, and cross sectional studies) were excluded, as well as conference abstracts, editorials, and commentaries. RCTs published without respective outcomes of the two interventions were also excluded.

Data extraction and study quality assessment

Two reviewers (L.C., S.Z.) independently searched the literature and extracted the data. Another reviewer (Y.H.) checked the data for completeness and accuracy. Information was collected on the study design, definition criteria, baseline patient characteristics, intervention procedures, and clinical outcomes. The authors (C.L., Y.H., X.L.) evaluated the quality and applicability of each study using the Cochrane Collaboration's tool for assessing risk of bias (random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other potential bias).[11]

Ethical approval statement

All analyses were conducted based on available published studies, thus no ethical approval or patient consent were required.

Statistical analysis

This meta-analysis of CAS versus CEA was performed according to the recommendations outlined in the Cochrane Collaboration tool.[11]

Odds ratios (ORs) and 95% confidence intervals (CIs) for dichotomous data (peri-procedural outcomes) were calculated. The I^2 test was performed to evaluate the heterogeneity.[12] A 0.5 continuity correction was applied for RCTs that included data with no events.[13,14] Comparisons of data were conducted using a fixed effects model; a random effects model was used when the test value of heterogeneity showed an $I^2 > 50\%$. A difference with a p value $< .05$ was considered statistically significant. Subgroup analysis results and mid- to long-term results were not available because of a paucity of information.

All statistical analyses were performed using Excel 2010 (Microsoft, Redmond, WA, USA) and the "meta" package of R (version 3.3.1).

RESULTS

Search results and study characteristics

In total, 678 records were identified using the search strategy. After reviewing duplicates, abstracts, and titles, 621 records were removed. Forty papers of five original RCTs finally met the inclusion criteria (Fig. 1), and 14 were used for quantitative analysis.[15−28] In total, 3901 participants were randomly assigned to stenting ($n = 2316$) or endarterectomy ($n = 1585$), treated, and followed up for a duration of 2−10 years (Table 1).[15−19,29]

With the exception of the RCTs mentioned above, the SAPPHIRE trial (238 asymptomatic patients)[30] was excluded for the following reasons: (i) patients with coronary artery disease accounted for 85% of all patients, which may have

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