Neuroradiology (2020) 62:1177–1184
https://doi.org/10.1007/s00234-020-02447-3

INTERVENTIONAL NEURORADIOLOGY

Risk factors for silent new ischemic cerebral lesions following carotid artery stenting

Xiaoyu Xu[1,2] · Yao Feng[1] · Xuesong Bai[1] · Yan Ma[1] · Yabing Wang[1] · Yanfei Chen[1] · Bin Yang[1] · Feng Ling[1] · Xiaoman Zhang[2] · Liqun Jiao[1]

Received: 10 December 2019 / Accepted: 22 April 2020 / Published online: 4 May 2020

Abstract

Purpose Silent new ischemic cerebral lesions (sNICL) detected by diffusion-weighted imaging (DWI) are common after carotid artery stenting (CAS). As part of the Revascularization of Extracranial Carotid Artery Stenosis (RECAS) study, this work aimed to determine predictors of sNICL detected by DWI following CAS.

Methods A total of 694 patients eligible for the RECAS study treated in Xuanwu Hospital, Capital Medical University, with complete imaging data were included in this retrospective study. The patients were asymptomatic after CAS, and those with stroke, transient ischemic attack (TIA), or death were excluded. The RECAS protocol specified that DWI was completed 1–7 days before the procedure and within 3 days after CAS. Several parameters were assessed for associations with sNICL occurrence after CAS in univariate analysis. Finally, multivariate analysis was performed to determine risk factors for sNICL.

Results The rate of post-procedural sNICL in CAS was 51.3% (356/694 patients with sNICL). All patients underwent stenting with embolic protection devices. Univariate analysis showed that diabetes mellitus ($P = 0.008$), ipsilateral calcified plaques ($P = 0.036$), ipsilateral ulcerated plaques ($P = 0.026$), pre-dilatation ($P = 0.003$), and open-cell stent use ($P < 0.001$) were significantly associated with sNICL occurrence in CAS. Multivariate analysis revealed that diabetes mellitus ($P = 0.006$), ipsilateral calcified plaques ($P = 0.024$), ipsilateral ulcerated plaques ($P = 0.021$), and open-cell stent use ($P < 0.001$) were independent risk factors for sNICL.

Conclusions Patients with diabetes, calcified or ulcerated plaques who undergo CAS with open-cell stent application, are at high risk of sNICL. Large-scale prospective randomized controlled trials are needed to confirm these findings.

Keywords Carotid artery stenosis · Silent new ischemic cerebral lesions · DWI · Risk factors

Introduction

Carotid artery stenting (CAS) has gradually become an alternative to carotid endarterectomy (CEA) for the treatment of carotid artery stenosis [1]. With the development of interventional devices and advances in minimally invasive surgery [2], patients with carotid artery stenosis are increasingly willing to undergo CAS. Diffusion-weighted imaging (DWI) may represent a surrogate tool for optimizing diagnostic and therapeutic vascular procedures [3]. Indeed, DWI could be performed to easily detect post-CAS cerebral emboli, which are asymptomatic and termed silent new ischemic cerebral lesions (sNICL) [4].

Embolization from plaque fragment mobilization is a common complication of endovascular procedures [5], and recent reports indicate sNICL rates ranging from 18 to 57% [6–10]. Even without a corresponding focal deficit, sNICL might lead to clinical consequences in the long term, including cognitive decline and dementia [11]. In addition, NICL could lead to an elevated risk of future stroke events [12].

Hence, evaluating risk factors associated with post-CAS sNICL has recently attracted increasing attention, but findings by various reports were limited and inconsistent [6, 7, 13]. Meanwhile, identifying potential risk factors for new cerebral

Xiaoyu Xu and Yao Feng contributed equally to this work.

✉ Liqun Jiao
liqunjiao@126.com

[1] Interventional Radiology Diagnosis and Treatment Center, Department of Neurosurgery, Xuanwu Hospital, Capital Medical University, Beijing, China

[2] Department of Neurology, 1st People's Hospital of Zhengzhou, Zhengzhou, China

lesions is essential in clinical practice. Therefore, the present work aimed to determine risk factors for sNICL detected by DWI following CAS. The associations of clinical and morphological variables with the occurrence of sNICL detected by DWI after CAS were assessed.

Materials and methods

Study design and patients

The present study retrospectively enrolled patients eligible for Revascularization of Extracranial Carotid Artery Stenosis (RECAS) study, which was a multicenter, prospective cohort study involving both CAS and CEA in Chinese patients with extracranial carotid artery stenosis. The RECAS study enrolled patients from 36 centers in China between December 2013 and February 2016. For the RECAS study, inclusion criteria were (1) age ≥ 18 years old and (2) symptomatic internal carotid artery (ICA) stenosis ≥ 50% or asymptomatic ICA stenosis ≥ 70% by computed tomography angiography (CTA) or digital subtraction angiography (DSA). Exclusion criteria were (1) stenosis combined with intracranial arteriovenous malformation or aneurysm; (2) severe stenosis or occlusion of the ipsilateral intracranial artery; (3) unstable angina, myocardial infarction (MI), or congestive heart failure within the previous 6 months; (4) uncontrolled diabetes mellitus (DM) defined as glucose > 300 mg/dL; (5) uncorrectable coagulation abnormalities; (6) pregnancy or being in the perinatal period for women; (7) severe concomitant disease with poor prognosis (life expectancy < 2 years); or (8) intolerance or allergies to any of the study medications, including aspirin and clopidogrel. Data of patients in our Hospital were extracted to perform the present single-center retrospective analysis. Patients without post-procedural symptomatic stroke were included, and those without pre-procedural or post-procedural DWI for any reason were excluded.

Carotid stenosis measurement was performed according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) [14], stenosis of 70–99% was defined as severe, and that of 50–70% as moderate. Patients with transient ischemic attack, retinal ischemic event, or ischemic stroke resulting from the narrowed carotid artery within the previous 6 months were considered to be recently symptomatic [15]. The degree of stenosis was morphologically evaluated by CTA of the supra-aortic trunks, agreeing with Doppler ultrasound examination results.

The RECAS study, registered on clinicaltrials.gov (NCT01994187), was approved by the ethics committees of all participating centers and performed according to the Declaration of Helsinki.

Preoperative data

The clinical variables evaluated included demographic data, stroke history, and cardiovascular risk factors such as atrial fibrillation (AF), hypertension, and DM. Stenosis characteristics, arch type, target carotid artery, and stenting procedure were also analyzed as potential risk factors for sNICL.

A neurological examination was performed the day before CAS. Neurological status recorded over the last 6 months before stenting was analyzed. The degree of artery stenosis and plaque characteristics in the ipsilateral and contralateral carotids, as well as vertebral arteries, were evaluated by preoperative ultrasound and/or CTA. Both common carotid arteries (CCA) and the carotid bifurcation were also assessed. All images were evaluated by qualified technicians blinded to clinical data. Plaques were classified as calcified, ulcerated, or other. Target carotid lesions were evaluated by diagnostic DSA during the stenting procedure. All angiograms were evaluated by qualified interventional technicians and neuroradiologists blinded to clinical data.

Stenting procedure

Patients received aspirin (100 mg/day) and clopidogrel (75 mg/day) for at least 3 days preoperatively. Heparin (1 mg/kg) was administered at the beginning of the intervention to maintain an activated clotting time at approximately twice the base value. After the procedure, the patients had both aspirin (100 mg/day) and clopidogrel (75 mg/day) as daily maintenance medications for 3 months. Those who could not tolerate aspirin or clopidogrel for any reason received cilostazol 0.1 g BID instead. Femoral access with an 8-French introducer and catheter was achieved under local anesthesia to introduce a guidewire up to the origin of the external carotid artery (ECA) in all patients. Carotid and cerebral angiography was subsequently performed to confirm the level and the degree of arterial stenosis. All stenting procedures were performed by surgeons highly experienced in angiographic procedures. Embolic protection devices (EPDs) were used in all patients. Pre-dilatation, if necessary, was performed after EPD placement. Above work was followed by stent deployment. Stent size was based on the estimated diameters of the CCA and ICA. In case of insufficient stent expansion, post-dilatation was performed. Atropine sulfate (0.5 mg) was administered intravenously during angioplasty balloon insufflation to prevent carotid sinus stimulation and bradycardia. The choice of catheters and guidewires was at the discretion of the surgeon. The stenting protocol in this study was similar to that reported previously [16].

DWI

The first magnetic resonance imaging (MRI) was performed before stenting to assess the pre-procedure condition and establish baseline information. The second MRI was performed within 3 days after stenting to assess post-procedural new ischemic cerebral lesions and at any time thereafter in case of neurological deterioration. The protocol included isotropic DWI sequences. MRI was performed on a 3.0T system (MAGNETOM Verio, Siemens Healthcare, Erlangen, Germany). The following brain MR sequences were applied, assessing apparent diffusion coefficients: axial plane T1-weighted spin-echo (TR = 135, TE = 2.55, slice thickness = 5 mm, and interslice gap = 1.2 mm); FLAIR (TR = 8800, TE = 84, TI = 8800, slice thickness = 5.0 mm, and interslice gap = 1.2 mm); and DWI (TR = 5500, TE = 90, *b* value = 1000, slice thickness = 5 mm, and interslice gap = 1.2 mm). The occurrence of new high-signal DWI lesions within any brain territory after stenting with corresponding low apparent diffusion coefficient indicated the existence of a new ischemic cerebral lesion [17]. MR images were evaluated by experienced neuroradiologists blinded to clinical data, angiograms, and ultrasound results.

Statistical analysis

Continuous data were given as mean ± standard deviation (SD). Categorical variables were presented as numbers and percentages. Differences between patients with and those without DWI lesions were analyzed by the chi-square test. Proportions were tested by the chi-square test or Fisher's exact test. To determine the univariate associations of lesion occurrence with potential risk factors, odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Multiple binary logistic regression using the backward and forward variable selection procedures was employed to determine risk factors for sNICL. Two-tailed $P < 0.05$ was considered statistically significant. Data were analyzed with SPSS 23.0 (IBM, NY, USA).

Results

Patient baseline characteristics

A total of 894 consecutive patients eligible for the RECAS study were initially enrolled. Of those, 19 patients with post-procedural complications, and 181 patients lacked DWI images were excluded. A total of 694 asymptomatic patients with complete imaging data were finally included in this study (Fig. 1). The patients were 66.03 ± 8.03 years old, and 83.3% of them were men. Symptomatic lesions before CAS accounted for 45.5%. Detailed patient characteristics are shown in Table 1.

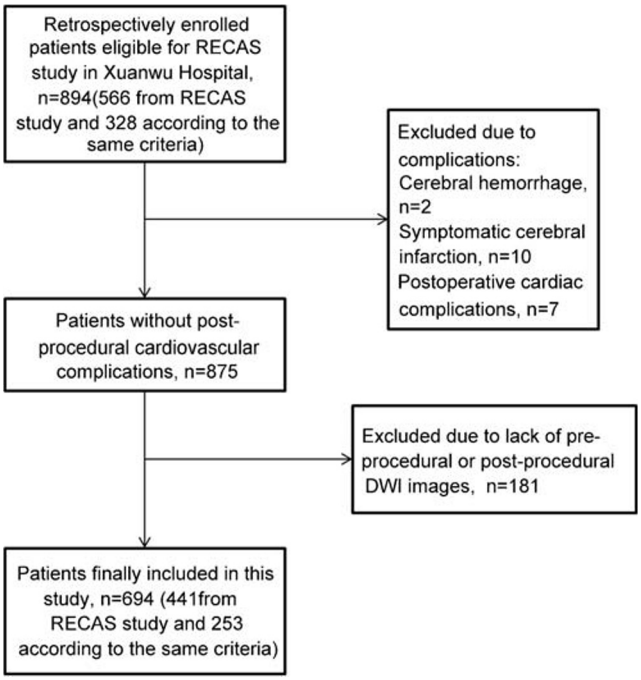

Fig. 1 Flowchart of the study population

Postoperative analysis

Stent placement and balloon angioplasty were successfully performed in all cases. Fifty-seven patients (8.2%) had unfavorable arch anatomy, which was defined as a type III or bovine arch. Meanwhile, 352 patients (50.7%) had right CAS, and the remaining 342 cases (49.3%) showed left CAS. A total of 414 patients (59.7%) were treated with open-cell stents. In this study, 524 (75.5%) and 203 (29.3%) patients had pre-dilatation and post-dilatation, respectively, with 79 of them having both pre-dilatation and post-dilatation.

We performed stenting without dilatation in 46 patients (6.6%); the stent delivery device had no difficulty in passing through the stenotic lesion, so there was no pre-dilatation; the stent was implanted satisfactorily, and the residual stenosis was < 30%, and post-dilatation was deemed unnecessary. At the end of the procedure, all patients had successful stenting, with ≤ 30% residual carotid stenosis on angiography (NASCET criteria). Postoperative DWI detected sNICL in 356 patients without persistent clinical deterioration, including 95 (26.7%) mono-infarct and 261 (73.3%) multiple infarct cases. Among these patients, 150 (42.1%) had lesions ipsilateral to the treated artery, 56 (15.8%) showed contralateral lesions, and 150 (42.1%) had ipsilateral and contralateral lesions. DWI lesions were mainly located in anterior vascular territories (54.8%). New infarcts were found in both anterior

Table 1 Patient demographics and stenosis characteristics

Characteristics	$N = 694$
Age, years	66.03 ± 8.03
≥ 70 years	222 (32.0)
Sex, male	578 (83.3)
Cardiovascular risk factors	
Smoking	381 (54.9)
Diabetes mellitus	267 (38.5)
Hypertension	505 (72.8)
Hypercholesterolemia	93 (13.4)
Coronary heart disease	129 (18.6)
Drinking (> 3 alcoholic drinks/day)	238 (34.3)
Previous stroke	254 (36.6)
Degree of carotid stenosis	
Moderate	22 (3.2)
Severe	672 (96.8)
Location of stenosis	
CCA	19 (2.7)
Carotid bulb	497 (71.6)
ICA	178 (25.6)
Contralateral severe stenosis	143 (20.6)
VA or BA severe stenosis	244 (35.2)
Type of plaque	
Calcified	91 (13.1)
Ulcerated	67 (9.7)
Not calcified, not ulcerated	536 (77.2)
Symptomatic stenosis	316 (45.5)

Data are numbers (percentages in parentheses)

CCA, common carotid artery; *ICA*, internal carotid artery; *VA*, vertebral artery; *BA*, basilar artery

Table 2 Surgical data and distribution of the new lesions

Characteristics	$N = 694$
Unfavorable arch anatomy	57 (8.2)
Operation side	
Left	342 (49.3)
Right	352 (50.7)
Open-stent	414 (59.7)
Stent type	
Acculink (open cell)	180 (25.9)
Invatec (open cell)	16 (2.3)
Precise (open cell)	183 (26.4)
Protege (open cell)	32 (4.6)
Wallstent (closed cell)	280 (40.3)
Express (open cell)	3 (0.4)
Balloon dilatation	
Pre-dilatation	524 (75.5)
Post-dilatation	203 (29.3)
Both pre-dilatation and post-dilatation	79 (11.4)
Without dilatation	46 (6.6)
Degree of residual carotid stenosis	
≤ 10%	365 (52.6)
10–20%	262 (37.8)
20–30%	67 (9.7)
Number of DWI+ patients	356 (51.3)
Mono	95 (26.7)
Multiple	261 (73.3)
Lesion localization	
Ipsilateral	150 (42.1)
Contralateral	56 (15.8)
Bi-lateral	150 (42.1)
Vascular territories	
Anterior	195 (54.8)
Posterior	39 (10.9)
Both	122 (34.3)
Brain structure	
Cortex	177 (49.7)
Subcortex	93 (26.1)
Watershed	16 (4.5)
Multiple sites	70 (19.7)

Data are numbers (percentages in parentheses). *DWI*, diffusion-weighted imaging

and posterior vascular territories in 122 patients (34.3%). A total of 19.7% of the patients had some scattered infarcts involving multiple sites, and 16 patients (4.5%) showed infarcts distributed mainly in the watershed districts (Table 2).

Univariate analysis

Univariate analysis identified significant factors associated with sNICL occurrence, including DM ($P = 0.008$), ipsilateral calcified plaques ($P = 0.036$), ipsilateral ulcerated plaques ($P = 0.026$), pre-dilatation ($P = 0.003$), and open-cell stent use ($P < 0.001$) (Table 3).

Multivariate analysis

Of the parameters significantly associated with sNICL occurrence in univariate analysis, multivariate analysis revealed four risk factors for sNICL, including DM (OR = 1.579, 95%CI 1.142–2.184; $P = 0.006$), ipsilateral calcified plaques (OR = 1.726, 95%CI 1.073–2.775; $P = 0.024$), ipsilateral ulcerated plaques (OR = 1.912, 95%CI 1.102–3.316; $P = 0.021$), and open-cell stent use (OR = 3.316, 95%CI 2.321–4.738; $P < 0.001$). In multivariate analysis, pre-dilatation was not a significant risk factor for sNICL (Table 4).

Table 3 Associations of demographic parameters with the occurrence of new ischemic brain lesions, assessed by univariate regression analysis

Characteristics	DWI (+), $N = 356$	DWI (−), $N = 338$	P
Age ≥ 70 years	113 (31.7)	109 (32.2)	0.886
Sex, male	291 (81.7)	287 (84.9)	0.263
Symptomatic	149 (42.1)	164 (48.8)	0.091
Hypertension	258 (72.5)	247 (73.1)	0.858
Diabetes mellitus	154 (43.3)	113 (33.4)	0.008
Hypercholesterolemia	45 (12.6)	48 (12.6)	0.546
Coronary heart disease	73 (20.5)	56 (16.6)	0.183
Ischemic history	131 (36.8)	123 (36.4)	0.911
Smoking	191 (53.7)	190 (56.2)	0.498
Drinking	120 (33.7)	118 (34.9)	0.739
Left side	178 (50.0)	164 (48.5)	0.697
Pre-dilatation	286 (80.3)	238 (70.4)	0.003
Post-dilatation	95 (26.7)	108 (32.0)	0.127
Contralateral stenosis	72 (20.2)	71 (21.0)	0.799
VA or BA stenosis	127 (35.7)	117 (34.6)	0.770
Calcified plaque	56 (15.7)	35 (10.4)	0.036
Ulcer plaque	43 (12.1)	24 (7.1)	0.026
Unfavorable arch anatomy	28 (7.9)	29 (8.5)	0.766
Open-cell stent	260 (73.0)	154 (45.6)	< 0.001

Data are numbers (percentages in parentheses). *DWI*, diffusion-weighted imaging; *VA*, vertebral artery; *BA*, basilar artery

Discussion

In this study, DM, ipsilateral calcified plaques, ipsilateral ulcerated plaques, and open-cell stent use were found to be independent risk factors for sNICL after CAS.

A total of 356 patients (51.3%) had postoperative new DWI-positive cerebral ischemic lesions. This was in line with previous reports revealing rates of ischemic lesions post-CAS of 18–57% [6–10]. In this study, sNICL occurrence had no associations with pre-procedural parameters, including symptomatic and asymptomatic stenoses, and the location of new lesions. This contradicted previous findings that symptomatic patients harbor a higher risk of post-procedural ipsilateral ischemic events [18], but corroborated Cosottini et al. who reported that symptomatic cases show no association with the incidence of silent ischemic lesions detectable by DWI [4].

Table 4 Risk factors for postoperative new ischemic brain lesions assessed by multivariate analysis

Characteristics	OR	95%CI	P
Diabetes mellitus	1.579	1.142–2.184	0.006
Pre-dilatation	1.000	0.665–1.503	0.999
Calcified plaque	1.726	1.073–2.775	0.024
Ulcer plaque	1.912	1.102–3.316	0.021
Open-cell stent	3.316	2.321–4.738	< 0.001

OR, odds ratio; *CI*, confidence interval

As shown above, four risk factors for sNICL occurrence after CAS were identified, including DM, ipsilateral calcified plaques, ulcerated plaques, and open-cell stent use. In previous trials, sex, stenosis severity, side of intervention, hypertension, DM, dyslipidemia, and smoking were not associated with periprocedural ischemic events in CAS [15]. We found a relationship between DM and new cerebral ischemic lesions after stenting. Interestingly, Henry et al. demonstrated that DM is associated with a specific pattern of compensatory remodeling based on ultrasound examination [19]. Thus, we hypothesized that differences in plaque consistency and surface appearance could result in variations of plaque vulnerability during invasive therapy, with DM-associated plaques being particularly prone to rupture and dispersal during treatment. However, further studies are required for confirmation.

Although unfavorable arch anatomy increases the difficulties of DSA and CAS, no relationship between arch anatomy and sNICL after CAS was found. In agreement, a previous report showed that neither arch type nor bovine arch is an independent risk factor for ischemic lesions associated with CAS [20]. Carotid plaque surface irregularity reflects plaque instability and causes solid cerebral embolism during CAS in symptomatic patients. Our results corroborated the aforementioned findings, demonstrating that ulcerated plaques detected on pre-procedural DSA increase the risk of DWI lesions after

stenting [21]. However, other authors hold a different view [22]. Such discrepancy could be explained by the fact that plaque characteristics evaluated by different imaging methods may vary, which results in errors. Moreover, Ichinose et al. reported that proximal calcification is an important predictor of new DWI lesions after CAS [23], which is consistent with our above results.

One of the main findings of this study was that, besides DM and plaque characteristics, open-cell stent use independently predicted post-procedural ischemic lesions after CAS. In a previous study, patients treated with open-cell stents had a significantly higher stroke and death rates after CAS compared with those treated with closed cell stents [24], indicating that the open-cell stent option has an intrinsically greater potential to cause cerebral embolism of plaque debris. Recently, a meta-analysis based on 46,728 procedures by de Vries et al. [25] demonstrated that open-cell stenting resulted in a significantly higher number of subclinical post-procedural new ischemic lesions detected on DWI compared with closed cell stenting. These findings were supported by the present study.

Khan et al. [26] suggested that the use of EPD may not be meaningful. At the beginning, 4 patients accepted CAS without successful EPD use for the badly tortuous carotid artery. However, these 4 patients were excluded out of the study for complications. Hence, we cannot evaluate our data in the same way as Khan did.

The rate of pre-dilatation was relatively high in our center. Pre-dilatation was usually performed after EPD placement, and individualized dilatation planning was performed based on information such as calcified plaque detected by ultrasound before surgery, residual stenosis, and so on.

This study had several limitations. The RECAS study was not originally designed to answer the question of the present post hoc study, and the data are limited because of the retrospective nature of the study. During its design, no consensus was reached on the platelet inhibition test or platelet function evaluation for guiding the medication plan in stenting patients. It is necessary to include this in follow-up studies. In addition, we did not evaluate the circle of Willis although several studies have demonstrated that the contralateral carotid artery becomes the primary collateral vessel supplying blood to it in patients with severe carotid stenosis, and vertebral or contralateral carotid severe stenosis or occlusion is positively associated with infarct volume [27, 28]. Some scholars proposed that unstable carotid plaques confer a high risk of embolism [29]. A meta-analysis demonstrated that patients with intraplaque hemorrhage on pre-procedural MRI have elevated rates of silent ischemia [30], while Chung et al. considered it the latter parameter is not a significant risk factor for cerebral embolism during CAS [18]. However, this study did not assess plaque details by high-resolution MRI or pathological examination. Therefore, it is plausible that not all unstable plaques were identified, especially in the case of intraplaque hemorrhage. ICA tortuosity, which may increase the risk of cerebral ischemia during CAS, should also be taken into account in future studies [31]. Serum biochemical or physiological indices, such as TNF-α levels, intra-arterial oxidative stress, and white matter damage, may be associated with new cerebral ischemic lesions [6, 7]. The plaque properties referred to in this article refer to the plaque properties of the stenotic lesions during surgery. Due to the limitations of the design of RECAS study, the present retrospective study could not complete the statistical evaluation of plaque morphology and stent type within the entire group of sNICL or within the group of sNICL located ipsilateral territory.

In conclusion, the rate of postoperative sNICL after CAS was 51.3% in this study. We also found that DM patients with calcified or ulcerated plaques who undergo CAS with open-cell stents are likely at a high risk of post-procedural ischemic events. This is a rare study involving the risk factors of sNICL after CAS in Chinese individuals, which may provide insights into patient selection for carotid stenosis. Nevertheless, large-scale prospective randomized controlled trials are needed to confirm these findings, which may be used to identify high-risk patients for CAS to prevent postoperative ischemic lesions.

Acknowledgements None.

Funding information This study was funded by the National Key Research and Development Program of China (2016YFC1301703) and Beijing Science and Technology Commission (D161100003816002).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee (Ethics committees of the Xuanwu Hospital Capital Medical University) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Abbreviations sNICL, silent new ischemic cerebral lesions; DWI, diffusion-weighted imaging; MRI, magnetic resonance imaging; CAS, carotid artery stenting; RECAS, Revascularization of Extracranial Carotid Artery Stenosis; TIA, transient ischemic attack; CEA, carotid endarterectomy; ICA, internal carotid artery; CTA, computed tomography angiography; DSA, digital subtraction angiography; MI, myocardial infarction; DM, diabetes mellitus; NASCET, North American Symptomatic Carotid Endarterectomy Trial; AF, atrial fibrillation; CCA, common carotid arteries; EPD, embolic protection device; SD, standard deviation; OR, odds ratio; CI, confidence interval

References

1. Bonati LH, Jongen LM, Haller S, Flach HZ, Dobson J, Nederkoorn PJ, Macdonald S, Gaines PA, Waaijer A, Stierli P, Jager HR, Lyrer PA, Kappelle LJ, Wetzel SG, van der Lugt A, Mali WP, Brown

MM, van der Worp HB, Engelter ST (2010) New ischaemic brain lesions on MRI after stenting or endarterectomy for symptomatic carotid stenosis: a substudy of the International Carotid Stenting Study (ICSS). Lancet Neurol 9(4):353–362. https://doi.org/10.1016/s1474-4422(10)70057-0

2. Ishii D, Sakamoto S, Okazaki T, Matsushige T, Shinagawa K, Ichinose N, Kurisu K (2018) Overlapped stenting is associated with postoperative hypotension after carotid artery stenting. J Stroke Cerebrovasc Dis 27(3):653–659. https://doi.org/10.1016/j.jstrokecerebrovasdis.2017.09.041
3. Bendszus M, Stoll G (2006) Silent cerebral ischaemia: hidden fingerprints of invasive medical procedures. Lancet Neurol 5(4):364–372. https://doi.org/10.1016/s1474-4422(06)70412-4
4. Cosottini M, Michelassi MC, Puglioli M, Lazzarotti G, Orlandi G, Marconi F, Parenti G, Bartolozzi C (2005) Silent cerebral ischemia detected with diffusion-weighted imaging in patients treated with protected and unprotected carotid artery stenting. Stroke 36(11):2389–2393. https://doi.org/10.1161/01.STR.0000185676.05358.f2
5. Yadav JS, Roubin GS, Iyer S, Vitek J, King P, Jordan WD, Fisher WS (1997) Elective stenting of the extracranial carotid arteries. Circulation 95(2):376–381. https://doi.org/10.1161/01.cir.95.2.376
6. Lin C, Tang X, Shi Z, Zhang L, Yan D, Niu C, Zhou M, Wang L, Fu W, Guo D (2018) Serum tumor necrosis factor alpha levels are associated with new ischemic brain lesions after carotid artery stenting. J Vasc Surg 68(3):771–778. https://doi.org/10.1016/j.jvs.2017.11.085
7. Maggio P, Altamura C, Lupoi D, Paolucci M, Altavilla R, Tibuzzi F, Passarelli F, Arpesani R, Di Giambattista G, Grasso RF, Luppi G, Fiacco F, Silvestrini M, Pasqualetti P, Vernieri F (2017) The role of white matter damage in the risk of periprocedural diffusion-weighted lesions after carotid artery stenting. Cerebrovasc Dis Extra 7(1):1–8. https://doi.org/10.1159/000452717
8. Kashiwazaki D, Kuwayama N, Akioka N, Noguchi K, Kuroda S (2017) Carotid plaque with expansive arterial remodeling is a risk factor for ischemic complication following carotid artery stenting. Acta Neurochir 159(7):1299–1304. https://doi.org/10.1007/s00701-017-3188-y
9. Kuliha M, Roubec M, Goldírová A, Hurtíková E, Jonszta T, Procházka V, Gumulec J, Herzig R, Školoudík D (2016) Laboratory-based markers as predictors of brain infarction during carotid stenting: a prospective study. J Atheroscler Thromb 23(7):839–847. https://doi.org/10.5551/jat.31799
10. Koyanagi M, Yoshida K, Kurosaki Y, Sadamasa N, Narumi O, Sato T, Chin M, Handa A, Yamagata S, Miyamoto S (2016) Reduced cerebrovascular reserve is associated with an increased risk of postoperative ischemic lesions during carotid artery stenting. J Neurointervention Surg 8(6):576–580. https://doi.org/10.1136/neurintsurg-2014-011163
11. Pendlebury ST, Rothwell PM (2009) Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis. Lancet Neurol 8(11):1006–1018. https://doi.org/10.1016/s1474-4422(09)70236-4
12. Gensicke H, van der Worp HB, Nederkoorn PJ, Macdonald S, Gaines PA, van der Lugt A, Mali WP, Lyrer PA, Peters N, Featherstone RL, de Borst GJ, Engelter ST, Brown MM, Bonati LH (2015) Ischemic brain lesions after carotid artery stenting increase future cerebrovascular risk. J Am Coll Cardiol 65(6):521–529. https://doi.org/10.1016/j.jacc.2014.11.038
13. Poppert H, Wolf O, Theiss W, Heider P, Hollweck R, Roettinger M, Sander D (2006) MRI lesions after invasive therapy of carotid artery stenosis: a risk-modeling analysis. Neurol Res 28(5):563–567. https://doi.org/10.1179/016164105X49391
14. Barnett HJM, Taylor DW, Haynes RB, Sackett DL, Peerless SJ, Ferguson GG, Fox AJ, Rankin RN, Hachinski VC, Wiebers DO, Eliasziw M (1991) Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 325(7):445–453. https://doi.org/10.1056/nejm199108153250701
15. Russjan A, Goebell E, Havemeister S, Thomalla G, Cheng B, Beck C, Krützelmann A, Fiehler J, Gerloff C, Rosenkranz M (2012) Predictors of periprocedural brain lesions associated with carotid stenting. Cerebrovasc Dis (Basel, Switzerland) 33(1):30–36
16. Jiao LQ, Song G, Li SM, Miao ZR, Zhu FS, Ji XM, Yin GY, Chen YF, Wang YB, Ma Y, Ling F (2013) Thirty-day outcome of carotid artery stenting in Chinese patients: a single-center experience. Chin Med J 126(20):3915–3920
17. Simonsen CZ, Madsen MH, Schmitz ML, Mikkelsen IK, Fisher M, Andersen G (2015) Sensitivity of diffusion- and perfusion-weighted imaging for diagnosing acute ischemic stroke is 97.5%. Stroke 46(1):98–101. https://doi.org/10.1161/strokeaha.114.007107
18. Chung GH, Jeong JY, Kwak HS, Hwang SB (2016) Associations between cerebral embolism and carotid intraplaque hemorrhage during protected carotid artery stenting. AJNR Am J Neuroradiol 37(4):686–691. https://doi.org/10.3174/ajnr.A4576
19. Henry RMA, Kostense PJ, Dekker JM, Nijpels G, Heine RJ, Kamp O, Bouter LM, Stehouwer CDA (2004) Carotid arterial remodeling: a maladaptive phenomenon in type 2 diabetes but not in impaired glucose metabolism: the Hoorn study. Stroke 35(3):671–676
20. Ikeda G, Tsuruta W, Nakai Y, Shiigai M, Marushima A, Masumoto T, Tsurushima H, Matsumura A (2014) Anatomical risk factors for ischemic lesions associated with carotid artery stenting. Interv Neuroradiol 20(6):746–754. https://doi.org/10.15274/inr-2014-10075
21. Wimmer NJ, Yeh RW, Cutlip DE, Mauri L (2012) Risk prediction for adverse events after carotid artery stenting in higher surgical risk patients. Stroke 43(12):3218–3224
22. Doig D, Hobson BM, Müller M, Jäger HR, Featherstone RL, Brown MM, Bonati LH, Richards T, Investigators I-MS (2016) Carotid anatomy does not predict the risk of new ischaemic brain lesions on diffusion-weighted imaging after carotid artery stenting in the ICSS-MRI substudy. Eur J Vasc Endovasc Surg 51(1):14–20
23. Ichinose N, Hama S, Tsuji T, Soh Z, Hayashi H, Kiura Y, Sakamoto S, Okazaki T, Ishii D, Shinagawa K, Kurisu K (2018) Predicting ischemic stroke after carotid artery stenting based on proximal calcification and the jellyfish sign. J Neurosurg 128(5):1280–1288. https://doi.org/10.3171/2017.1.jns162379
24. Wodarg F, Turner EL, Dobson J, Ringleb PA, Mali WP, Fraedrich G, Chatellier G, Bequemin JP, Brown MM, Algra A, Mas JL, Jansen O, Bonati LH (2018) Influence of stent design and use of protection devices on outcome of carotid artery stenting: a pooled analysis of individual patient data. J Neurointervention Surg 10(12):1149–1154. https://doi.org/10.1136/neurintsurg-2017-013622
25. de Vries EE, Meershoek AJA, Vonken EJ, den Ruijter HM, van den Berg JC, de Borst GJ, Group ES (2019) A meta-analysis of the effect of stent design on clinical and radiologic outcomes of carotid artery stenting. J Vasc Surg 69(6):1952–1961 **e1951**. https://doi.org/10.1016/j.jvs.2018.11.017
26. Khan M, Qureshi AI (2014) Factors associated with increased rates of post-procedural stroke or death following carotid artery stent placement: a systematic review. J Vascular Intervention Neurol 7(1):11–20
27. Park KY, Chung PW, Kim YB, Moon HS, Suh BC, Yoon WT (2011) Post-interventional microembolism: cortical border zone is a preferential site for ischemia. Cerebrovasc Dis (Basel, Switzerland) 32(3):269–275
28. Zhou W, Baughman BD, Soman S, Wintermark M, Lazzeroni LC, Hitchner E, Bhat J, Rosen A (2017) Volume of subclinical embolic infarct correlates to long-term cognitive changes after carotid revascularization. J Vasc Surg 65(3):686–694. https://doi.org/10.1016/j.jvs.2016.09.057

29. Gupta A, Baradaran H, Schweitzer AD, Kamel H, Pandya A, Delgado D, Dunning A, Mushlin AI, Sanelli PC (2013) Carotid plaque MRI and stroke risk: a systematic review and meta-analysis. Stroke 44(11):3071–3077
30. Brinjikji W, Lehman VT, Huston J, Murad MH, Lanzino G, Cloft HJ, Kallmes DF (2017) The association between carotid intraplaque hemorrhage and outcomes of carotid stenting: a systematic review and meta-analysis. J Neurointervention Surg 9(9):837–842. https://doi.org/10.1136/neurintsurg-2016-012593
31. Muller MD, Ahlhelm FJ, von Hessling A, Doig D, Nederkoorn PJ, Macdonald S, Lyrer PA, van der Lugt A, Hendrikse J, Stippich C, van der Worp HB, Richards T, Brown MM, Engelter ST, Bonati LH (2017) Vascular anatomy predicts the risk of cerebral ischemia in patients randomized to carotid stenting versus endarterectomy. Stroke 48(5):1285–1292. https://doi.org/10.1161/strokeaha.116.014612