Stenting Versus Endarterectomy for Restenosis Following Prior Ipsilateral Carotid Endarterectomy

An Individual Patient Data Meta-analysis

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Objective: To study perioperative results and restenosis during follow-up of carotid artery stenting (CAS) versus carotid endarterectomy (CEA) for restenosis after prior ipsilateral CEA in an individual patient data (IPD) meta-analysis.

Background: The optimal treatment strategy for patients with restenosis after CEA remains unknown.

Methods: A comprehensive search of electronic databases (Medline, Embase) until July 1, 2013, was performed, supplemented by a review of references. Studies were considered for inclusion if they reported procedural outcome of CAS or CEA after prior ipsilateral CEA of a minimum of 5 patients. IPD were combined into 1 data set and an IPD meta-analysis was performed. The primary endpoint was perioperative stroke or death and the secondary endpoint was restenosis greater than 50% during follow-up, comparing CAS and CEA.

Results: In total, 13 studies were included, contributing to 1132 unique patients treated by CAS (10 studies, n = 653) or CEA (7 studies; n = 479). Among CAS and CEA patients, 30% versus 40% were symptomatic, respectively ($P < 0.01$). After adjusting for potential confounders, the primary endpoint did not differ between CAS and CEA groups (2.3% vs 2.7%, adjusted odds ratio 0.8, 95% confidence interval (CI): 0.4–1.8). Also, the risk of restenosis during a median follow-up of 13 months was similar for both groups (hazard ratio 1.4, 95% (CI): 0.9–2.2). Cranial nerve injury (CNI) was 5.5% in the CEA group, while CAS was in 5% associated with other procedural related complications.

Conclusions: In patients with restenosis after CEA, CAS and CEA showed similar low rates of stroke, death, and restenosis at short-term follow-up. Still, the risk of CNI and other procedure-related complications should be taken into account.

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Restenosis after carotid endarterectomy (CEA) hampers the long-term durability of CEA in terms of stroke-free survival.[1,2] The reported incidence of restenosis is variable according to its definition, method of measurement, and duration of follow-up. The rate of restenosis at 2 years has varied from 6% to 14% using duplex ultrasound with more than 50% restenosis as criterion.[3,4] Restenotic lesions have been shown to be clinically important, because recurrent lesions with more than 70% stenosis have been related to an increased risk for ipsilateral stroke.[5] However, the optimal treatment strategy of significant restenotic lesions remains unclear.[6–8] Redo-CEA potentially leads to a more challenging procedure,[9,10] and therefore restenosis following prior CEA has been adapted among the "high-risk" criteria within several registries and clinical trials comparing outcome after carotid artery stenting (CAS) versus CEA.[11,12] CAS has been suggested and applied as an alternative for CEA in these deemed high-risk cases.[13] However, there is no evidence suggesting that the (peri)procedural risk for stroke in these patients is lower for CAS when compared with CEA. Although the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial is the only randomized controlled trial comparing CAS versus CEA that included a subgroup of patients with restenosis after prior ipsilateral CEA, no subgroup analysis was performed in these patients.[11] Numerous single centers and several larger registries have reported on outcome of patients treated for restenosis after prior ipsilateral CEA through CAS or CEA,[14–16] but only few (nonrandomized) studies reported on outcome of both treatment modalities.[16–22] Generally, small number of patients in each registry limits the current evidence on the most desirable treatment strategy for restenosis. Most studies were underpowered to stratify patients in different risk categories (ie, based on symptoms). In addition, confounding by indication is a severe threat for these registries when evaluating both treatment modalities and not adjusting for potential confounders such as cardiovascular risk factors. While a randomized control trial is beyond perspective, accurate outcome analysis with the use of individual patient data (IPD) seems the highest retrievable level of evidence at present.

Therefore, we pooled all the publically available evidence regarding surgical and endovascular treatment of patients with restenosis after prior CEA into a dataset with IPD, and compared outcome

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after CAS and CEA. We hypothesized that CAS is not superior to CEA regarding perioperative results and outcome during follow-up.

METHODS

The study protocol defining the process for obtaining patient level data and the preplanned analyses was designed by the core study group (M.F., J.V., H.R., F.M., G.J.B.) and approved by all collaborating authors of the TREAT CARE (optimal TREATment of CArotid REstenosis) study group. The guidelines for meta-analyses of observational studies were followed.[23]

Search Strategy and Study Selection

A systematic search was performed on PubMed and Embase databases until July 1, 2013. Synonyms for "recurrent carotid stenosis" and "carotid endarterectomy" and/or "carotid angioplasty and stenting" were used to identify relevant studies. No filters or restrictions were applied (see Table 1 for search query). References of relevant articles were screened for additional relevant studies. Two independent researchers (M.F. and J.V.) screened all publications on predefined inclusion criteria: (1) patients who underwent CEA or CAS for restenosis after prior ipsilateral CEA; (2) data on the primary endpoint reported; (3) publications in English, Dutch, German, French, or Spanish; and (4) original data. Studies were excluded if there was no full-text version available or if the number of patients treated was less than 5. Duplicates were removed manually. All citations that met the inclusion criteria were thoroughly assessed for final inclusion.

Our search resulted in 1334 articles on PubMed and 1207 on Embase. After removing duplicates, 1521 articles remained, of which 1428 were excluded after screening citations. Of the remaining 93 articles, another 14 were excluded because they did not meet the inclusion criteria. Reference check of these 93 articles yielded 5 relevant studies. This resulted in a final number of 84 eligible articles (Fig. 1).

Individual Patient Data Acquisition

Authors of eligible articles were contacted per e-mail or per post with a request to join the TREAT CARE initiative. We obtained the contact details of any author listed on the article (sequence of contact: corresponding author, first author, senior author, other coauthors). If we did not receive a response after 1 week, the authors were contacted again, with a maximum of 4 attempts within a timeframe of 3 months. From the 84 eligible articles (7609 patients, possibly including duplicate patients and interventions others than CEA/CAS), we received IPD from 13 studies.[15,16,18,19,24–32] From the remaining 71 studies, IPD could not be retrieved because 30 authors did not respond, 26 did respond but the data were not available [no access to the data anymore without a clear reason why (13); no access to the data anymore because of change of institution, retirement, or institutional/study group restrictions (7); data destroyed or lost (4); data not digital (2)]. Three studies replied, but only provided summary data, and 11 study groups responded that they were not willing to participate (unknown reasons). One study cohort[33] was not contacted because the cohort was a duplicate of another study.[29] Of the studies that provided IPD, patients treated with interposition grafting (n = 43), carotid bypass (n = 24), or angioplasty only (n = 2) were excluded from the database. Furthermore, 32 bilateral or tertiary procedures were excluded, resulting in a total of 1132 unique patients (479 CEA, 653 CAS) (Fig. 1 and Table 2).

TABLE 1. Search Strategy

Recurrent stenosis OR Recurrent carotid stenosis OR Restenosis OR Post-CEA stenosis OR Post carotid endarterectomy stenosis OR Post endarterectomy stenosis
AND
CEA OR carotid endarterectomy OR carotid surgery OR Carotid revascularization OR OCS OR Open surgical repair OR Redo surgery OR Endarterectomy OR CAS OR Carotid artery stenting OR Carotid angioplasty OR Carotid stenting

Data Extraction and Outcome

Demographics, patient-related risk factors, procedural details, perioperative outcome, and follow-up data were extracted from the received IPD files and aggregated into 1 database after careful data examination. The primary endpoint of the current study was any perioperative stroke or death (a 30-day postoperative timeframe for all studies except for 1 (a 1-week timeframe). A combined endpoint was chosen because of the low event rate, and the inherent inability to compare treatments with enough power. Use of a combined endpoint is limited by difficulties in interpretation (ie, potentially opposite treatment effects of separate endpoints) and differences in importance to patients. More important events such as death are often associated with lower event rates and smaller treatment effects, which can be misleading. To partly overcome this limitation, we have also analyzed the individual endpoints (stroke and death) separately.

The secondary endpoint was recurrent carotid restenosis (>50%) during follow-up. Other procedural complications such as cranial nerve injury (CNI), neck hematoma, wound infection, bradycardia/arrhythmia during the procedure, residual stenosis (>30%), technical failure, and access site complications were also examined.

Statistical Analysis

Baseline characteristics between CEA and CAS patients were compared using the Fisher exact test for categorical variables, and parametric (Student *t* test) or nonparametric test (Mann-Whitney *U* test) for continuous variables.

The primary endpoint (any perioperative stroke or death) was compared between CEA and CAS with the Fisher exact test. For adjusted analyses, potential confounders were previously determined on the basis of availability (<75% missing values) and clinical relevance by 4 members of the core study group (M.F., J.V., H.R., and G.B.). To prevent confounding by indication and improve the reliability of our results, factors that were assumed to influence outcome, but also treatment decisions (and thus bias estimates of treatment effects), were chosen. These variables were age, gender, smoking, hypertension, degree of ipsilateral stenosis, symptom status, diabetes, and coronary artery disease. To prevent bias due to exclusion of observations because of missing values in these variables, single imputation was used (using the multivariate imputation by chained equations algorithm in R with 1 imputation).[34,35] Predictors in the imputation model included all variables to be imputed, including the primary endpoint, as recommended previously.[26] Because of low power in this analysis due to the low event rate of stroke or death, a propensity score including the previously listed variables was constructed. In short, the propensity score is a method to control for confounding and is derived from a logistic regression model to estimate the probability of being exposed to a certain treatment. Hence, patients with the same score will on average be balanced in confounder characteristics and comparing subjects with the same score will not be confounded by these characteristics.[36] With our score, we obtained considerable balance between treatment groups. The primary endpoint comparing CEA and CAS was subsequently analyzed by logistic regression model (events were recorded mostly in a 30-day postoperative timeframe), adjusted for the propensity score. Odds ratios (ORs) and 95% confidence intervals (CIs) are reported.

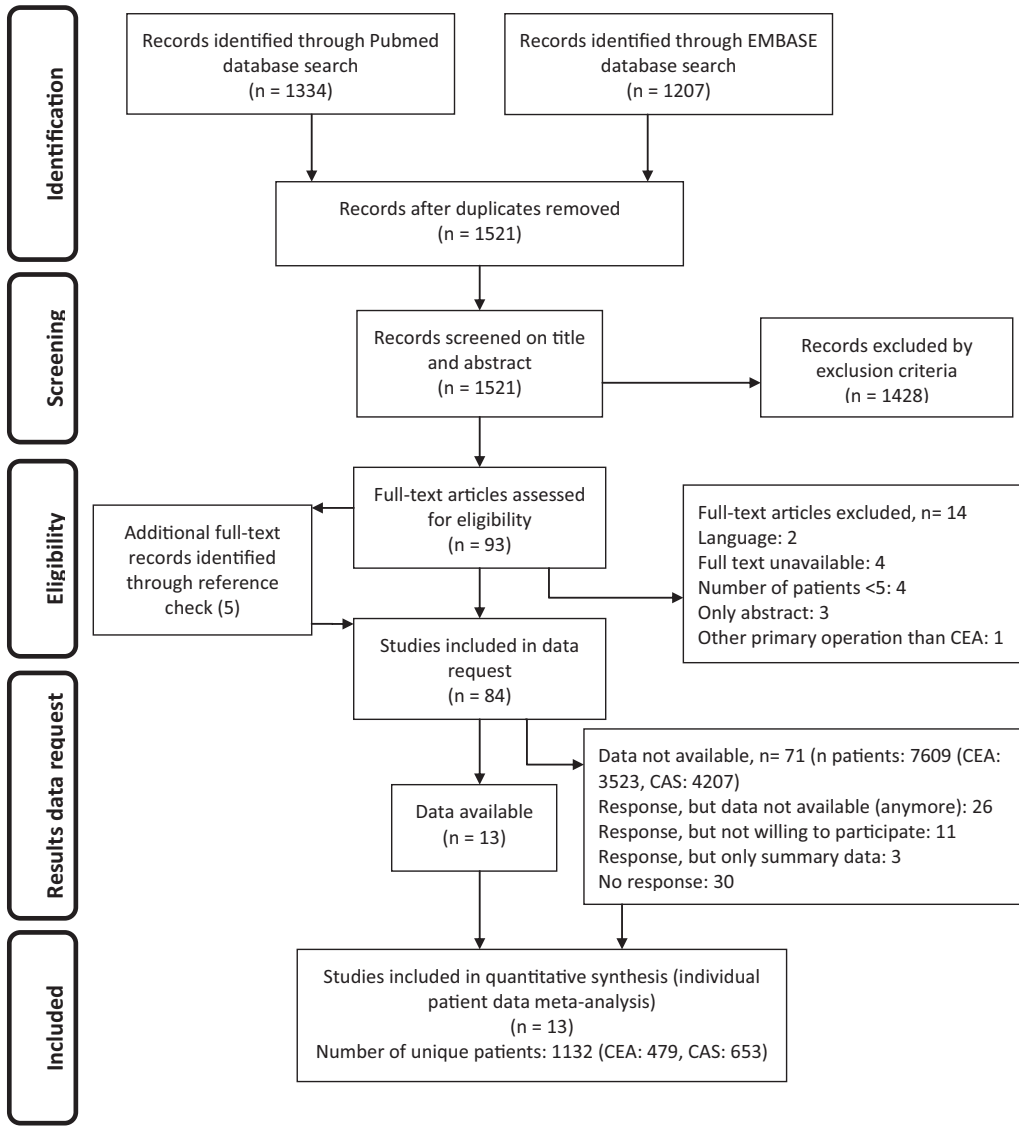

FIGURE 1. Flow diagram of TREAT CARE study.

TABLE 2. Overview of Included Studies

Article	Type of Study	Years of Inclusion	CEA (N)	CAS (N)
Alric et al[24]	Single center	1997–2000	0	15
Attigah et al[19]	Single center	1989–2007	28	41
Benitez et al[25]	Single center	1996–1997	0	5
Bettendorf et al[18]	Single center	1998–2006	28	29
Domenig et al[15]	Single center	1990–2001	82	0
Dorigo et al[26]	Single center	2005–2011	37	58
Eskandari et al[27]	Single center	2001–2009	0	70
Fokkema et al[16]	Multicenter	2003–2012	212	220
Halabi et al[28]	Single center	1998–2004	0	72
Jain et al[29]	Single center	1988–2005	80	0
Kadkhodayan et al[30]	Single center	1996–2005	0	73
Radak et al[31]	Multicenter (2 centers)	2000–2008	12	0
Vos et al[32]	Single center	1997–2006	0	70
		Total	479	653

The secondary endpoint (restenosis during follow-up) was analyzed using a multivariable Cox proportional hazard model to allow time to event analyses, adjusted for the same propensity score as mentioned earlier. Hazard ratios (HRs) and 95% CIs are reported.

SPSS version 20.0 (IBM Corp, IBM SPSS Statistics for Windows, Armonk, NY) and R Statistical software[37] were used for statistical analyses (R packages "mice" and "survival"). *P*'s < 0.05 were considered significant in all statistical analyses.

RESULTS

Baseline Characteristics

Baseline characteristics of patients undergoing CEA (n = 479) and CAS (n = 653) for restenosis after prior ipsilateral CEA are shown in Table 3. Although CAS patients were more likely to be older (mean age 70 vs 68 years, $P < 0.01$), CEA patients were more often symptomatic (40% vs 30%, $P < 0.01$). Severe ipsilateral stenosis greater than 70% was also found more frequently compared with CAS patients (94% vs 85%, $P < 0.01$). Data on time to restenosis from the initial CEA were available for 56% (n = 639) of patients. Median time from primary CEA to reintervention was significantly shorter for CAS when compared with CEA patients (14 vs 52 months, $P < 0.01$). Time to reintervention was also shorter for asymptomatic versus symptomatic patients (18 vs 33 months, $P < 0.01$). Of these 639 patients, 55% of patients (80% CAS and 20% CEA) had early restenosis (<24 months after primary CEA). Inclusion periods for CAS and CEA were similar, as shown in Table 4. Specifically, median year of start of inclusion was 1997.5 for CAS and 1998 for CEA.

Primary Endpoint

Perioperative stroke or death rate did not differ between CAS and CEA (2.3% vs 2.7%, OR = 0.8, 95% CI: 0.4–1.8). After propensity score adjustment, no difference was observed in the direction and significance of this endpoint (adjusted OR = 0.8, 95% CI: 0.4–1.8).

In addition, no differences in adjusted ORs for myocardial infarction, any stroke, and mortality were found between the 2 treatment modalities (Table 5). Similarly, no differences in stroke or death rate were identified between symptomatic and asymptomatic patients (3.4% vs 2.0%, $P = 0.15$). Comparing CAS and CEA also showed no significant differences between symptomatic (3.1% vs 3.7%, adjusted OR = 0.8, 95% CI: 0.3–2.6) and asymptomatic patients (2.0% vs 2.1%, adjusted OR = 0.8, 95% CI: 0.3–2.3). Although patients treated for early restenosis tended to have lower stroke or death rates with CAS than with CEA (1.1% vs 2.9%, adjusted OR = 0.3, 95% CI: 0.04–1.8), the difference did not reach statistical significance. Among all patients with late restenosis, stroke or death rate after CAS was 2.6% and after CEA was 2.2% (adjusted OR = 1.6, 95% CI: 0.3–7.8).

Secondary Endpoint

Data on restenosis during follow-up was available for 712 (400 CAS, 312 CEA) patients from 10 studies,[14,16,18,19,24,26,28–31] with a median follow-up time of 13 months (interquartile range: 8.7–26). In the CAS group, restenosis greater than 50% occurred in 34 patients (8.5%), and in 16 patients (4.0%) when using 70% as cutoff. For CEA patients, these numbers were 23 (7.3%) and 24 (7.7%), respectively, and there were 5 occlusions. In the adjusted analysis, no statistically significant difference was found regarding restenosis greater than 50% or 70% (including occlusions) between CAS and CEA patients (>50%: adjusted HR = 1.4, 95% CI: 0.7–2.2 and >70%: adjusted HR = 0.7, 95% CI: 0.4–1.4). Adjusted restenosis risk with a 50% cutoff was similar for both symptomatic (HR = 1.8, 95% CI: 0.8–3.7) and asymptomatic patients (HR = 1.3, 95% CI: 0.8–2.2).

Regarding clinical outcome during follow-up, there were 7 strokes (1 in the CAS group and 6 in the CEA group) and 7 cardiovascular-related deaths (2 in the CAS group and 5 in the CEA group) during 453 person years of follow-up in CAS patients and 731 person years of follow-up in CEA patients. These limited numbers did not allow for a reliable comparison between the treatment groups or for multivariable analysis.

Other Complications

After CAS, technical failure rate was 1.3%, residual stenosis was seen in 0.3%, access site complications in 1.9%, and bradycardia or arrhythmia during the procedure occurred in 1.4% of cases. After CEA, CNI was identified in 5.5% (N = 26) of patients, bleeding in 2.7% (N = 13), and wound infections in 0.2% (N = 1). From the 26

TABLE 3. Baseline Characteristics

	CEA (n = 479)		CAS (n = 653)		
	N/Total	%	N/Total	%	*P*
Age, mean ± SD, yr	67.8 ± 9.3		69.7 ± 8.7		**.001**
Gender (male)	238/479	49.7	345/653	52.8	0.31
Time to reintervention, median (IQR), mo	52 (77)		14 (39)		**<.001**
Patch (vs primary) closure during primary CEA	30/37	81.1	68/87	78.2	0.81
Side (right)	182/399	45.6	241/504	47.8	0.55
Symptomatic	189/479	39.5	193/653	29.6	**.001**
Degree of ipsilateral stenosis					**<.001**
50%–69%	30/459	6.5	86/589	14.6	
>70%	429/459	93.5	503/589	85.4	
Hypertension	400/479	83.5	504/573	88.0	**0.041**
Diabetes mellitus	147/479	30.7	175/570	30.7	1.0
Coronary artery disease	201/479	42.0	220/592	37.2	0.12
Renal failure	18/295	6.1	45/428	10.5	**0.044**
Hypercholesterolemia	170/209	81.3	209/341	61.3	0.067
Smoking (prior or current)	388/468	82.9	332/570	58.2	**<0.001**
Antiplatelet therapy	354/414	85.5	444/457	97.2	**<0.001**
Statin use	270/360	75.0	284/364	78.0	0.38
Contralateral occlusion	30/318	9.4	58/566	10.2	0.73

The bold values indicate statistical significance.
IQR indicates interquartile range.

TABLE 4. Perioperative Stroke and Death Rate of 13 Included Studies

	CEA, N (%)	95% CI	CAS, N (%)	95% CI
Alric et al[24]	NA	NA	0/15 (0)	0%–25%
Attigah et al[19]	2/28 (7.1)	0%–25%	0/41 (0)	0%–11%
Benitez et al*[25]	NA	NA	0/5 (0)	0%–54%
Bettendorf et al[18]	1/28 (3.6)	0%–20%	1/29 (3.4)	0%–20%
Domenig et al[15]	2/82 (2.4)	0%–9.4%	NA	NA
Dorigo et al[26]	0/37 (0)	0%–12%	0/58 (0)	0%–7.8%
Eskandari et al[27]	NA	NA	1/70 (1.4)	0%–8.7%
Fokkema et al[16]	7/212 (3.3)	1.5%–7.0%	7/220 (3.2)	1.4%–6.7%
Halabi et al[28]	NA	NA	2/72 (2.8)	0%–11%
Jain et al[29]	1/80 (1.2)	0%–7.8%	NA	NA
Kadkhodayan et al[30]	NA	NA	4/73 (5.5)	1.8%–14%
Radak et al[31]	0/12 (0)	0%–30%	NA	NA
Vos et al*[32]	NA	NA	0/70 (0)	0%–6.5%

All percentages are stroke and death rate adapted from individual patient data. All rates are 30-day postoperative event rate, unless indicated otherwise.
*7-day postoperative event rate.
NA indicates not applicable.

TABLE 5. Perioperative Outcome in All Patients Undergoing CEA or CAS

	CEA, N/Total	% (95% CI)	CAS, N /Total	% (95% CI)	Adjusted OR (95% CI)
Primary outcome					
Any stroke or death	13/479	2.7 (1.5–4.7)	15/653	2.3 (1.3–3.9)	0.8 (0.4–1.8)
Any stroke	12/479	2.5 (1.4–4.5)	13/653	2.0 (1.1–3.5)	0.8 (0.4–1.8)
Death	3/479	0.6 (0.2–2.0)	4/653	0.6 (0–1.2)	0.9 (0.2–4.4)
Myocardial infarction	7/400	1.8 (0.8–3.7)	8/653	1.2 (0.6–2.5)	0.7 (0.2–1.9)
Other complications					
Cranial nerve injury	26/474	5.5 (3.7–8.0)	1/126	0.8 (0–5.0)	NA*
Bleeding	13/474	2.7 (1.5–4.7)	1/72	1.4 (0–8.5)	NA*
Wound infections	1/462	0.2 (0–1.4)	NA	NA	NA
Technical failure	NA	NA	8/640	1.3 (0.6–2.6)	NA
Residual stenosis	NA	NA	2/640	0.3 (0–1.3)	NA
Access site complication	NA	NA	11/580	1.9 (1.0–3.5)	NA
Bradycardia/arrhythmia during procedure	NA	NA	6/441	1.4 (0.6–3.1)	NA

ORs for CAS compared to CEA are shown and are adjusted for a propensity score including age, gender, smoking, hypertension, degree of stenosis, symptom status, diabetes, and coronary artery disease.
*No statistical comparison done because of many missing cases in the CAS group.
NA indicates not applicable.

CNIs, information on reversibility was available for 23 patients. The majority of lesions were transient (N = 22), and 1 persistent CNI was reported.[29] One transient CNI occurred in the CAS group; however, this endpoint was only recorded in 2 studies.[26,27]

Sensitivity Analysis

Event rates of the included studies varied from 0% to 5.5% for CAS and 0% to 7.1% for CEA (Table 4). Sensitivity analysis was performed by excluding patients from the largest study.[16] In this subset analysis, a similar effect size and direction was identified for both primary and secondary endpoints compared with the entire cohort of 1132 patients (stroke or death, OR = 1.0, 95% CI: 0.3–3.1 and restenosis, HR = 1.1, 95% CI: 0.6–2.0). In addition, outcome in the 4 studies with both treatments were analyzed separately to differentiate treatment effect and study effects. This led to similar results (OR for primary endpoint = 0.65, 95% CI: 0.26–1.7).

DISCUSSION

This meta-analysis of individual patients data from 13 studies showed that in symptomatic and asymptomatic patients with restenosis after prior ipsilateral CEA, CAS was not superior to CEA regarding perioperative stroke and death rate and restenosis rate during follow-up. These results indicate that this criterion should not be used to preferentially treat restenosis with CAS. As a consequence, both CAS and CEA seem suitable options to treat restenosis after prior ipsilateral CEA. Although CEA may be counterbalanced by a 5.5% risk for CNI, CAS is limited by other complications such as access site complications and technical failure. Our results indicate that choice of treatment should probably be based on patient characteristics that may influence outcome after CAS or CEA, such as severe comorbidities, aortic arch anatomy, and poor anatomical accessibility such as excessive subcutaneous fat and/or a short neck. Unfortunately, these factors were not readily available in this IPD analysis, as was physician experience.

The criteria that determine "high-risk" for CEA have been a matter of debate for a long time.[13,38] It remains unclear whether these patients are considered at increased risk for stroke, death, or other periprocedural complications after CEA. Consequently, patients were excluded from the major carotid trials comparing CAS and CEA[39,40] and the optimal treatment for these patients remains a matter of debate.

We found that the durability of both procedures at follow-up was comparable, regardless of symptom status at baseline. However, the mean follow-up duration was only 13 months, and especially for the post-CAS situation increasing restenosis rates have been reported.[14] As a consequence, with longer follow-up duration, the restenosis rate after CAS might further increase whereas the restenosis rate after CEA may be more subtle. Furthermore, the 50% cutoff

point to determine restenosis after CAS is questionable. Stent stiffness and tortuosity in CAS patients may lead to higher velocity patterns and subsequent increased degree of reported stenosis.[41,42] Therefore, the rate of restenosis in CAS patients may be overestimated when compared with CEA patients. A prior study reported an increased incidence of restenosis greater than 50% in CAS compared with CEA, whereas this difference was absent when looking at restenosis greater than 80%.[21] In the current study, however, severe restenosis greater than 70% or 80% was not statistically analyzed, because most of the received IPD only reported on restenosis greater than 50%. Besides the possible apparent in-stent restenosis in CAS patients, patients were followed for a median of 13 months in this study, possibly indicating that some restenosis cases have represented residual stenosis, instead of new, recurrent stenotic lesions. In a clinical perspective, it is important to consider that restenosis is usually asymptomatic.[43]

Although an increased risk for CNI in patients undergoing redo-CEA has been reported previously,[10,21] our rate of 5.5% was very comparable to the risk of nerve injury in primary CEA (4.7%–8.6%).[12,44,45] A recent report on CNI did also not identify redo-CEA as a risk factor for CNI.[46] Other factors (such as urgency and reexploration) proved to be important predictors. Importantly, the CREST (Carotid Revascularization and Stenting Trial) found that CNI was not associated with a sustained impact on quality of life at 1 year.[47] This can be explained because most lesions seem to be transient and completely resolving (permanent rates $<1\%$).[47,48] We also found that the majority of lesions had a transient nature. However, it should be reaffirmed that permanent CNI can be a serious and invalidating complication limiting the benefit of carotid surgery in preventing stroke. The risk of CNI should be taken into account at all times when selecting optimal treatment for patients with restenosis after prior CEA.

The strength of this study is that we were able to adjust for various risk factors, which may have had a significant impact on treatment decisions and outcome after carotid intervention to prevent confounding by indication. Although in most comparative analyses CAS patients generally have increased risk factors compared with CEA patients,[13] in this study we found that comorbidities between CEA and CAS patients were quite similar. This was also indicated by the finding that adjustment for risk factors did not substantially change outcome and may be a possible explanation for the absence of differences between symptomatic and asymptomatic patients; the propensity score took into account multiple factors which seemed to be balanced between the groups. We were also able to perform stratified analyses for time elapse to restenosis. This is important, because early restenosis might follow a different pathophysiology pattern, possibly influencing outcome. Excellent results with CAS in early restenosis can be explained by a more stable plaque in restenotic lesions caused by intimal hyperplasia, compared with primary lesions or late restenosis with atherosclerotic plaque.[49,50]

LIMITATIONS

Although the response rate on our IPD data request was acceptable, we could not acquire data from all studies. This could potentially lead to selection bias, because results from acquired studies could report a more positive outcome than excluded studies. We cannot make inferences regarding the possible influence of excluded data, because analyzing aggregate data from these studies would be less reliable than IPD.[51] In a similar manner, publication bias and poor reporting could be an issue, as positive results are more likely to be published, leading to an underestimation of the "real" risks of treatment. This could have affected our study through an imbalance of the number of studies conducted on CEA and CAS groups. Also, secondary outcomes such as CNI can have a heterogenic character by differences in definitions across studies. For CNI, the rate is also influenced by method of assessment (eg, otolaryngeal examinations vs clinical assessment), which may influence outcome. Unfortunately, these aspects are inherent in meta-analyses. Another concern with IPD is that certain studies may have a greater impact on outcome than others. However, we addressed this issue by conducting a sensitivity analysis by excluding the largest study,[16] and results did not change. Finally, we could not completely adjust for confounding due to clustering of patients within studies so residual confounding may still be present. Ideally, in IPD meta-analysis, this is taken into account by analyzing the data using a random effects model. However, for a number of studies included in our analysis, all patients in the particular studies were treated with the same treatment modality. Consequently, our analysis could not differentiate between study effects (ie, differences between studies such as expertise) and the actual treatment effect.

Nonetheless, this seems the best available evidence to date given that a randomized controlled trial in this small group of patients, accompanied by low event rates after the intervention, would not be feasible in an achievable period of time.

CONCLUSIONS

In patients with restenosis after previous ipsilateral CEA, CAS does not seem to be superior to redo-CEA in terms of procedural stroke and death and prevention of short-term restenosis. This suggests that both CAS and CEA may be considered as a treatment modality in patients with an indication for intervention for recurrent stenosis, though the risk of CNI and other procedure-related complications should be taken into account.

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