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Silent Micro-Infarct in Carotid Artery Stenting: Who Has it and Why?

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ABSTRACT

AIM: To compare the postprocedural cerebral diffusion-weighted imaging (DWI) findings in cases of carotid stenosis (CS)-related carotid plaques in terms of plaque morphology, degree of stenosis, and the use of a distal protection filter. Moreover, we used DWI to assess the asymptomatic cerebral embolism rates during carotid artery stending (CAS) operations performed for noncalcified versus calcified carotid plaques.

MATERIAL and METHODS: Our study included 99 patients admitted to the Ankara City Hospital Stroke Center in 2022. All of our patients have been evaluated and scheduled for CAS as a result of a decision made by the council. Cases of stenosis of >50% in symptomatic patients and >70% in asymptomatic patients were included. The patients were grouped according to their Doppler ultrasonography results. All of the patients underwent DWI within the first 24 hours after the procedure, and then two groups of patients were compared.

RESULTS: A statistically significant difference was found between the distributions of the presence of silent micro-infarcts on DWI in terms of plaque characteristics ($p<0.001$). In the patients with normal DWI findings, the percentage of calcified plaques was 38.7%, while the percentages of hypoechoic plaques, plaques with low echogenicity, and ulcerated plaques were 91.3%, 85.7%, and 78.8%, respectively. The rates of calcified plaques and ulcerated plaques differed in the group of patients with silent micro-infarcts. The rate of silent micro-infarcts was 61.3% in the patients with calcified plaques, 8.7% in those with hypoechoic plaques, 14.3% in those with low-echogenicity plaques, and 21.2% in those with ulcerated plaques.

CONCLUSION: The study found that carotid stents implanted in calcified and ulcerated plaques had a higher correlation with the presence of periprocedural asymptomatic ipsilateral DWI findings than those implanted in hypoechoic plaques and low-echogenicity plaques.

KEYWORDS: Carotid artery stenosis, Stroke, Cerebral embolism, Silent micro-infarct

ABBREVIATIONS: CS: Carotid stenosis, **DW-MRI:** Diffusion-Weighted Magnetic Resonance Imaging, **DWI:** Diffusion Weighted Imaging, **CAS:** Carotid artery stenting, **USG:** Ultrasonography, **ICA:** Internal Carotid Artery, **ECA:** External Carotid Artery, **ASA:** Acetylsalicylic Acid, **AP:** Anteroposterior, **ADC:** Apparent Diffusion Coefficient, **AH:** Arterial Hypertension, **LVH:** Left Ventricular Hypertrophy, **TCD:** Transcranial Doppler, **MES:** Micro-Embolic Signals, **PHD:** Persistent Hemodynamic Depression

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INTRODUCTION

Cerebrovascular diseases are the second leading cause of death in people aged over 60 and the first leading cause of disability and labor force loss (5,29). Despite advances in thrombolysis and other treatments for acute stroke (1,26), primary prevention remains the most effective strategy for reducing the occurrence of cerebrovascular diseases. In fact, the risk of stroke can be minimized by identifying and addressing modifiable risk factors.

Carotid stenosis (CS) is a modifiable risk factor for stroke that has become more common because of advances in imaging methods and their widespread use (30). There is a significant correlation between CS severity and the risk of stroke (14). Although the definition of clinically significant stenosis varies among guidelines, it is generally defined as a stenosis of >50% or >60%, and severe asymptomatic CS is defined as stenosis of >70% (24). Fortunately, carotid artery stenting (CAS) can be performed to manage asymptomatic patients with symptomatic or severe CS (11).

Different guidelines publish varying recommendations for treating CS. The American Stroke Association's (2014) recommendations vary according to stenosis severity and vascular risk factors (20). They state that CAS is a viable option for carotid endarterectomy in symptomatic individuals with a low/average complication rate and a stenosis of >70% diagnosed by noninvasive methods or a stenosis of >50% diagnosed by digital substrate angiography (category 1, evidence B). Citing a lack of evidence, the National Institute for Health and Clinical Excellence guideline recommends that CS be treated only in exceptional cases in asymptomatic patients, while CAS is recommended for symptomatic CS (13). Also, in the Carotid Revascularization Endarterectomy Versus Stenting Trial, endarterectomy was compared to CAS, and it was found that both treatments provided similar rates of benefit (17).

In asymptomatic CS, the annual risk of ipsilateral stroke is 1–2% (18). CS can be asymptomatic or lead to recurrent stroke. Currently, endovascular treatment of CS is performed with stenting and angioplasty in selected eligible patients (6). Patients who are asymptomatic but have hemodynamic changes benefit from revascularization procedures rather than medical treatment (28). However, patients who have successful revascularization procedures may still be at risk of stroke due to atherosclerotic stenosis originating from other vessels or cardioembolic causes. Therefore, medical treatment will always play an important role in the treatment and prevention of stroke (21).

The CAS procedure carries a risk of embolization, and several factors can contribute to the development of new ischemic lesions after CAS. The patient's cerebral status, vascular system, and aortic arch type, as well as the device(s) used, the surgeon's expertise, and the plaque morphology are all critical factors. Therefore, the patient's characteristics, the lesion type, and the equipment used all play important roles in reducing distal lesions (3,8,19,23,32,33,36,37).

We aimed to compare the postprocedural cerebral diffusion-weighted magnetic resonance imaging (DW-MRI) findings in cases of CS-related carotid plaques in terms of plaque morphology, degree of stenosis, and use of a distal protection filter. We also used diffusion-weighted imaging (DWI) to assess the asymptomatic cerebral embolism rates during CAS operations performed for noncalcified versus calcified carotid plaques.

MATERIAL and METHODS

Our study included 99 patients admitted to the Ankara City Hospital Stroke Center in 2022. The ethics committee approved the study (Date: 01.02.2022, Decision no: E1-22-2365). All the included patients had been evaluated and scheduled for CAS by the council of neurologists, radiologists, and neurosurgeons. Symptomatic patients with stenosis of >50% and asymptomatic patients with stenosis of >70% were included. It was ensured that all included patients had a glomerular filtration rate greater than 60 mL/min/1.73 m^2. The patients were grouped according to their Doppler ultrasonography results. All of the patients underwent DW-MRI within the first 24 h after the procedure, and then two groups of patients were compared.

The inclusion criteria were as follows: symptomatic internal carotid artery (ICA) stenosis >50%, asymptomatic ICA stenosis >70%, no need for predilatation before crossing the lesion with a filter, presence of patent contralateral ICA, and lack of total occlusion of the contralateral external carotid artery (ECA). The exclusion criteria were as follows: symptomatic complications, periprocedural hemodynamic instability, differential bilateral-restricted diffusion on DWI and diffusion restriction in the watershed area, receiving radiotherapy, and a history of malignancy and rheumatologic diseases.

Preparation of Patients for CAS

The patients' regular use of antihypertensive, antihyperlipidemic, and antiplatelet treatments was confirmed. It was ensured that antiplatelet treatment was administered on a regular basis and that acetylsalicylic acid (ASA) and clopidogrel were administered together regularly for at least one week. Patients not already using this medication protocol were administered a loading dose of ASA (300 mg) and clopidogrel (600 mg) before the procedure.

The patients received dual antiplatelet treatments at least three days before the procedure. As per the standard regimen, they were administered clopidogrel (75 mg/day) and aspirin (100 mg/day).

CAS Procedure

Tapered and non-tapered self-expandable stents with open- and closed-cell designs were used. The sheath on the stent was peeled off to allow the stent to expand. A cobalt braided-wall stent (Boston Scientific, Natick, USA) and a nitinol open-cell Protégé Covidien stent (Irvine, USA) were used in the study. Nitinol stents expand and conform to a predetermined shape. In cobalt stents, the gaps between the stent's cells are small and expand with a spring-like motion. Stents with open-cell designs have larger gaps between the cells and are more flexible, allowing for better access to tortuous vessels and a better fit to the wall because they do not shorten in length.

Endovascular Procedure

The femoral artery was punctured under local anesthesia. After performing catheterization with a vertebral catheter or Simmons 2 catheter, angiograms showing both carotid arteries and vertebral artery orifices in the anteroposterior (AP) and lateral planes were obtained, and the degree of stenosis and hemodynamics were evaluated accordingly. The degree of stenosis was calculated using the North American Symptomatic Carotid Endarterectomy Trial method: % ICA stenosis = 1 – (narrowest ICA diameter/normal ICA diameter) × 100. Following the stenting decision, the patient was heparinized to ensure a clotting time of 250–300 s. A guiding catheter was inserted into the common carotid artery through the exchange guidewire placed in the ECA. First, the stenosis was crossed with a guidewire (Synchro 0.014" microguidewire; Stryker Neurovascular, Fremont, USA), and a distal embolic protection filter (Spider fx; ev3 Covidien, Plymouth, USA) was placed distally to the stenosis. In cases of severe stenosis, predilatation angioplasty was performed to allow the stent to pass through the stenosis. After the stent was advanced over the guidewire, taking care to keep the filter in place in the vessel, it was expanded to center the stenosis. Angioplasty was performed using a balloon of an appropriate size to ensure full coverage of the vessel wall with the stent. During angioplasty, atropine was made available to treat bradycardia caused by the stimulation of the carotid sinus. After collecting the distal embolic protection filter, AP and lateral radiographs were obtained to assess stent patency and intracranial branch loss. The closure of the femoral arterial access was performed using a vascular closure device.

Factors Considered after CAS

After CAS, the clinical and hemodynamic parameters of all the patients were monitored in the neurology intensive care unit for 24 hours. The patients underwent DW-MRI within the first 24 hours. All the patients were discharged with dual antiplatelet therapy and statin therapy (if their low-density lipoprotein cholesterol level was >70 mg/dL). After ensuring that there were no contraindications, the patients were assessed for their adherence to the treatment prescribed with dual antiplatelet use for 6–12 months during their outpatient follow-up.

Carotid Plaque Characteristics

When evaluating carotid artery plaques, the localization, extension, degree of stenosis, and surface structure of the plaque should be considered. The structure of the plaque is particularly important in terms of embolism and any subsequent symptoms that may develop.

As the degree of stenosis increases, calcification in the plaque structure degrades image quality and makes it difficult to determine the lumen diameter. Soft plaques may be difficult to distinguish, as their echogenic structure is similar to that of blood. In total occlusions, plaque appearance may be minimal. Therefore, gray-scale examination alone is insufficient for imaging stenoses. Spectral Doppler provides information that can be used to calculate the degree of stenosis. Doppler waveforms should be obtained in the longitudinal plane. Generally, maximum systolic velocity values are the most important spectral parameters used in the assessment of stenosis.

In terms of their echogenicity and appearance on the gray scale, atheromatous plaques are classified into four types. Type 1 plaques have a thin capsular structure that is echogenic but are completely hypoechoic. Type 2 plaques are almost completely hypoechoic, with a small focal echogenic area. Type 3 plaques are predominantly echogenic, with focal radiolucent areas. Type 4 plaques are completely echogenic.

Hypoechoic plaques (Types 1–2) include those with a "fibrofatty" structure. On USG examination, they have an echo content that is equivalent to the echogenicity of the sternocleidomastoid muscle. Gray-scale examination may not always be sufficient to detect hypoechoic plaques. However, they appear as filling defects on color Doppler examination.

Plaques with low echogenicity (Type 3) have a high collagen fiber content and a low lipid content. They are also known as fibrous plaques. They are more echogenic than the sternocleidomastoid muscle but have a lower echo than the adventitia. They generally have a homogeneous internal structure.

Echogenic plaques (Type 4) are formed as a result of dystrophic calcification of the hemorrhagic and necrotic areas of plaques. Calcification can appear in a focal area of the plaque or as a diffuse pattern. In our study, ulcerated echogenic plaques were classified as Type 4a, while those with prominent focal calcifications were classified as Type 4b.

DWI

Cerebral DWI was performed with a 1.5-Tesla Magnetom Sonata (Siemens, Erlangen, Germany). The cerebral MRI (DW-MRI and apparent diffusion coefficient [ADC] maps) results were evaluated by an interventional neurologist before and after CAS. Silent cerebral embolisms were defined as new ipsilateral hyperintense lesions on DWI that had not been detected prior to CAS. When comparing the affected area to the corresponding contralateral area in cases with a lesion detected using DWI, we also reviewed the ADC map and noted whether high-signal areas on the b1000 image showed low, high, or normal signal intensity on the ADC map.

Statistical Analysis

The data analysis was performed with IBM SPSS V23. Normality tests of the data were performed using the Shapiro–Wilk test. Normally distributed data in the paired groups were compared using an independent samples t-test. Yate's correction, Fisher's exact test, and Pearson's χ^2 test were used to compare categorical data. Multiple comparisons were made using the Z test with Bonferroni correction. The results of the analysis are presented as mean ± standard deviation and median (minimum–maximum) for quantitative parameters and as frequency (percentage) for categorical data. $p<0.050$ was considered statistically significant.

Table I: Frequency Distributions and Descriptive Statistics of the Variables

	n (%)
Doppler USG Plaque Characteristics	
Hypoechoic	23 (24)
Slightly echogenic	7 (7.3)
Echogenic calcified	31 (32.3)
Echogenic ulceration	35 (36.4)
DWI	
Normal	65 (67.7)
Silent Microinfarct	29 (30.2)
Infarct	2 (2.1)
Sex	
Male	68 (70.8)
Female	28 (29.2)
Right Symptomatic	
50–70	6 (35.3)
70–99	10 (58.8)
Occluded	1 (5.9)
Right Asymptomatic	
50–70	3 (17.6)
70–99	13 (76.5)
Occluded	1 (5.9)
Left Symptomatic	
50–70	10 (40.0)
70–99	15 (60.0)
Left Asymptomatic	
50–70	3 (9.1)
70–99	30 (90.9)
mRS Discharge	
0	61 (72.6)
1	20 (23.8)
2	2 (2.4)
3	1 (1.2)
mRS at 3 months	
0	19 (59.4)
1	11 (34.4)
2	1 (3.1)
3	1 (3.1)
Arcus Type	
1	81 (89.0)
2	9 (9.9)
3	1 (1.1)
Filter	
Yes	72 (79.1)
No	19 (20.9)
Predilatation	
Yes	2 (2.2)
No	88 (97.8)
Postdilatation	
Yes	89 (98.9)
No	1 (1.1)

DWI: *Diffusion weighted imaging,* ***mRS:*** *Modified Rankin scale.*

RESULTS

Of the patients who participated in the study, 70.8% were male and 29.2% were female (Table I). When the risk factors were evaluated, it was found that one patient had more than one and that the most common was arterial hypertension (AH) (72.53%) (Table II).

No significant difference was found between the risk factor distributions in terms of the presence of silent micro-infarcts detected using DWI (p=0.529). The most common risk factor encountered in patients with normal DWI results was AH (72.3%), while the most common risk factors in those with silent micro-infarcts detected using DWI were AH and previous left ventricular hypertrophy (LVH) (58.6%) (Table III).

In our study, filters were not used in 18 patients for technical and anatomical reasons, while filters were used in 71 patients. In the group of patients with filter use, 67.6% had normal MRI results, while 32.4% had silent micro-infarcts. In the group of patients without filter use, 72.2% had normal MRI results, while 27.8% had silent micro-infarcts. As a result, no statistically significant difference was found between the use and non-use of filters and the detection of silent micro-infarcts using DW-MRI (p=0.926) (Table IV).

In all patients, both symptomatic and asymptomatic, the rates of silent plaques detected using DWI did not differ statistically significantly in terms of the degree of stenosis (p=0.336). The MRI findings were normal in 77.3% of the patients with

Table II: Frequency Distributions and Descriptive Statistics of the Variables (to be continued)

	n (%)
Risk Factor*	
Lung Carcinoma (CTx-RTx)	1 (1.1)
AF	3 (3.3)
ALCOHOL	2 (2.2)
AMAUROSİS	1 (1.1)
BY PASS	2 (2.2)
CA	1 (1.1)
DM	41 (45.05)
FUGAX	1 (1.1)
HL	14 (15.38)
AH	66 (72.53)
CAD	22 (24.18)
CRF	1 (1.1)
CF	2 (2.2)
Smoking	9 (9.89)
CVA	49 (53.85)
TIA	4 (4.4)
NO	1 (1.1)
Medication used*	
Acetylsalicylic acid	91 (98.91)
Warfarin	1 (1.09)
Apixaban	1 (1.09)
Clopidogrel	87 (94.57)
Rivaroxaban	1 (1.09)

	AO ± ss	Mean (min–max)
Age (years)	67.93 ± 7.97	68.5 (44–84)
NIHSS, admission	0.77 ± 1.6	0 (0–10)
NIHSS, 1-hour	1.01 ± 2.25	0 (0–15)
NIHSS, 24-hour	0.93 ± 2.08	0 (0–15)
NIHSS AT DISCHARGE	0.7 ± 1.36	0 (0–6)

Multiple response.* ***CTx:* *Chemotherapy,* ***RTx:*** *Radiation therapy,* ***AF:*** *Atrial fibrillation,* ***CA:*** *Cancer,* ***CABG:*** *Coronary artery bypass grafting* ***DM:*** *Diabetes mellitus,* ***HL:*** *Hyperlipidemia,* ***AH:*** *Arterial hypertension,* ***CAD:*** *Coronary artery disease,* ***CRF:*** *Chronic renal failure,* ***CF:*** *Cardiac failure,* ***CVA:*** *Cerebrovascular accident,* ***TIA:*** *Transient ischemic attack.*

a stenosis of 50–69% and in 64.6% of the patients with a stenosis of 70–99%. Silent micro-infarcts were found in 22.7% of the patients with a stenosis of 50–69% and in 35.4% of the patients with a stenosis of 70–99%.

In the group of symptomatic patients, no statistically significant difference was found between the distributions of the presence of normal MRI findings in terms of the degree of stenosis (p=0.397). The MRI findings were normal in 75% of the patients with a stenosis of 50–70%, in 58.3% of those with a stenosis of 70–99%, and in 100% of the patients with occlusion. Silent micro-infarcts were found in 25% of the patients with a stenosis of 50–70%, and micro-infarcts were found in 41.7% of those with a stenosis of 70–99% (Table V).

In the group of asymptomatic patients, no statistically significant difference was found between the distributions of the presence of normal MRI findings in terms of the degree of stenosis (p=0.667). The MRI findings were normal in 83.3% of the patients with a stenosis of 50–70%, in 68.3% of those with a stenosis of 70–99%, and in 100% of the patients with occlusion. Silent micro-infarcts were found in 16.7% of the patients with a stenosis of 50–70% and in 31.7% of the patients with a stenosis of 70–99% (Table VI).

A statistically significant difference was found between the distributions of the presence of silent micro-infarcts detected using DWI in terms of plaque characteristics (p<0.001). In the patients with normal DWI findings, 91.3% of the plaques were hypoechoic, 85.7% of the plaques had low echogenicity, 78.8% of the plaques were ulcerated, and 38.7% of the plaques were calcified. The occurrence of calcified plaques and ulcerated plaques differed in the group of patients with silent micro-infarcts. The rate of silent micro-infarcts was 61.3% in the patients with calcified plaques, 21.2% in those with ulcerated plaques, 14.3% in those with low-echogenicity plaques, and 8.7% in those with hypoechoic plaques (Table VII).

DISCUSSION

In this study, we aimed to compare the postprocedural cerebral DWI findings in cases of CS-related carotid plaques in terms of their morphologic characteristics, the degree of stenosis, and the use of a distal protection filter.

To achieve this aim, we compared periprocedural ipsilateral cerebral DWI findings of CS-related carotid plaques classified into different groups. DWI is a highly sensitive method for detecting silent cerebral micro-infarcts. We found that carotid stents implanted in calcified and ulcerated plaques correlated more closely with the presence of periprocedural asymptomatic ipsilateral lesions detected using DWI than those implanted in hypoechoic and low-echogenicity plaques.

Others have reported silent microembolisms developing in 40% of CAS cases (10). In our study, the rate of silent micro-infarcts was found to be 30.2%, which is similar to the rates reported in the literature (34). This prevalence can be reduced to 33% by using embolic protection methods (31).

Table III: Distribution of the Risk Factors by Presence of Silent Micro-Infarct on DWI

	DWI		Total	Test Station	p-value
	Normal	Silent Micro-infarct Present			
Risk Factor**	**n (%)**	**n (%)**	**n (%)**		
DM	31 (47.7)	9 (31.0)	40 (42.6)	5.114	0.529
HL	9 (13.9)	5 (17.2)	14 (14.9)		
AH	47 (72.3)	17 (58.6)	64 (68.1)		
CAD	14 (21.5)	7 (24.1)	21 (22.3)		
CVA	32 (49.2)	17 (58.6)	49 (52.1)		
Others	59 (90.8)	27 (93.1)	86 (91.5)		

*Pearson Chi-Square Test; * Not included in the comparison because the frequency of the infarct option was not suitable for comparison; **Multi-response.*

Table IV: Distributions of the Presence of DWI by Presence of Filter

	Filter		Total	Test Station	p-value
	Yes	No			
DWI	**n (%)**	**n (%)**	**n (%)**		
Normal	48 (67.6)	13 (72.2)	61 (68.5)	0.009	0.926
Silent Micro-infarct Present	23 (32.4)	5 (27.8)	28 (31.5)		

*Yate's Correction; **

Table V: Distribution of the Normal MRI in Symptomatic Patients by Degree of Stenosis

	Degree of stenosis (Symptomatic)			Test Station	p-value
	50–70	70–99	OCCLUDED		
DWI	**n (%)**	**n (%)**	**n (%)**		
Normal	12 (75.0)	14 (58.3)	1 (100.0)	2.963	0.397
Silent Micro-infarct Present	4 (25.0)	10 (41.7)	0 (0.0)		

Pearson Chi-Square Test.

Table VI: Distribution of the Normal MRI in Asymptomatic Patients by Degree of Stenosis

	Degree of stenosis (Asymptomatic)			Test Station	p-value
	50–70	70–99	OCCLUDED		
DWI	**n (%)**	**n (%)**	**n (%)**		
Normal	5 (83.3)	28 (68.3)	1 (100.0)	1.566	0.667
Silent Micro-infarct Present	1 (16.7)	13 (31.7)	0 (0.0)		

Pearson Chi-Square Test.

Table VII: Distribution of the Normal MR by Plaque Characteristics

	Characteristics of plaque on Doppler USG				Total	Test Station	p-value
	Hypoechoic plaques	Plaques with low echogenicity	Echogenic calcified plaques	Echogenic ulcerated plaques			
DWI	**n (%)**	**n (%)**	**n (%)**	**n (%)**			
Normal	21 (91.3)[a]	6 (85.7)[ab]	12 (38.7)[b]	26 (78.8)[a]	65 (69.1)	21.094	**<0.001**
Silent Micro-infarct Present	2 (8.7)[a]	1 (14.3)[ab]	19 (61.3)[b]	7 (21.2)[a]	29 (30.9)		

Pearson Chi-Square Test; a-b There is no difference between the groups with the same letter; ***DM:*** *Diabetes mellitus,* ***HL:*** *Hyperlipidemia,* ***AH:*** *Arterial hypertension,* ***CAD:*** *Coronary artery disease,* ***CVA:*** *Cerebrovascular accident.*

It is thought that cerebral embolism during CAS is caused by two mechanisms: emboli generated by plaque destruction and thrombosis caused by intimal damage. Protection filters, heparinization, and periprocedural antiaggregants are used to hinder these two mechanisms. Dual antiaggregant therapy has been shown to be superior to monotherapy in preventing early and late ischemic events after stenting (7).

Regarding risk factors, in their 2020 study, Xiaoyu et al. showed that diabetes mellitus, ipsilateral calcified plaque, ulcerated plaque, predilatation, and open-cell stent use were independent risk factors for silent cerebral lesions during CAS (37). In addition, Hunt et al. analyzed material collected from carotid plaques during endarterectomy and found that noncalcified plaques had a greater association with cerebrovascular events than calcified plaques (12). In our study, the presence of echogenic calcified plaques was found to be a risk factor for silent micro-infarcts.

In symptomatic patients, existing atherosclerotic plaques may be more unstable and thus sources of microemboli during and after interventional procedures. However, Tulip et al. evaluated 23 asymptomatic and 17 symptomatic patients using transcranial Doppler (TCD) and DWI and observed similar rates of embolic signal intensities in the two groups after CAS (35). Similarly, in our research, there was no discernible difference between the embolic signal intensities in the symptomatic and asymptomatic patients after CAS.

Several studies have been conducted to investigate the association between cerebral embolization and microembolic signals (MES) detected by TCD that originate from the plaque itself or are associated with endovascular treatment. For example, Almekhlafi et al. used TCD to record MES during CAS and DWI after the procedure in a study with 30 patients and found that 76.9% of the patients had new ischemic lesions after stenting (2).

Measures to reduce the formation of embolic lesions include the use of different types of filters and flow diverters. Montorsi et al. used proximal protection filters in 26 patients and distal protection filters in 27 patients and found that the rate of new lesions detected using DWI was significantly lower in the group in which proximal protection filters were used than in the group in which distal protection filters were used; however, the former group had a higher rate of plaque ulceration (2). In contrast, in a meta-analysis by Schnaudigel et al., distal protection filters were found to be superior to proximal protection filters and stents (31). In our unit, distal protection filters are used during CAS. While some studies have reported that anti-embolism systems are not beneficial (3,4), others have reported that they reduce the risk of ipsilateral stroke (16). A systematic review by Kastrup et al. reported lower periprocedural stroke and mortality rates with the use of embolization prevention systems (15). Despite studies on the efficacy of these systems and the course of the procedure becoming more complicated with prolonged procedure time, the majority of interventionalists who perform CAS believe that embolism prevention systems should be used (15,16). In our study, there was no discernible difference in the rate of new lesions detected using DWI between individuals in whom filters were or were not used (for technical and anatomical reasons).

Our findings are consistent with those in the current literature; however, this study has the following limitations. The study was retrospective by design, and the sample size of the study group was limited because we did not include patients with border-zone infarcts. Despite the study group consisting of patients with carotid occlusion, data were only collected from a single center. It was also difficult to acquire long-term patient data, and there was a lack of data available on other key parameters, such as the time between each patient's stroke and CAS.

Persistent hemodynamic depression (PHD) is observed when a patient's blood pressure falls below 90/60 mmHg and/or heart rate falls below 60 beats per minute for more than 6 h. If the patient does not respond to volume replacement therapy and/or inotropic usage, the condition is referred to as "resistant PHD." In a study conducted by Nii et al. on 95 patients who underwent CAS, 32.6% of the patients had postprocedural PHD and 30.6% had postprocedural new cerebral emboli; however, no significant relationship was found between these two complications (25). In the current study, postprocedural monitoring data was not collected; therefore, PHD among the study cohort cannot be ruled out. This is another limitation of this study.

Symptomatic or asymptomatic periprocedural cerebral embolism is a critical limitation of CAS. Silent cerebral embolism

associated with CAS has been shown to cause dementia, cognitive decline (9), and even ischemic stroke in later years (27). Although the risk of stroke is significantly lower in asymptomatic patients than in symptomatic patients, the risk of new emboli developing as a result of the procedure should also be considered in asymptomatic patients (24). It is also suggested that these patients be followed up with medical treatment only if it is deemed necessary, depending on an individual patient's other risk factors, degree of stenosis, and plaque characteristics (21).

CONCLUSION

One of the most serious consequences of CAS is asymptomatic or symptomatic periprocedural cerebral embolism. Silent cerebral embolism associated with CAS has been linked to dementia, cognitive decline, and potentially ischemic stroke in later life. In the current study, we compared periprocedural cerebral DWI findings from CS-related carotid plaques classified into different groups. The findings show that the carotid stents implanted in calcified and ulcerated plaques had a higher correlation with the presence of periprocedural asymptomatic ipsilateral DWI findings than those implanted in hypoechoic and low-echogenicity plaques.

AUTHORSHIP CONTRIBUTION

Study conception and design: BA

Data collection: BA, UG, RD

Analysis and interpretation of results: BA

Draft manuscript preparation: BA, UG

Critical revision of the article: BA, UG

Other (study supervision, fundings, materials, etc...): BA, UG, RD, GO

All authors (BA, UG, RD, GO) reviewed the results and approved the final version of the manuscript.

REFERENCES

1. Akmangit I, Sayin B, Karaman A, Daglioglu E, Arli B, Sahin MH, Orhan G: Endovascular stroke therapy focused on direct clot aspiration using the SOFIA TM catheter for acute ischemic stroke. Turkish Neurosurg 32(5):720-726, 2022
2. Almekhlafi MA, Demchuk AM, Mishra S, Bal S, Menon BK, Wiebe S, Clement FM, Wong JH, Hill MD, Goyal M: Malignant emboli on transcranial Doppler during carotid stenting predict postprocedure diffusion-weighted imaging lesions. Stroke 44: 1317-1322, 2013
3. Barbato JE, Dillavou E, Horowitz MB, Jovin TG, Kanal E, David S, Makaroun MS: A randomized trial of carotid artery stenting with and without cerebral protection. J Vasc Surg 47: 760-765, 2008
4. Bonati LH, Jongen LM, Haller S, Flach HZ, Dobson J, Nederkoorn PJ, Macdonald S, Gaines PA, Waaijer A, Stierli P, Jäger HR, Lyrer PA, Kappelle LJ, Wetzel SG, van der Lugt A, Mali WP, Brown MM, van der Worp HB, Engelter ST; ICSS-MRI study group: 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, 2010
5. Centers for Disease Control and Prevention (CDC): Prevalence of stroke-United States, 2005. MMWR Morb Mortal Wkly Rep 56:469-474, 2007
6. Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, de Borst GJ, Lo TH, Gaines P, Dorman PJ, Macdonald S, Lyrer PA, Hendriks JM, McCollum C, Nederkoorn PJ, Brown MM: Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): An interim analysis of a randomised controlled trial. Lancet 375:985-997, 2010
7. Enomoto Y, Yoshimura S: Antiplatelet therapy for carotid artery stenting. Interv Neurol 1(3-4):151-163, 2013
8. Faggioli G, Ferri M, Rapezzi C, Tonon C, Manzoli L, Stella A: Atherosclerotic aortic lesions increase the risk of cerebral embolism during carotid stenting in patients with complex aortic arch anatomy. J Vasc Surg 49:80-85, 2009
9. 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: Ischemic brain lesions after carotid artery stenting increase future cerebrovascular risk. J Am Coll Cardiol 65:521-529, 2015
10. Hammer FD, Lacroix V, Duprez T, Grandin C, Verhelst R, Peeters A, COSNARD G: Cerebral microembolization after protected carotid artery stenting in surgical high-risk patients: Results of a 2-year prospective study. J Vasc Surg 42(5):847-853, 2015
11. Hajiyev K, Hellstern V, Cimpoca A, Wendl C, Bäzner H, Henkes H, von Gottberg P: Carotid artery stenting in patients with symptomatic and asymptomatic stenosis: In-hospital clinical outcomes at a single neurovascular center. J Clin Med 11(8):2086, 2022
12. Hunt JL, Fairman R, Mitchell ME, Carpenter JP, Golden M, Khalapyan T, Wolfe M, Neschis D, Milner R, Scoll B, Cusack A, Mohler 3rd ER: Bone formation in carotid plaques: A clinicopathological study. Stroke 33:1214-1219, 2002
13. Interventional procedures guidance. April 27, 2011. Available at: https://www.nice.org.uk/guidance/ipg389/chapter/3-Further-information. Accessed September 22, 2022
14. Inzitari D, Eliasziw M, Gates P, Sharpe BL, Chan RK, Meldrum HE, Barnett HJ: The causes andrisk of stroke in patients with asymptomatic internalcarotid-artery stenosis. N Engl J Med 342:1693-1670, 2000
15. Kastrup A, Gröschel K, Nägele T, Riecker A, Schmidt F, Schnaudigel S, Ernemann U: Effects of age and symptom status on silent ischemic lesions after carotid stenting with and without the use of distal filter devices. AJNR Am J Neuroradiol 29:608-612, 2008
16. Macdonald S, Evans DH, Griffiths PD, McKevitt FM, Venables GS, Cleveland TJ, Gaines PA: Filter-protected versus unprotected carotid artery stenting: A randomised trial. Cerebrovasc Dis 29:282-289, 2010
17. Mantese VA, Timaran CH, Chiu D, Begg RJ, Brott TG; CREST Investigators: The carotid revascularization endarterectomy versus stenting trial (CREST) stenting versus carotid endarterectomy for carotid disease. Stroke 41 Suppl 10: S31-S34, 2010

18. Marquardt L, Geraghty OC, Mehta Z, Rothwell PM: Low risk of ipsilateral stroke in patients with asymptomatic carotid stenosis on best medical treatment: A prospective, population-based study. Stroke 41(1):e11-e17, 2010
19. Mazurek A, Partyka L, Trystula M, Jakala J, Proniewska K, Borratynska A, Tomaszewski T, Slezak M, Malinowski KP, Drazkiewicz T, Podolec P: Highly-calcific carotid lesions endovascular management in symptomatic and increased-stroke-risk asymptomatic patients using the CGuard™ dual-layer carotid stent system: Analysis from the PARADIGM study. Catheter Cardiovasc Interv 94:149-156, 2019
20. Meschia JF, Bushnell C, Boden-Albala B, Braun LT, Bravata DM, Chaturvedi S, Creager MA, Eckel RH, Elkind MSV, Fornage M, Goldstein LB, Greenberg SM, Horvath SE, Iadecola C, Jauch EC, Moore WS, Wilson JA; American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; Council on Functional Genomics and Translational Biology; Council on Hypertension: Guidelines for the primary prevention of stroke: A statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 45:3754-3832, 2014
21. Mohd AB, Alabdallat Y, Mohd OB, Ghannam RA, Sawaqed S, Hasan H, Ellebedy M, Turkmani K, Al-Ezzi S: Medical and surgical management of symptomatic and asymptomatic carotid artery stenosis: A comprehensive literature review. Cureus 15(8):e43263, 2023
22. Montorsi P, Caputi L, Galli S, Ciceri E, Ballerini G, Agrifoglio M, Ravagnani P, Trabattoni D, Pontone G, Fabbiocchi F, Loaldi A, Parati E, Andreini D, Veglia F, Bartorelli AL: Microembolization during carotid artery stenting in patients with high-risk, lipid-rich plaque. A randomized trial of proximal versus distal cerebral protection. J Am Coll Cardiol 58:1656-1663, 2011
23. Nakagawa I, Kotsugi M, Park HS, Furuta T, Sato F, Myochin K, Nishimura F, Yamada S, Motoyama Y, Nakase H: Near-infrared spectroscopy carotid plaque characteristics and cerebral embolism in carotid artery stenting. EuroIntervention 17:599-606, 2021
24. Naylor R, Rantner B, Ancetti S, de Borst GJ, De Carlo M, Halliday A, Kakkos SK, Markus HS, McCabe DJH, Sillesen H, van den Berg JC, de Ceniga MV, Venermo MA, Vermassen FEG, Esvs Guidelines Committee, Antoniou GA, Goncalves FB, Bjorck M, Chakfe N, Coscas R, Dias NV, Dick F, Hinchliffe RJ, Kolh P, Koncar IB, Lindholt JS, Mees BME, Resch TA, Trimarchi S, Tulamo R, Twine CP, Wanhainen A, Document Reviewers, Bellmunt-Montoya S, Bulbulia R, Darling 3rd RC, Eckstein HH, Giannoukas A, Koelemay MJW, Lindström D, Schermerhorn M, Stone DH: Editor's Choice–European Society for Vascular Surgery (ESVS) 2023 clinical practice guidelines on the management of atherosclerotic carotid and vertebral artery disease. Eur J Vasc Endovasc Surg 65(1):7-111, 2023
25. Nii K, Tsutsumi M, Aikawa H, Hamaguchi S, Etou H, Sakamoto K, Kazekawa K: Incidence of hemodynamic depression after carotid artery stenting using different self-expandable stent types. Neurol Med Chir (Tokyo) 51(8):556-560, 2011
26. Onal Y, Velioglu M, Demir U, Celikoglu E, Karakas HM: Feasibility of distal mechanical thrombectomy in m3, a3, and p3 segments via a 0.013-inch delivery system: Preliminary experience. Turk Neurosurg 30(4):614-620, 2020
27. Pendlebury S, Rothwell P: Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: A systematic review and meta-analysis. Lancet Neurol 8:1006-1018, 2009
28. Rangel-Castilla L, Rajah GB, Shakir HJ, Davies JM, Snyder KV, Siddiqui AH, Siddiqui AH, Levy EI, Hopkins LN: Endovascular prevention and treatment of stroke related to extracranial carotid artery disease. J Cardiovasc Surg (Torino) 58:35-48, 2017
29. Rosamond W, Flegal K, Furie K, Go A, Greenlund K, Haase N, Hailpern SM, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell C, Roger V, Sorlie P, Steinberger J, Thom T, Wilson M, Hong Y: Heart disease and stroke statistics 2008 update a report from the american heart association statistics committee and stroke statistics subcommittee. Circulation 117:e25-e146, 2008
30. Saxena A, Ng EYK, Lim ST: Imaging modalities to diagnose carotid artery stenosis: Progress and prospect. Biomed Eng Online 18:66, 2019
31. Schnaudigel S, Gröschel K, Pilgram SM, Kastrup A: New brain lesions after carotid stenting versus carotid endarterectomy: A systematic review of the literature. Stroke 39:1911-1919, 2008
32. Stabile E, Sannino A, Schiattarella GG, Gargiulo G, Toscano E, Brevetti L, Scudiero F, Giugliano G, Perrino C, Trimarco B, Esposito G: Cerebral embolic lesions detected with diffusion-weighted magnetic resonance imaging following carotid artery stenting: A meta-analysis of 8 studies comparing filter cerebral protection and proximal balloon occlusion. JACC Cardiovasc Interv 7:1177-1183, 2014
33. Stojanov D, Ilic M, Bosnjakovic P, Zivkovic M, Jolic S, Vukasinovic N, Ignjatovic A, Ilic B, Benedeto-Stojanov D: New ischemic brain lesions on diffusion-weighted MRI after carotid artery stenting with filter protection: Frequency and relationship with plaque morphology. AJNR Am J Neuroradiol 33:708-714, 2012
34. Traenka C, Engelter ST, Brown MM, Dobson J, Frost C, Bonati LH: Silent brain infarcts on diffusion-weighted imaging after carotid revascularisation: A surrogate outcome measure for procedural stroke? A systematic review and meta-analysis. Eur Stroke J 4:127-143, 2019
35. Tulip HH, Rosero EB, Higuera AJ, Ilarraza A, Valentine RJ, Timaran CH: Cerebral embolization in asymptomatic versus symptomatic patients after carotid stenting. J Vasc Surg 56: 1579-1584, 2012
36. Wissgott C, Brandt-Wunderlich C, Kopetsch C, Schmidt W, Andresen R: Initial clinical results and in vitro testing of the new cguard micronet-covered "one-size-fits-all" carotid stent. J Endovasc Ther 26:578-582, 2019
37. Xu X, Feng Y, Bai X, Ma Y, Wang Y, Chen Y, Yang B, Ling F, Zhang X, Jiao L: Risk factors for silent new ischemic cerebral lesions following carotid artery stenting. Neuroradiology 62: 1177-1184, 2020