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ORIGINAL ARTICLE

Importance of brain MRI to evaluate immediate intracranial complications after carotid stenting in patients with significant carotid stenosis

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Abstract

Objective: *This prospective study aimed to fill the current knowledge gap in the literature by identifying the demographic and clinical characteristics of patients with carotid stenosis who undergo carotid arterial stenting.* **Methods:** *A cohort of 49 patients who underwent carotid artery stenting (CAS) from January 2021 to August 2022 was analyzed. Demographic information and data related to the existence of adverse neurological events were collected.* **Results:** *Stent placement achieved a 93.8% success rate when measured using the NASCET measurement criteria. Post-CAS neuroimaging revealed multifocal diffusion-weighted imaging (DWI) restriction in 8.16% of patients, hypointensity on susceptibility-weighted imaging in 8.16%, and focal DWI restriction in 32.65%, with no clinically significant deficits observed. A statistically significant association (p = 0.015) between severe stenosis and multifocal neuroimaging events was observed.* **Conclusions:** *Neurological complications observed by neuroimaging after CAS were not an indicator of an increased risk of clinically important adverse events at follow-up.*

Keywords: *Carotid stenosis. Self expandable metallic stents. Magnetic resonance spectroscopy. Radiology. Interventional.*

Importancia de la RM cerebral para evaluar las complicaciones intracraneales inmediatas después de la colocación de un stent carotídeo en pacientes con estenosis carotídea significativa

Resumen

Objetivo: *Este estudio prospectivo tuvo como objetivo llenar el vacío de conocimiento actual en la literatura mediante la identificación de las características demográficas y clínicas de los pacientes con estenosis carotídea que se someten a la colocación de stents arteriales carotídeos.* **Métodos:** *Se analizó una cohorte de 49 pacientes sometidos a stent arterial carotídeo (CAS) entre enero de 2021 y agosto de 2022. Se recogió información demográfica y datos relacionados con la existencia de eventos neurológicos adversos.* **Resultados:** *La colocación del stent alcanzó una tasa de éxito del 93,8% cuando se midió utilizando los criterios de medición NASCET. La neuroimagen posterior al NASCET reveló una restricción multifocal en la imagen ponderada por difusión (DWI) en el 8.16% de los pacientes, hipointensidad en la imagen ponderada por susceptibilidad (SWI) en el 8,16% y restricción focal en la DWI en el 32,65%, sin que se observaran déficits clínicamente*

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significativos. Se observó una asociación estadísticamente significativa (p = 0.015) entre la estenosis grave y los eventos de neuroimagen multifocales. **Conclusiones:** *Las complicaciones neurológicas observadas por neuroimagen después de la EAC no fueron un indicador de un mayor riesgo de eventos adversos clínicamente importantes durante el seguimiento.*

Palabras clave: *Estenosis carotídea. Stent metálico autoexpandible. Espectroscopia por resonancia magnética. Radiología. Intervencionismo.*

Introduction

Ischemic stroke has become a major global health problem, due to its high prevalence and the significant social and economic impact attributed to it. Regarded as a medical emergency, comparable to acute ischemic heart disease, the incidence of stroke within the European population is approximately 186.96 cases/100,000 inhabitants annually. Notably, 87% of these cases are ischemic strokes, with the remaining incidents attributed to cerebral hemorrhages (10%) and subarachnoid hemorrhages (3%)[1].

A primary contributor to ischemic strokes is extracranial carotid artery stenosis (CAS). This condition is characterized by severe atherosclerosis in the carotid arteries, significantly elevating the risk of subsequent strokes[2]. Such stenosis can induce cerebral hypoperfusion, potentially leading to brain atrophy, dementia, or cognitive impairment[3]. To mitigate the risk of further strokes in patients with CAS, carotid revascularization procedures, such as carotid endarterectomy (CEA) and CAS, are employed. CEA, considered the gold standard, is particularly effective in patients with low morbidity and mortality rates < 6% in symptomatic patients and under 3% in asymptomatic individual[4]. In contrast, CAS, noted for its rapid recovery, minimal surgical risks, and continuous neurological monitoring during the procedure, has gained popularity, especially among high-risk patients.

CAS offers several advantages over traditional surgical techniques: a recovery period of merely 24 h, reduced hospital stay, no risk of cranial nerve damage in the neck, and less surgical invasiveness. The patient remains conscious throughout the procedure, allowing for continuous neurological monitoring and observation of carotid blood flow. Due to these benefits, CAS has been widely adopted, particularly in patients with elevated surgical risks.

The study's principal objective is to examine neuroimaging changes in patients with carotid stenosis, both pre- and post-revascularization and to evaluate the impact of new neurological events, as observed through neuroimaging post-procedure, differentiating between asymptomatic and symptomatic cases.

Materials and methods

Study design

Prospective single-center study from November 2021 to May 2022, was approved by the local ethical committee (reference number: C.P.-C.I. PI20/126) and was carried out in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants for both the procedure and the study. The primary outcome was technical success objectively assessed by post-CAS angiography. Secondary outcomes evaluated CAS-related complications by comparing pre- and post-CAS treatment brain magnetic resonance imaging (MRI).

Study population and eligibility

From November 2021 to May 2022, a total of 49 consecutive patients were performed with the intention of CAS. All patients had CAS with or without contralateral stenosis. Stenosis was documented by neck duplex ultrasound, computed tomography angiography, or MR angiography.

Patients were selected according to the following inclusion and exclusion criteria.

Inclusion criteria

Age over 18 years without upper limit, symptomatic stenosis > 50% demonstrated by imaging tests and angiography; or asymptomatic stenosis > 70% and more than one risk factor for future embolism (progressive carotid stenosis) confirmed by Doppler study of the supra-aortic trunks or magnetic resonance angiography, transient ischemic attack, or ischemic stroke occurring in the supply area blood from the ipsilateral carotid artery in the past 6 months and complying with the indications for CAS.

Exclusion criteria

The existence of dementia caused by other reasons (such as Alzheimer's disease), people with problems of consciousness or confusion without the ability to cooperate, subarachnoid hemorrhage, cerebral hemorrhage or history of intracranial tumor, people with neuropsychiatric diseases, hydrocephalus, claustrophobia or inability to perform a brain MRI.

CAS pretreatment assessment

The pretreatment evaluation included assessment of the degree of stenosis using non-invasive imaging, neurological evaluation (NIH Stroke Scale) performed by a neurologist with more than 15 years of experience in the treatment and follow-up of stroke patients, laboratory results, and a 12-lead electrocardiogram.

Patients received antiplatelet therapy with oral enteric-coated aspirin (100 mg/day) and clopidogrel (75 mg/day) per day at least 3 days before the procedure to reduce periprocedural platelet embolism. Patients using long-term anticoagulation changed their treatment to heparin.

CAS procedure protocol

All CAS procedures were performed by two interventional radiologists with extensive experience in endovascular techniques. The endovascular procedure was performed with local anesthesia at the puncture site and conscious sedation for continuous neurological monitoring of the patient. The technique used in previous studies[5].

Through a femoral approach, selective carotid angiography was performed using a 5F diagnostic catheter (Seldinger technique). Standard anteroposterior and lateral intracranial views were obtained in all cases to establish the adequacy of the intracranial collateral circulation through the external carotid and anterior communicating arteries and to document any intracranial stenotic lesions. The location, length and degree of stenosis, flow compensation through the circle of Willis, and the presence of anastomosis between the internal and external carotid arteries were evaluated. To maintain activated clotting time during the procedure, a bolus of intravenous heparin (5000-7000 IU) was administered.

A 0.035-inch guidewire (Terumo Medical Corporation, USA) was advanced through a spinal microcatheter (5F) to engage the stump of the internal carotid artery internal stenosis. After confirming the tip in the distal true lumen with multiple angiographic projections with Ioversol 320 mg (optiray guerbet) with a flow rate of 12 mL and 4 cc/s. An embolic protection device (EPD) (Emboshield, Abbott Vascular, Santa Clara, CA, USA) was advanced and deployed distally if the anatomical conditions and degree of stenosis permitted. A self-expanding stent (Acculink, Abbott Vascular, Santa Clara, CA, USA) was placed across the stenosis, usually a 6-8 mm × 40 mm cone-shaped stent. Finally, a final intracranial angiogram was obtained to confirm antegrade perfusion and evaluate residual stenosis.

Depending on the operators, the decision was made to postdilate the lesion using balloon angioplasty. The decision was made to predilate in cases where it was impossible to cross the stenosis with the protection system and/or stent system. After stent placement, anteroposterior and lateral cerebral angiograms were obtained to exclude any embolic branch occlusion and document new flow patterns. Technical success was defined as a final residual diameter stenosis < 50% with distal antegrade filling of the middle cerebral and anterior cerebral arteries after the intervention. Residual stenosis was measured using the NASCET measurement criteria.

After the procedure, percutaneous closure devices were used to remove the femoral sheath. All patients were monitored in the neurology unit for 24-48 h after treatment. Antiplatelet agents were administered after the procedure using clopidogrel 75 mg for 4-6 weeks and aspirin 100 mg indefinitely.

The technical success of the CAS stent was defined as the ability to recanalize stenotic carotid lesions and correct deployment of the stent with better cerebral blood flow compared to the subsequent angiographic study.

Pre-CAS and post-CAS brain MRI evaluation

All 49 patients underwent brain MRI (Ingenia S 1.5T; Philips, Germany) with the following weighted sequences: T1, T2, FLAIR, diffusion, and susceptibility-weighted images. Brain MRI and MRI angiography were performed 24 or 48 h before CAS and follow-up MRI imaging 24 h after CAS.

The degree of stenosis was defined as mild (0-50%), moderate (50-70%), and severe (more than 70%) according to the European Carotid Surgery Trial criteria.

Based on the imaging findings observed on post-procedure MRI, patients were classified into the following categories:

- Absence of adverse neurological findings: if the patient does not present new images in the post-procedure brain MRI.

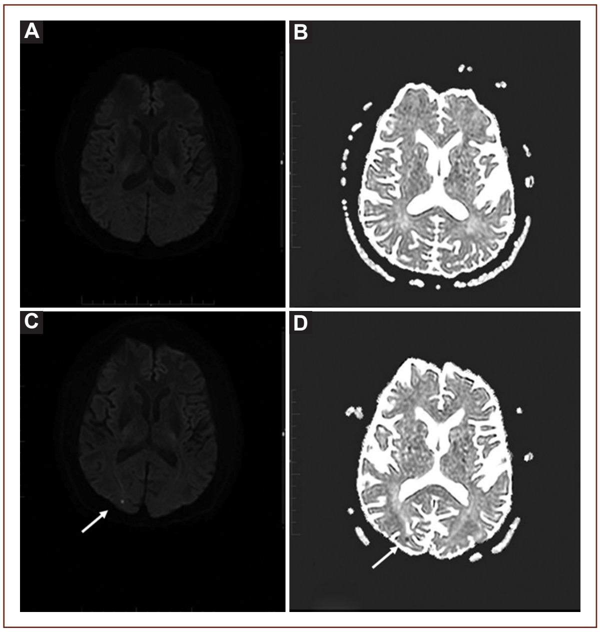

Figure 1. A: magnetic resonance imaging of the brain with diffusion-weighted imaging, and the apparent diffusion coefficient map (**B**). It was conducted 24 h before the placement of the right carotid stent, showing no significant findings. **C** and **D**: a white arrow indicates an area with focal restricted fluid diffusion located in the right occipital hemisphere, performed 24 h after the insertion of the left carotid stent.

Table 1. Demographic data of the study sample

Variable	Patients (n = 49) (%)
Age (years)	71.52 ± 9.52
Sex	
Male	40/49 (81.6)
Risk factors	
Hypertension	42/49 (85.7)
Dyslipidemia	43/49 (87.7)
Diabetes mellitus	25/49 (51)
Smoking	28/49 (57)
Cardiac arrhythmias-atrial fibrillation	15/49 (30.6)
Chronic kidney disease	11/49 (22.4)
Cervical radiation therapy	4/49 (8.16)
Neuroimaging findings 24 h	
No events	25/49 (51)
Focal restriction DWI	16/49 (32.65)
Multifocal restriction DWI	4/49 (8.16)
Hypointensity susceptibility-weighted imaging	4/49 (8.16)
Right or left carotid stenting	
Right internal carotid artery	23/49 (47)
Left internal carotid artery	26/49 (53)
RICA stenosis	
Moderate	3/49 (6.1)
Severe	20/49 (40.8)
LICA stenosis	
Moderate	8/49 (16.3)
Severe	18/49 (36.7)

DWI: diffusion-weighted imaging.

- Focal ischemia: it was defined as small ischemic areas not visualized in the brain MRI before CAS belonging to a single vascular territory (Fig. 1).
- Multifocal ischemia: visualization of ischemic areas not visualized in the brain MRI before CAS belonging to more than one vascular territory (Fig. 2).
- Cerebral microhemorrhage: visualization of hemorrhagic or microhemorrhagic areas not seen on brain MRI before CAS (Fig. 3).

Statistic analysis

To describe the different qualitative variables of the sample, absolute frequencies (n) and relative frequencies expressed in percentages (%) were used. For the quantitative variables, the mean and standard deviation were calculated.

For the inferential analysis and to determine the association between qualitative variables, the Pearson $\chi 2$ test (X2) or the likelihood ratio test was used. By analyzing the association between a qualitative and quantitative variable, the normality of the sample was determined. If the hypothesis of normality was not rejected, parametric tests were used to compare means: Student's t for independent samples in the case of two means and analysis of variance in cases where there were more than two means.

The level of significance (α error) was set in all cases at 0.05 for a confidence level of 95%. All statistical calculations and analyzes were performed with the statistical analysis program IBM Statistical Package for the Social Sciences 22.0 for Windows.

Results

A total of 49 patients with a mean age of 71.52 years (range 50-90) were treated with CAS. Patient demographics, risk factors, and morbidities are listed in (Table 1).

Technical success was achieved in 93.8% (46/49) of intervened carotids. Protective devices were used in 75.5% (37/49) of patients. Post-stent balloon dilation was performed in 93.8% of patients (46/49), with predilation being necessary in 14.2% (7/49).

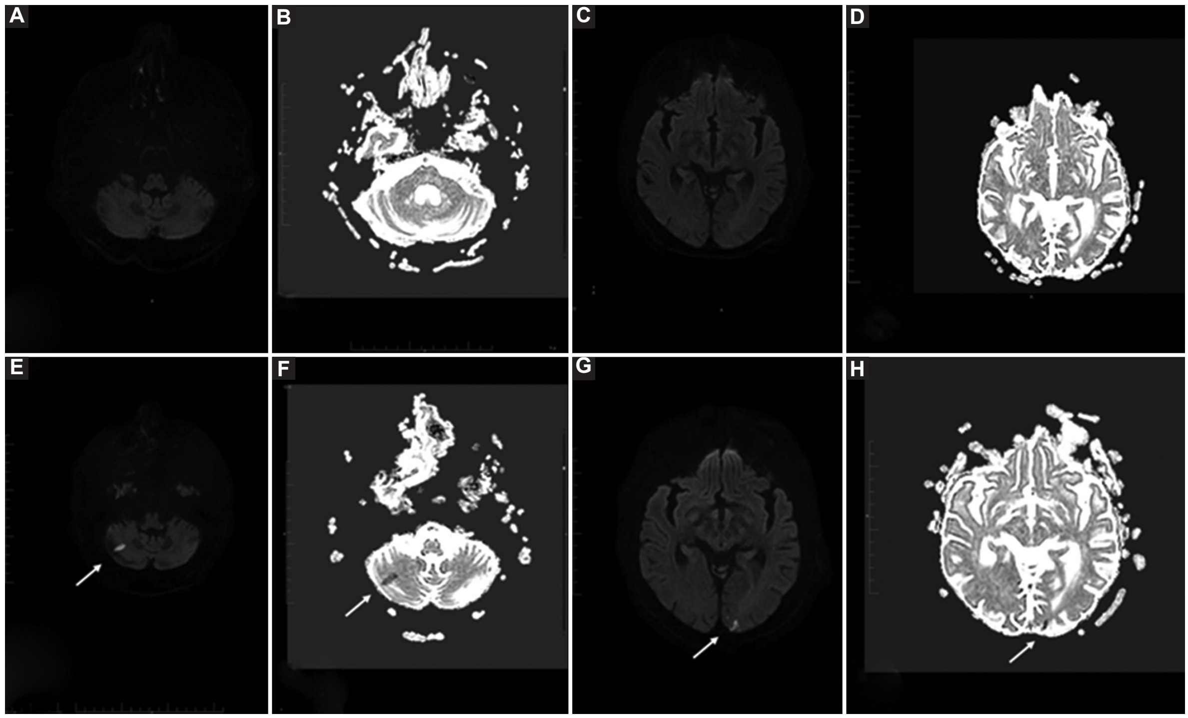

Figure 2. Magnetic resonance imaging of the brain with diffused weighted imaging (**A** and **C**), and apparent diffusion coefficient maps (**B** and **D**), performed 24 h before placement of the left carotid stent. No important findings are seen in the supratentorial and infratentorial. **E-H:** white arrows indicate multifocal areas with restriction of fluid diffusion located in the right cerebellar hemisphere and in the left occipital cortico-subcortical region, performed 24 h after left carotid stenting. No relevant clinical symptoms were observed in this patient.

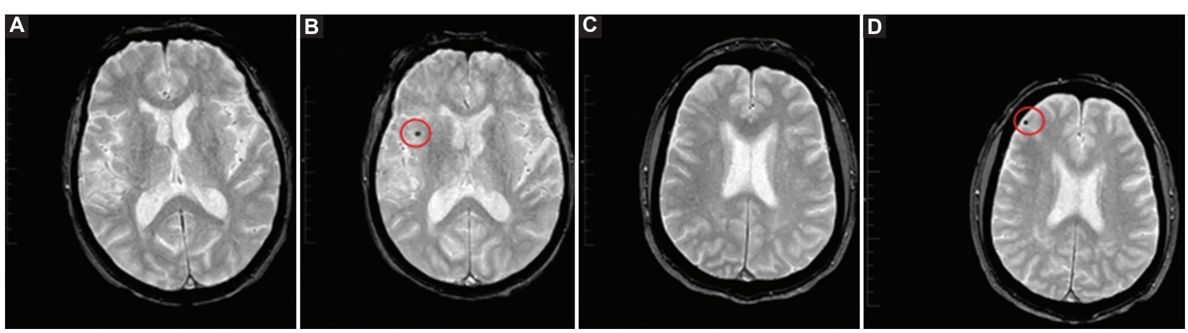

Figure 3. A: brain magnetic resonance imaging study with gradient echo sequence, performed 24 h before insertion of the right carotid stent. No significant findings were seen in the supratentorial sections. **B-D:** a red circle indicates a punctate area, compatible with a focal hypointensity in susceptibility weighted imaging area located in the right hemisphere, performed 24 h after right carotid stenting. No relevant clinical symptoms were observed in this patient.

Regarding the neurological events observed by neuroimaging after CAS, multifocal ischemia occurred in 4/49 patients (8.16%), microbleeds in another 4/49 patients (8.16%), and focal ischemia in 16/49 patients (32.65%), although none of the patients reported a relevant clinical deficit. The degree of stenosis demonstrated a statistically significant correlation ($p = 0.015$) with the appearance of adverse neurological events manifested after CAS in neuroimaging (Table 2), so patients who presented post-procedural ischemia were more likely to

Table 2. Influence of the degree of stenosis and MRI findings

Variable	No MRI findings			Focal restriction DWI			Multifocal restriction DWI			Hypointensity susceptibility-weighted imaging		
	n	%	p	n	%	p	n	%	p	n	%	p
Moderate stenosis (50-70%)	8/13	61.50	$0.427^{\chi 2}$	3/13	23.10	$0.376^{\chi 2}$	0/13	0%	$0.015^{\chi 2}$	2/13	15.30	$0.279^{\chi 2}$
Total cases of moderate stenosis	13			13			13			13		
Severe stenosis (> 70%)	17/36	47.20		13/36	36.10		4/36	11.10		2/36	5.50	
Total cases of severe stenosis	36			36			36			36		

MRI: magnetic resonance imaging.

have a high grade of stenosis. All patients who presented multifocal ischemia (n = 4) had a stenosis > 70%.

Middle cerebral artery involvement represented 20.8% of the sample with 10 patients, compared to 79.2% (n = 38) who did not have middle cerebral artery involvement.

The procedure time measured in minutes was an average of 44.33 min with a range between 26 and 89 min.

On the NIHHS scale upon admission, the most frequent values were 0, n = 36 (75%); 1, n = 2 (4.2%); 2, n = 2 (4.2%); 5, n = 2 (4.2%); 9, n = 2 (4.2%); while the predominant results at discharge were values 0, n = 37 (77.1%); 1, n = 6 (12.5%); 2, n = 2 (4.2%), which shows an improvement in the neurological status compared to the values upon the patients' arrival at our center.

A total of 3/49 patients (6.12%) died in this 12-month follow-up period. Of these patients, only 1 case occurred due to a neurological etiology, due to an ipsilateral stroke of the treated carotid artery, more than 30 days after CAS implantation. The rest of the cases were due to other non-neurological causes in relation to the patients' comorbidities. A survival of 94.23% of the sample was demonstrated 1 year after carotid stent implantation.

Discussion

Carotid revascularization is a widely used endovascular procedure for stroke prevention. Some studies have been published to evaluate factors associated with embolization during CAS, either using transcranial Doppler ultrasound or comparing imaging studies before and after stent placement. In all of them, the risks of the procedure are associated with comorbidities, unfavorable anatomy, and the characteristics of the injury[6,7]. In a study of 728 patients published by Bijuklic et al.[8], the rate of new brain lesions was analyzed in patients with carotid stenosis, undergoing CAS with EPD, using diffusion MRI, as in our study. The frequency of new ipsilateral ischemic lesions was 33% (241/728), associated with advanced age and HBP, and only 5% (37/72) of patients who showed an alteration in diffusion MRI developed clinical neurological deficits.

In the current study, the results of ischemic complications were somewhat higher, being 40.81% (20/49), including within this percentage small focal and multifocal ischemias in white matter, clinically irrelevant. The complications evidenced by microhemorrhagic neuroimaging were along the same lines somewhat higher, being 8.16% (4/49), compared to the study by Bijuklic et al. (5.8%)[8], although none of our patients reported a relevant clinical deficit.

The only factors that influenced the appearance of post-procedural complications were cardiac arrhythmias and the presence of dyslipidemia (Table 3). The most plausible explanation is that these patients have a higher risk of stroke, since the possibility of releasing thrombi of atheromatous plaque, with the consequent embolic phenomenon, is higher than in patients without these risk factors.

Table 3. Influence of different clinical risk factors on the presentation of adverse neurological events

Variable	No magnetic resonance imaging findings				Focal restriction DWI				Multifocal restriction DWI				Hypointensity susceptibility-weighted imaging			
	N/Y	n	%	p^{RV}	N/Y	n	%	p^{RV}	N/Y	n	%	p^{RV}	N/Y	n	%	p^{RV}
Hypertension	No	4	57.1	0.606	No	2	28.6	0.892	No	1	14.3	0.482	No	0	0	0.412
	Yes	21	46.7		Yes	14	31.1		Yes	3	6.7		Yes	4	8.9	
Dyslipidemia	No	1	14.3	0.054	No	3	42.9	0.074	No	0	0	0.074	No	2	28.6	0.026
	Yes	24	53.3		Yes	13	28.9		Yes	4	8.9		Yes	2	4.4	
Diabetes mellitus	No	14	56	0.271	No	7	28	0.677	No	1	4	0.336	No	2	8	0.936
	Yes	11	40.7		Yes	9	33.3		Yes	3	11.1		Yes	2	7.4	
Smoking	No	9	39.1	0.250	No	8	34.8	0.577	No	2	8.7	0.809	No	2	8.7	0.809
	Yes	16	55.2		Yes	8	27.6		Yes	2	6.9		Yes	2	6.9	
Cardiac arrhythmias	No	20	54.1	0.175	No	10	27	0.358	No	0	0	0.001	No	4	10.8	0.007
	Yes	5	33.3		Yes	6	40		Yes	4	26.7		Yes	0	0	
Chronic kidney disease	No	18	45	0.417	No	13	32.5	0.622	No	4	10	0.254	No	3	7.5	0.924
	Yes	7	58.3		Yes	3	25		Yes	0	0		Yes	1	8.3	
Cervical radiation therapy	No	23	47.9	0.936	No	14	29.2	0.386	No	4	8.3	0.548	No	4	8.3	0.548
	Yes	2	50		Yes	2	50		Yes	0	0		Yes	0	0	

DWI: diffusion-weighted imaging.

73.1% of the patients in our study had a stenosis > 70%. In the majority of cases in which some metabolic or non-metabolic risk factor was present, there was a stenosis > 70%, highlighting its presence in 71.1% of patients with HTN and 75.9% of patients with a habit. Smoking, these findings can be considered a risk factor for carotid stenosis, although like the other risk factors they did not show a statistical association with the degree of stenosis.

Regarding the analysis that related the degree of stenosis and the presentation of new adverse neurological events observed by neuroimaging after revascularization with CAS, ischemia had statistically significant results, so we can affirm that patients who presented ischemia after the procedure had more probability of having high-grade stenosis > 70%. In fact, all patients targeted for new-onset ischemia after CAS had > 70% stenosis, although the number of patients was small (n = 4).

In the present study, neuroimaging neurological complications after CAS were not an indicator of an increased risk of clinically important adverse events at follow-up. The same happened with other well-known risk factors such as diabetes, smoking, or hypertension.

Conclusion

This study reveals that neurological complications objectified by neuroimaging after CAS were not an indicator of a higher risk of clinically important adverse events in the follow-up. The same happened with other risk factors well known such as diabetes, smoking, or hypertension. MRI may overestimate neuroimaging findings following CAS that might ostensibly indicate ischemic or hemorrhagic pathology; however, fortunately, in our study, these findings were not clinically relevant.

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The authors declare that this work was carried out with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical responsibilities

Protection of people and animals. The authors declare that no experiments have been carried out on humans or animals for this research.

Data confidentiality. The authors declare that they have followed their workplace's protocols regarding the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Use of artificial intelligence to generate texts. The authors declare that they have not used any type of generative artificial intelligence in the writing of this manuscript or for the creation of figures, graphs, tables, or their corresponding captions or legends.

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