Vascular anatomy predicts the risk of cerebral ischemia in patients randomized to carotid stenting versus endarterectomy

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Abstract

Background and Purpose: Complex vascular anatomy might increase the risk of procedural stroke during carotid artery stenting (CAS). Randomized-controlled-trial evidence that vascular anatomy should inform the choice between CAS and endarterectomy (CEA) has been lacking.

Methods: 184 patients with symptomatic carotid (ICA) stenosis were randomly assigned to CAS or CEA in the International Carotid Stenting Study and underwent baseline MR (n=126) or CT angiography (n=58), as well as brain MRI before and after treatment. We investigated the association between aortic arch type, angles of supra-aortic arteries, degree and length of stenosis and plaque ulceration with the presence of ≥1 new ischemic brain lesion on diffusion-weighted MRI (DWI+) after treatment.

Results: 49/97 patients in the CAS group (51%) and 14/87 in the CEA group (16%) were DWI+ (odds ratio [OR] 6.0, 95% CI 2.9-12.4, p<0.001). In the CAS group, aortic arch type 2/3 (OR 2.8, 95% CI 1.1-7.1, p=0.027) and the degree of the largest ICA angle (≥60°vs. <60°; OR 4.1, 95% CI 1.7-10.1, p=0.002) were both associated with DWI+, also after correction for age. No predictors for DWI+ were identified in the CEA group. The extra DWI+ risk in CAS increased further over CEA if the largest ICA angle was ≥60° (OR 11.8, 95% CI 4.1-34.1) than if it was <60° (OR 3.4, 95% CI 1.2-9.8, interaction p=0.035).

Conclusion: Complex anatomy of the aortic arch and ICA tortuosity increase the risk of cerebral ischemia during CAS, but not during CEA. Vascular anatomy should be taken into account when selecting patients for stenting.

List of abbreviations

CCA	Common Carotid Artery
CEA	Carotid endarterectomy
CI	Confidence interval
CTA	Computed Tomography Angiography
DSA	Digital subtraction angiography
DWI	Diffusion-weighted imaging
ECA	External carotid artery
EVA-3S	Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis
ICA	Internal carotid artery
ICC	Intra-class correlation coefficient
ICSS	International Carotid Stenting Trial
MRI	Magnetic Resonance Imaging
NASCET	North American Symptomatic Carotid Endarterectomy Trial
OR	Odds Ratio
TIA	Transient ischemic attack

Introduction

Atherosclerotic disease of the carotid artery is an important cause of stroke. The selection of patients to whom carotid artery stenting (CAS) can be offered as an alternative to carotid endarterectomy (CEA) has remained a controversial issue. In the International Carotid Stenting Study (ICSS), 1710 patients with symptomatic carotid stenosis greater than 50% were randomly allocated to CAS or CEA and followed for up to 10 years. An interim analysis in ICSS showed that CAS was associated with a higher risk of non-disabling, procedure-related stroke than CEA.[1] The long-term outcomes of ICSS showed that beyond the procedural period, CAS was as effective as CEA in preventing recurrent stroke.[2] Thus, the choice of the optimal treatment for an individual patient should be based on minimizing procedural risks. In patients with symptomatic carotid stenosis, the excess risk of procedural stroke in CAS versus CEA appears to be limited to patients above the age of 70,[3] yet the mechanisms behind this association remain unclear. Observational studies suggest that certain anatomical features of the aortic arch and supra-aortic vessels may increase procedural risk in CAS,[4-9] but also in CEA.[10] However, evidence from randomized trials whether vascular anatomy constitutes a risk factor for procedural stroke independently of age, and if so, whether it should inform the choice between CAS and CEA has been lacking.

In the magnetic resonance imaging (MRI) substudy of ICSS, about three times more patients had new ischemic brain lesions after CAS than after CEA.[11] In the present analysis of the ICSS-MRI substudy, we aimed to investigate the association between vascular anatomy observed on baseline contrast-enhanced MR or CT angiography and the risk of subsequent procedure-related cerebral ischemia in patients randomly assigned to CAS or CEA. We hypothesized that increased difficulty of vascular anatomy would pose patients at greater risk of cerebral ischemia during CAS than during CEA.

Methods

ICSS-MRI Substudy

In the ICSS-MRI substudy 231 patients (124 patients in the CAS group and 107 patients in the CEA group) were examined with brain MRI 1-7 days before intervention (pre-treatment scan) and 1-3 days thereafter (post-treatment scan). All imaging protocols included diffusion-weighted sequences (DWI) to detect ischemic brain lesions. MRI scans were evaluated by a neurologist and neuroradiologist, who were both blinded to treatment allocation and vascular anatomy.[11] The primary outcome measure of the ICSS-MRI substudy was procedural cerebral ischemia, defined as the presence of at least one new DWI lesion on the post-treatment MRI scan which had not been present on the pre-treatment scan. The study was approved by local ethics committees for non-UK centers and by the Northwest Multicentre Research Ethics Committee in the UK. Patients provided written informed consent to undergo MRI when the scans were not part of clinical routine.

In the present study we evaluated pre-defined anatomical parameters of the aortic arch and supra-aortic arteries along with the morphology of the atherosclerotic plaque in patients with available non-invasive contrast-enhanced MR (CE-MRA) or CT-based angiography (CTA) obtained at baseline, and assessed their impact on the risk of procedural cerebral ischemia.

Assessment of vascular anatomy and stenosis characteristics

The following anatomical parameters were defined prior to assessment and then evaluated on baseline CE-MRA or CTA in each patient by a single neurologist (MM) trained in the reading technique and blinded to the findings on post-treatment brain MRI. To test the reproducibility of her assessments, the scans of the first 40 patients were additionally assessed by a neuroradiologist (FA), and interrater reliability was determined.

Degree of stenosis in the internal carotid artery (ICA) considered for treatment and in the ipsilateral external carotid artery was calculated according to NASCET criteria,[12, 13] expressed as the percentage of narrowing of the lumen at the site of maximum stenosis compared to the diameter of the non-diseased ICA measured distal to the bulb, where the artery walls run parallel. Patients with near occlusion of the carotid artery were not eligible to participate in ICSS. Length of stenosis was defined as the distance between the proximal and the distal shoulder of the stenotic plaque. If the shoulders of the stenotic plaque were not clearly visible, the length of the stenosis was defined as the distance between the proximal and distal point where the vessel reached 80% of its original diameter.[10] The stenosis was considered ulcerated if it fulfilled the radiographic criteria of an ulcer niche, "seen in profile as a crater penetrating into a stenotic plaque".[14] Aortic arch configuration was classified using a modification of the original definition,[15] in line with previous studies:[9] type 1, if the supra-aortic arteries originated at the level of the outer curvature of the aortic arch; type 2, if the supra-aortic arteries originated between the levels of the outer and inner curvature; and type 3, if the supra-aortic arteries originated below the level of the inner curvature (**Figure 1**). Aortic arch anomalies, such as the left common carotid artery (CCA) originating from the brachiocephalic artery, were recorded.[9, 16]

The angle between the aortic arch and CCA (or brachiocephalic artery) was measured on the plane defined by the aortic arch by first, drawing a tangential line along the outer curvature of the aortic arch connecting the origin of the left subclavian artery and the brachiocephalic artery. Then the angle apex was positioned at the origin of the CCA or brachiocephalic artery, one angle leg was drawn parallel to the tangential line and the second one was placed in the center of the CCA or brachiocephalic artery (**Figure 2A**). Subsequently, choosing the projection on which the angle was most pronounced, each angle along the course of the brachiocephalic artery, between the brachiocephalic artery and the CCA (in case of carotid stenosis on the right or stenosis on the left and CCA originating the brachiocephalic artery), and along the CCA and extracranial ICA was recorded if greater than 30°. The angle between the CCA and ICA was always recorded. For measurement of each angle the apex was positioned at the turning point of the artery, and the angle legs in the center of the artery proximal and distal to the turning point (**Figure 2B**). Each angle was measured as the change in direction of the course of the artery by subtracting the angle between the two legs from 180°, as shown by an asterisk (*) in figure 2.

In addition, we calculated for each patient a previously published score of anatomic features which experts considered to increase procedural risk in CAS.[8] The score includes type of aortic arch, arch atheroma, presence of "bovine arch", i.e. origin of the left CCA from the brachiocephalic artery, CCA disease defined as >50% stenosis, pinhole stenosis (>90%), ECA stenosis >50%, CCA tortuosity defined as any vessel angulation >90° and ICA tortuosity defined as any vessel angulation > 60°.

Statistical Analysis

Inter-observer agreement of anatomical parameters between the two raters was assessed in 40 patients. For the continuous variables (degree of stenosis, length of stenosis, aortic/CCA angle, largest CCA angle, largest ICA angle) we used intra-class correlation coefficients (ICC), with values >0.75 indicating excellent, 0.40-0.75 fair to good, and < 0.40 poor reliability.[17] For categorical variables (type of aortic arch) we used Cohen's kappa, with values >0.81 indicating excellent, 0.61-0.80 substantial, and 0.41-0.60 moderate agreement.[18]

The association between the following anatomical parameters and occurrence of the primary outcome measure was investigated with binary logistic regression analysis in each treatment group separately: degree of stenosis, length of stenosis, plaque ulceration, angle between aortic arch and brachiocephalic artery or CCA, angle between the brachiocephalic artery and CCA (if applicable), largest angle in the CCA, CCA/ICA angle, largest angle in the ICA and type of aortic arch. Continuous variables (degree and length of stenosis, angles and expert score of anatomic suitability) were dichotomized at the population median. All analyses were adjusted for the time interval between treatment and the post treatment MRI, which was previously shown to be longer in the CEA group than in the CAS group.[11] Analyses were additionally adjusted for age, which is the strongest known clinical predictor for procedural stroke or death associated with CAS and may itself be associated with complex vascular anatomy. In addition, we tested whether anatomical parameters which were significantly associated with the primary outcome measure in one treatment group also modified the odds ratio of the primary outcome measure between CAS and CEA, by formal testing of statistical interaction. Statistical analysis was performed using SPSS version 22.0, IBM Corp (Chicago, IL, USA).

Results

Patient and intervention characteristics

Baseline CE-MRA (n= 126) or CTA (n=58) was available in 184 of the 231 patients (80%) included in the ICSS-MRI substudy. Of those 184 patients, 97 were assigned to CAS and 87 to CEA (**Figure 3**). Baseline and intervention characteristics were well balanced between groups and there were no substantial differences in anatomical characteristics (**Table 1**).

Interrater reliability of anatomical assessment

Testing of interrater reliability of the anatomical assessments in the first 40 patients showed excellent agreement between the two readers for degree of stenosis (ICC=0.951), length of stenosis (ICC=0.886), aortic/CCA angle (ICC=0.948), largest CCA angle (ICC=0.968), CCA/ICA angle (ICC=0.887) and largest ICA angle (ICC=0.944; p<0.001), as well as substantial agreement for aortic arch type (0.724; 95% CI 0.535 -0.912; p<0.001).

Anatomical predictors of cerebral ischemia

Procedural cerebral ischemia was found in 49 patients in the CAS group (51%) and 14 patients in the CEA group (16%; OR 6.0, 95% CI 2.9-12.4, p<0.001). In 6 of the 49 patients in the CAS group and in 2 of the 14 patients in the CEA group, the new DWI lesions on the post-treatment scan were associated with symptoms of an ischemic hemispheric stroke occurring between initiation of treatment and the post-treatment scan. DWI lesions in the remaining patients were silent, as these patients did not experience focal neurological events up to the time of their post-treatment scan. [11]

In the CAS group, aortic arch type 2 or 3 as opposed to type 1 (OR 2.8, 95% CI 1.1-7.1, p=0.027), as well as the largest angle along the course of the ICA separated at the population median (≥60° vs. <60°; OR 4.1, 95% CI 1.7-10.1, p=0.002) were associated with cerebral ischemia (**Figure 4**). Both associations remained significant after correction for age (OR 2.9, 95% CI 1.1-7.7, p=0.032; and OR 3.4, 95% CI 1.4-8.9, p=0.01; respectively). To account for the duration of the stenting procedure as a possible confounder, we additionally corrected both associations for the duration of the stenting procedure (OR 2.93, 95% CI 1.06-8.1, p=0.038 for ICA angle; and OR 2.59, 95% CI 0.89-7.49, p=0.079 for aortic arch type, respectively). None of the other anatomical variables or stenosis characteristics (degree and length of ipsilateral stenosis, plaque ulceration, ECA stenosis) measured at baseline predicted the occurrence of cerebral ischemia. In addition, patients with a higher score of anatomic difficulty[8] were at increased risk for cerebral ischemia (OR 3.2, 95% CI 1.3-7.9, p=0.014, values separated at the population median 4.3), but no longer so after correction for age (OR 2.16, 95% CI 0.8-5.7, p=0.123).

In the CEA group, none of the assessed parameters for vascular anatomy or stenosis characteristics (nor the score for anatomic difficulty) were associated with procedural cerebral ischemia.

We performed a sensitivity analysis excluding patients without available arch angiography from all analyses: Among 89 remaining patients in the CAS group, the association between cerebral ischemia and largest ICA angle ≥60° remained statistically significant (OR 3.2, 95% CI 1.2-8.5, p=0.023). In the remaining 76 patients in the CEA group, we again found no significant associations.

The interaction between the largest ICA angle and the effect of treatment (CAS versus CEA) on the occurrence of cerebral ischemia was statistically significant: The extra risk of DWI lesions in CAS increased further over CEA if the largest ICA angle was ≥60° (OR 11.8, 95% CI 4.1-34.1) than if it was <60° (OR 3.4, 95% CI 1.2-9.8, interaction p=0.035). The interactions between treatment effect and aortic arch type or anatomic suitability score were not significant (**Figure 5**).

Discussion

In this randomized study of patients with symptomatic carotid stenosis, difficult anatomy of the aortic arch as well as tortuosity of the ICA were found to increase the risk of procedural cerebral ischemia detected on MRI in patients treated with stenting, but not in patients treated with endarterectomy.

In most previous studies investigating the association between anatomical risk factors and procedure-related stroke in CAS, vascular anatomy was assessed on digital subtraction angiography (DSA) performed as part of the CAS procedure. Data on the importance of vascular anatomy in CEA have been much more limited, and to date, no study has compared the impact of vascular anatomy on procedural risks between CAS and CEA. Nowadays, DSA is rarely performed for diagnostic workup of carotid stenosis. In our study we assessed baseline non-invasive carotid imaging (CE-MRA and CTA) obtained at the time of random assignment to CAS or CEA, before treatment was initiated. These tests are commonly available and used in routine diagnostic work-up of patients with carotid disease. Hence, our findings seem more relevant to inform the choice between CAS and CEA in routine practice than the results of studies based on pre-procedural DSA.

Several authors have previously postulated that difficult anatomy of the aortic arch and vessel tortuosity are associated with a higher risk of adverse events following CAS.[5-8, 11, 16] Faggioli et al. reported a statistically significant association between type of aortic arch as well as aortic arch anomalies, such as origin of the left CCA from the brachiocephalic artery, also referred to as "bovine arch", and the incidence of neurological complications in patients undergoing CAS.[16] In our study, we were able to confirm an increased incidence of cerebral ischemia on the post-treatment scan after CAS in patients with type 2 or 3 aortic arch. The aortic arch variant where the left CCA originated from the brachiocephalic artery was present in 11% of our study population, which is within the frequency range reported in the literature, and showed no association with the occurrence of new lesions on MRI after treatment, possibly due to a lack of power.

With regard to tortuosity of the supra-aortic arteries, the investigators of the Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) reported a higher risk of stroke or death within 30 days of CAS in patients with ICA-CCA angulation ≥60° on pre-procedural angiography.[7] Other authors described a significant association between tortuosity of the CCA and proximal ICA and the occurrence of complications in CAS, but found no increase in adverse events in patients with tortuous ICA distal to the stenosis.[6] We were able to confirm that patients undergoing CAS were at greater risk of procedural cerebral ischemia if the largest measured ICA angle was ≥60° (the population median) than if it was <60°. Moreover, our results suggest that angulation along the course of the ICA is a more important anatomical risk factor for CAS than tortuosity in the more proximal access vasculature. Catheterization of the aortic arch and the supra-aortic vessels using femoral access (which was the standard access route in ICSS) may cause endothelial micro-trauma and dislodge atherosclerotic plaque debris, especially in patients with unfavorable anatomy. CAS using trans-cervical access might avoid this problem.[19]

A scoring system derived from expert opinion has been developed to grade the difficulty of vascular anatomy (and hence to judge the suitability of the patient) for CAS.[8] Our results suggest that this system might indeed be able to predict the occurrence of ischemic brain lesions after CAS, although perhaps not independently of age.

We found no significant association between supra-aortic vascular anatomy or stenosis characteristics and procedural cerebral ischemia in the surgery group. There was a strong non-significant trend, that patients with aortic arch type 2 or 3 had a higher risk of cerebral ischemia. In lack of a plausible biological explanation for this association, we cannot rule out that this trend was caused by chance. Problems in CAS related to navigating difficult vascular anatomy do not apply to endarterectomy where the atherosclerotic lesion can be directly accessed. Thus, the lack of an increased surgical risk in patients with difficult vascular anatomy seems plausible.

Owing to the randomized allocation of treatment in our study and unlike in previous research, we were able to investigate whether a given anatomical risk predictor in one treatment group would also modify the relative risk of cerebral ischemia between the two procedures, by formal testing for statistical interaction. The extra risk of DWI lesions associated with CAS increased further over CEA if the largest measured ICA angle was ≥60° than if it was <60°. ICA tortuosity therefore appears to be a feature which should specifically be taken into account when deciding between CAS and CEA.

We have previously shown in a smaller subset of the ICSS-MRI substudy that characteristics of the carotid plaque evaluated by pre-procedural catheter angiography (degree and length of ipsilateral stenosis and plaque ulceration) did not predict the occurrence of new DWI lesions after CAS,[20] and our present study using non-invasive CE-MRA and CTA confirms this. Ulceration has been established as an indicator of unstable plaque and therefore of increased risk for cerebral ischemia under conservative therapy.[21] In contrast with our findings, several studies with DSA showed that the presence of an ulcerated plaque also increases the likelihood of the occurrence of DWI lesions after stenting.[22-24] In addition, lesion length has been found to constitute a risk factor for adverse events in CAS,[10, 22-24] but also in CEA.[10] These discrepant findings might be explained by the fact that CE-MRA and CTA are inferior to DSA in accurately depicting plaque ulceration and lesion length.

In a meta-analysis of individual patient data from several randomized controlled trials, patients 70 years or older had almost double the risk of procedural stroke or death than younger patients when undergoing CAS, while no such association was found for CEA.[3] It has been speculated whether the association between age and procedural stroke risk in stenting might be mediated by vascular anatomy. Elongation of the aortic arch and supra-aortic arteries were found to be more prevalent in elderly patients,[5, 9] possibly leading to more difficulties during the CAS procedure. Notably in our analysis, the associations between ICA angulation and aortic arch type 2 or 3 with cerebral ischemia in the stenting group remained significant after correction for age. Hence, vascular anatomy should be taken into account when selecting the appropriate treatment option for an individual patient, independent of their age.

This analysis has several limitations. The fact that the ICSS protocol excluded patients with a stenosis that was thought to be unsuitable for stenting because of proximal tortuous anatomy is likely to have limited the number of patients with very unfavorable anatomy. The full impact of vascular anatomy on CAS risk may therefore have been underestimated. Secondly, although allocation of treatment was randomized, only seven out of 50 study sites participated in the ICSS-MRI substudy, and not all patients enrolled in ICSS at these sites completed the substudy for various reasons, as previously reported.[11] Analyzing a subset of a clinical trial implies a number of potential risks: although baseline characteristics of patients in the present study were comparable to the main trial and similar between treatment groups, populations may still differ in characteristics not measured in the trial, due to selection bias. Thirdly, our study was too small to rule out a true effect of vascular anatomy or stenosis characteristics on the risk of cerebral ischemia in patients undergoing CEA. It may also have been underpowered to detect an association between a common origin of the brachiocephalic artery and the left CCA and risk of cerebral ischemia in the stenting group, contrasting with the findings of a larger study.[16] Limited power also meant that the observed trends and associations must be interpreted with caution: it seems likely that the trend for an association between aortic arch type and risk of cerebral ischemia might be the result of chance. Nonetheless, we believe that the observed associations between vascular anatomy and cerebral ischemia in the stenting group are valid, as they confirm the findings of previous, non-randomized studies. Furthermore, technical advances in stent design and cerebral protection devices have likely lowered the risk of thromboembolic complications in CAS since the time of recruitment in ICSS. Protection devices were only used in a minority of patients and they were mostly of the distal filter type. A previous analysis of the ICSS-MRI data showed that, contrary to their intended purpose, the use of distal protection devices was associated with an increased risk of DWI lesions.[11] Finally, the protocol did not prescribe other technical aspects of CAS such as limiting guidewire maneuver time between flushing, syringe aspiration and cleansing, concentration of heparin in saline flush, use of constant infusion via infusion ports to stopcocks, etc. Procedural safety may have been optimised in the trial by a more rigorous technical stenting protocol and strict monitoring of centres' adherence to such a protocol. Indeed, we cannot rule out the possibility that the observed associations between vascular anatomical characteristics and occurrence of cerebral lesions may no longer have been significant if the overall rate of thromboembolic complications would have been substantially lower.

Conclusion

In this MRI substudy of a randomized trial we have shown that ICA tortuosity and difficult aortic arch anatomy both increase the risk of cerebral ischemia during stenting independent of patient age, but not during endarterectomy. These results support the hypothesis that vascular anatomy should be taken into account before selecting patients for stenting, irrespective of their age.

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Bayer and Boehringer Ingelheim and on the editorial board of Stroke. LHB has served on scientific advisory boards for Bayer. The other authors have no conflicts of interest.

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Figure legends

Figure 1 - Classification of aortic arch type according to the origin of the supra-aortic arteries on contrast-enhanced magnetic resonance angiography*. The two horizontal lines mark the levels of the outer and inner curvature of the aortic arch. The figure illustrates a type 2 aortic arch.*

Figure 2 – Measurement of vessel angles on contrast-enhanced magnetic resonance angiography.

2A. *Assessment of the angle between aortic arch and left CCA: first, a parallel line to the upper curvature of the aortic arch is drawn by connecting the origin of the brachiocephalic artery and the left subclavian artery. Then, one angle leg is positioned parallel to the tangent and the other in the center of the left CCA respecting its distal course.* ***2B.*** *Assessment of angles in the course of the ICA: the angle apex is positioned at the turning point of the vessel and the legs at the center of the ICA respecting its distal and proximal course. Angles were measured as the change in direction of the course of the artery by subtracting the angle between the two legs from 180°, as shown by an asterisk (*) in figure 2.*

Figure 3 - Study flow diagram *- Diagram depicting the two treatment arms of the study, including events that precluded patients from analysis. Scans are magnetic resonance imaging (MRI). BMT = best medical treatment; CAS = carotid artery stenting; CEA = carotid endarterectomy; DWI = diffusion weighted imaging; MI = myocardial infarction*

Figure 4 – Risk factor analysis *- Impact of vascular anatomy on the risk of new DWI lesions after carotid artery stenting (CAS) and carotid endarterectomy (CEA). Data are numbers of*

patients with new DWI lesions on post-treatment MRI scans (n) and total numbers of patients (N) per group. Circles and horizontal lines are odds ratios (OR) and 95% confidence intervals (CI) for presence of new DWI lesions in patients with versus without each risk factor, adjusted for interval between treatment and post-treatment scan and age. Continuous variables (degree and length of stenosis, angles and expert score for anatomic suitability) were separated at the median values of the study population. Missing data: In the CAS group the aortic arch was not visible in 8 patients; in the CEA group the aortic arch was not visible in 11 patients. CCA = common carotid artery; ICA = internal carotid artery.

Figure 5 – Subgroup analysis. *Data are numbers of patients with new DWI lesions on post-treatment scans (n) and total numbers of patients (N) per treatment group. Circles and horizontal lines are odds ratios (OR) and 95% confidence intervals (CI) for presence of new DWI lesions in patients treated with carotid artery stenting (CAS) versus carotid endarterectomy (CEA), adjusted for interval between treatment and post-treatment scan. Continuous variables were separated at the median values of the study population. Interaction p-values are shown. Missing data: In the CAS group the aortic arch was not visible in 8 patients; in the CEA group the aortic arch was not visible in 11 patients. ICA = internal carotid artery.*

Tables

Table 1- Patient and intervention characteristics

	CAS (n=97)	CEA (n=87)
Age (years) *median (IQR)*	70.45 (14.4)	71.65 (13.8)
Male *n (%)*	65 (67%)	65 (74.7%)
Vascular risk factors *n (%)*		
Hypertension	67 (69.1%)	63 (72.4%)
Diabetes	18 (18.6%)	19 (21.8%)
Hyperlipidemia	56 (57.7%)	55 (63.2%)
Smoking	73 (75.3%)	65 (74.7%)
Peripheral artery disease	17 (17.5%)	12 (13.8%)
Coronary heart disease	24 (24.7%)	20 (23.0%)
Qualifying event type *n (%)*		
Retinal or TIA	56 (57.7%)	52 (59.7%)
Hemispheric stroke	41 (42.3%)	35 (40.2%)
Contralateral severe stenosis or occlusion *n (%)*	20 (20.6%)	16 (18.4%)
Delay to treatment (days) *median (IQR)*	30 (63)	40 (52)
Anatomical risk factors		
Left sided stenosis *n (%)*	47 (48.5%)	38 (43.7%)
Type of aortic arch		
Aortic arch type 1 *n (%)*	37 (38.1%)	28 (32.2%)
Aortic arch type 2 or 3 *n (%)*	52 (53.6%)	48 (55.2%)
Left CCA originating from the brachiocephalic artery *n (%)*	11 (11.3%)	10 (11.5%)
Aortic arch not visible *n (%)*	8 (8.2%)	11 (12.6%)
Largest CCA angle *median (IQR)*	48 (45)	52.5 (35)
Angle CCA-ICA *median (IQR)*	24 (22)	27 (21)
Largest ICA angle *median (IQR)*	57 (32)	66 (47)
Degree of stenosis *median (IQR)*	72.13 (20)	75.0 (23)
Length of stenosis *median (IQR)*	6.3 (6)	6.0 (4)

Plaque ulceration *n (%)*	16 (16.5%)	19 (21.8%)
Expert score of anatomic suitability *median (IQR)*	4.0 (2.2)	4.3 (2.2)
Cerebral protection device		
Cerebral protection device used *n (%)*	31 (36%)	-
No cerebral protection device used *n (%)*	55 (64%)	-
Stent design		
Open cell *n (%)*	53 (61.6%)	-
Closed cell *n (%)*	33 (38.4%)	-
Type of anesthesia		
General anesthesia *n (%)*	-	71 (81.6%)
Local anesthesia *n (%)*	-	10 (11.5%)
Patch		
Patch used *n (%)*	-	49 (56.3%)
No patch used *n (%)*	-	19 (21.8%)
Shunt		
Shunt used *n (%)*	-	11 (12.6%)
No Shunt used *n (%)*	-	76 (87.4%)

Baseline data of patients in the stenting and endarterectomy group as well as details of stenting and endarterectomy procedure. Percentages exclude missing data; missing data were: Carotid artery stenting (CAS) group: n=11 patients no interventional details known; carotid endarterectomy (CEA) group: n= 6 patients no information on type of anesthesia available, n=19 patients no information on patch use available. IQR = interquartile range; TIA = transient ischemic attack; CCA = common carotid artery; ICA = internal carotid artery.