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Treatment results of carotid artery stenting in a developing country

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SUMMARY

OBJECTIVE: The purpose of this study was to investigate the details of minor complications of carotid artery stenting in a developing country.

METHODS: This was a retrospective, single-center study conducted on the target group consisting of 65 symptomatic patients who underwent carotid artery stenting. We assessed technical success rate, periprocedural complication within 30 days (hypotension, bradycardia, acute kidney injury, vasospasm, a transient ischemic attack, stroke, myocardial infarction, and death), and the differences between groups with and without complications.

RESULTS: Minor periprocedural complications occurred in 15 patients. In all, 8 (12.3%) had transient hypotension, 6 (9.2%) had bradycardia, 7 (10.7%) had acute kidney injury, 2 (3.1%) had vasospasm, and 1 (1.5%) had transient ischemic attack. A greater rate of minor complications was observed in women (p=0.051).

CONCLUSION: The results of the carotid artery stenting procedures performed in a developing country were acceptable.

KEYWORDS: Risk. Complications. Carotid artery diseases. Stents.

INTRODUCTION

Carotid artery stenting (CAS) is considered an alternative to carotid endarterectomy (CEA) for symptomatic patients when the rate of periprocedural stroke or death is <6%, the risk of complications is considered to be at average or low, and the stenosis of the internal carotid artery (ICA) is more than 50% by digital subtraction angiography or noninvasive neuroimaging, according to the American Heart Association/American Stroke Association guidelines (Recommendation Class IIa, Level B)[1].

Therefore, to perform CAS as an intervention to prevent recurrent strokes, it is necessary to determine whether the risk of periprocedural stroke or death is <6% within the center where the procedure will be carried out. Most of the information about the risks of CAS originates from studies conducted in developed countries, and there is a gap in information about rates of complications in developing countries[2-8].

Previously, we reported the rates of major and minor periprocedural complications of CAS in 65 patients with symptomatic carotid stenosis at a reference academic hospital in São Paulo, Brazil[9]. The rate of stroke, myocardial infarction (MI), or death was 4.6%, similar to reports in the real-world series or clinical trials (2–9%)[5,6,10]. So far, few studies reported the details of treatment results after CAS in developing or developed countries[5,8,11].

We extended our investigation by explaining, in the same dataset, the types of minor complications. Also, we compared demographic characteristics, risk factors, use of antithrombotic drugs, and types of cerebrovascular events between patients with and without major or minor complications.

METHODS

Study design

This is a retrospective, single-center study that evaluated medical records of consecutive patients submitted to CAS for the treatment of symptomatic carotid stenosis at a university hospital in a developing country.

Subjects

Inclusion criteria include age 18 years or above, CAS performed according to the institutional protocol (see Supplementary material) and follow-up by neurologists.

Exclusion criterion includes a lack of follow-up by neurologists.

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Information retrieved from medical records were as follows: age, gender, ethnicity, comorbidities (hypertension, diabetes, hypercholesterolemia, cardiopathy, coagulopathy, smoking, prior stroke); days between the onset of symptoms and the procedure; the use of antiplatelet or anticoagulant drugs; the type of cerebrovascular event (stroke or TIA); and the National Institutes of Health Stroke Scale (NIHSS) scores. These scores, if not recorded in medical records, were calculated based on the neurological examination described in medical records[12].

Outcomes

We described the rates of different types of minor complications after the procedure: TIA, hypotension, vasospasm, bradycardia, ICA dissection, and acute kidney injury (AKI) (creatinine blood levels>1.5×baseline)[13] during the first 96 h after the procedure. The severity of AKI was classified according to the Acute Kidney Injury Network (AKIN)[13]. Complications were assessed according to notes from medical records, until hospital discharge. Major complications were stroke, MI, or death during the periprocedural period[1].

In addition, we compared demographic characteristics; risk factors; the use of aspirin, clopidogrel, or anticoagulants prior to the procedure; and types of cerebrovascular events (stroke or TIA) in patients with or without minor or major complications. Post-hoc comparisons were performed in patients with and without AKI with regard to baseline creatinine, glomerular filtration rate according to Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equations, administration of intravenous hydration, or N-acetylcysteine before or after the intervention.

Ethics

The study was approved by the institutional Ethics Committee (protocol 1.981.536). Informed consent was waived because data were obtained from medical records.

Data analysis

Continuous variables are presented as mean, medians, standard deviations (SD), and minimum and maximum values. Percentages of complications were calculated. Comparisons between characteristics of the groups of patients with and without major or minor complications were performed with unpaired t-test, chi-square test, or Fisher's exact test. Fisher's exact test was used instead of chi-square tests when at least one cell had counts less than 5. Unplanned, post-hoc comparisons were performed using the chi-square test, Fisher's exact test, unpaired t-test, or Mann-Whitney U test, according to the nature and distribution of the data. Multivariate regression was planned in order to analyze predictors of minor complications, in case between-group differences were observed in bivariate analysis, regarding more than one variable.

Carotid artery stenting and follow-up

The recommended antiplatelet regimen is aspirin (100 mg qd) and clopidogrel (75 mg qd) at least 5 days before treatment or aspirin (300 mg) and clopidogrel (300 mg) at least 4 h before CAS. These drugs are continued for at least 1 month later. When an anticoagulant is indicated for secondary stroke prevention, only 100 mg daily aspirin is maintained. Double antiplatelet in combination with anticoagulants is never prescribed. The time to discharge depends on the follow-up, but patients typically remain in the hospital from 24 to 96 h after the procedure. According to the institutional protocol, cardiac biomarkers and creatinine are measured within this time frame.

On average, 20 CAS procedures are performed for symptomatic ICA stenosis per year in our institution. All procedures are performed by a high-volume interventional neuroradiologist (>20 procedures per year)[14]. The chief in the procedure is always an attending physician, with the assistance of a fellow. Cerebral embolic protection devices are used whenever possible, and the amount of contrast varies between 60 and 150 mL, depending on the characteristics of the artery. ICA tortuosity and calcifications render the intervention more difficult, increasing the length of the procedure and requiring a greater volume of contrast. In general, a low osmolality nonionic contrast (Ultravist) is administered, but for patients with prior renal failure an isosmolar agent (Vasipaque) is preferred. An embolic protection device (EZ filter, Boston Scientific) was used for protection in all patients.

RESULTS

A total of 73 patients who underwent CAS were identified, of whom 8 were excluded due to a lack of follow-up by neurologists. The mean±SD age was 67.7±9.9 years. Only 10 (15.3%) patients were ≥80 years. The mean NIHSS score was 2.5 (range 0–10, median 2). Other baseline characteristics are shown in Table 1. Patients were followed up until the end of hospital admission, ranging from 4 to 42 days (18.6±7.1). The median interval between cerebrovascular event and procedure was 20 days (range 3–193 days).

Primary outcome

The rate of any minor complication was 15 (23.1%) of 65. Some patients had more than one minor complication, so the

overall rate of all minor complications was 36.9% (24/65). Among minor complications, 8 (12.3%) patients had transient hypotension, 6 (9.2%) had bradycardia, 7 (10.7%) had AKI, and 2 (3.1%) had vasospasm.

Table 1. Characteristics of the patients.

Characteristics	n (%)
Male	40 (61.5)
Ethnicity	
White	46 (70.7)
Black	14(21.5)
No information	5 (7.7)
Arterial hypertension	50 (76.9)
Diabetes mellitus	25 (38.5)
Cardiopathy	22 (33.8)
Hypercholesterolemia	32 (49.2)
Smoking	28 (43)
Carotid-related stroke	55 (84.6)
Transient ischemic attack	10 (15.4)

Creatinine was measured in all patients up to 96 h post-CAS (7.7% up to 24 h after the procedure, 40% between 24 and 48 h, 52.3% between 48 and 96 h). In the seven patients who had AKI, the severity was AKIN grade 1, and the patients do not require hemodialysis. We could not retrieve the creatinine data of two patients in the study.

One (1.5%) patient had a TIA, with no evidence of stroke in a computed tomography (CT) performed 24 h after the onset of the symptoms. Magnetic resonance imaging (MRI) was not performed. This patient also presented hypotension.

Secondary outcomes

There were no significant differences in age between groups with (64.6±21.5 years) and without (67.9±9.3 years) major complications (p=0.589), or between the groups with (64.7±12.3 years) and without (68.6±9.1 years) minor complications (p=0.185).

Minor complications were more common in women than in men (p=0.051) (Table 2).

Baseline creatinine levels were higher in patients with AKI than in those without, but the between-group difference in this variable did not reach statistical significance (Table 3). The difference between creatinine levels on the first day after CAS,

Table 2. Characteristics of subgroups of patients with or without major and minor complications.

Characteristics	Subgroups according to major complications		p-value[a]	Subgroups according to minor complications		p-value[a]
	With (%) (n=3)	Without (%) (n=62)		With (%) (n=15)	Without (%) (n=50)	
Sex (male)	33.3	62.9	0.55	40	68	0.051
Ethnicity (non-white)	33.3	22.8	0.55	21.4	23.9	1.0
Arterial hypertension	66.7	77.4	0.55	80	76	1.0
Diabetes mellitus	33.3	38.7	1.0	46.7	36	0.46
Cardiopathy	33.3	33.8	1.0	33.3	34	0.96
Dyslipidemia	33.3	50	1.0	60	46	0.34
Smoking	33.3	43.5	1.0	60	38	0.13
Previous TIA	33.3	9.7	0.3	6.7	12	1.0
Previous stroke	33.3	25.8	1.0	20	28	0.74
Blood dyscrasia	33.3	3.2	0.13	6.7	2	0.52
Aspirin	66.7	96.8	0.13	93.3	96	0.55
Clopidogrel	66.7	96.8	0.13	86.7	98	0.13
Anticoagulation	50	6.4	0.22	13.3	6	0.32
Type of event						
Stroke	100	83.9	1.0	86.7	84	1.0
TIA	0	16.1	1.0	13.3	16	1.0

TIA: transient ischemic attack. [a]Chi-square or Fisher's exact test.

Table 3. Comparisons mong patients with or without transient acute kidney injury.

	Worsening in renal function		p-value
	Yes (n=7)	No (n=56)	
Hydration before intervention (%)	85.7	78.6	1.0[a]
Hydration after intervention (%)	71.4	53.6	0.448[a]
Treatment with N-acetylcysteine (%)	0	23.2	0.328[a]
Creatinine at admission (average±standard deviation) (mg/dL)	1.21±1.2	1.02±0.3	0.088[b]
Glomerular filtration rate calculated according to CKD-EPI equations, mL/min/1.73 m^2 (average±standard deviation)	75.3±30.5	71.7±18.9	0.653[c]

[a]Fisher's exact test. [b]Mann-Whitney U test. [c]Unpaired t-test.

compared to creatinine at admission, was -0.03±0,17 mg/dL (range, -0.48 to 0.38 mg/dL) in patients who did not present worsening in renal function and 0.68±0.7 mg/dL (range, 0.22–2.21 mg/dL) in those who did (p=0.056).

Post-hoc assessment of the time from the onset of neurologic symptoms and CAS showed no significant difference (p=0.9) between patients who presented hypotension (n=8; mean=28.8; SD±25.1) or bradycardia (n=6; mean=26.8; SD±22.0; p=1.0) and those who did not (without hypotension: n=57; mean=28.9; SD±29.4; without bradycardia: n=59; mean=29.1; SD±29.4).

DISCUSSION

To the best of our knowledge, this is the first study to address specifically different types of minor complications after CAS. The most common minor complications were hypotension and bradycardia. The main strengths of this study were the detailed assessment of consecutive patients and evaluation of different minor complications.

Overall, major complication rates, previously published by our group[10], were low, meeting international recommendations. Cerebral infarction as a perioperative complication related to CAS is an issue, and previous studies reported that risk factors for cerebral infarction included protection devices, operator's skill, patient age, plaque properties, stent design, and statin use. Kotsugi et al. reported that plaque protrusion (PP), as a new risk factor, was strongly associated with cerebral infarction[15-17].

The good results obtained in this study may be explained by the use of embolic protection devices, double antiplatelet regimen, and performance of procedures by experienced neurointerventional radiologists[18]. This result may not be externally valid for low-volume centers in Brazil or other countries.

Our rates of hypotension (12.3%) and bradycardia (9.2%) are within the wide range of reported rates (6.8–75.9% and 2.3–47.6%, respectively)[8,19-24]. These effects, expected to be transient, are explained by mechanical dilation of the carotid artery bulb during the procedure, leading to decreased sympathetic output and, possibly, increased parasympathetic discharge[22-24]. Alcade-Lopez et al reported low rates of hypotension (3.6%) and bradycardia (4.4%)[8]. The authors suggested that early CAS (<14 days after the event) is associated with fewer transient hemodynamic events. Our results do not support this hypothesis because we found no significant differences in the timing of CAS in patients with or without these minor complications.

As for the rate of AKI found in our study (10.7%), it was 2–10 times greater than rates previously reported in patients receiving greater (250 mL)[25] or the same (150 mL)[26] volume of contrast. All but one of the seven patients with AKI in our series received intravenous fluids before the procedure. None of the patients received sodium bicarbonate or N-acetylcysteine, which have already been considered inefficient to prevent contrast-associated AKI[27]. Baseline creatinine levels were higher in patients with AKI; therefore, these had a greater risk for this outcome and could benefit from the use of low osmolarity contrast media[28]. However, we could not retrieve information about the type of contrast media used in these patients. Still, there were no cases of permanent renal damage. As expected, the change in creatinine levels after CAS was greater in subjects who developed kidney injury than in patients without, but the difference did not reach statistical significance. However, glomerular filtration rates before CAS were similar in these two subgroups of patients.

Vasospasm is a possible reaction to the use of distal protection devices used in the CAS procedure. The device's basket and its movement might cause endothelial injury, leading to vasospasm, which may cause neurological symptoms[29]. Our vasospasm rate (3.1%) was low, when compared to the one reported by Alcade-Lopez et al (15.8%)[8]. Intra-arterial administration of nitroglycerin may be used to treat vasospasm, but not for prophylaxis, because it increases the risk of hypotension[29].

We found no significant differences in the age of subjects who presented and those who did not present complications, in contrast with the concept that older age is a predictor of the occurrence of complications after CAS[24]. The reason for this result is unclear, and the relatively small sample size of this study may have influenced, as well as the trend for a greater proportion of women in the group who had minor complications.

This study has some limitations: sample size, retrospective design, and relatively short-term follow-up. Still, it demonstrates that, in a high-volume center in a developing country, minor complications were more frequent than major. These findings are useful to inform patients before CAS procedures. In centers and patients with a comparable profile, considering the high risks of stroke recurrence in patients with carotid stenosis ≥70%[1], the overall risk-benefit of CAS is highly favorable. Future studies may compare rates of minor complications in different settings, such as low- and high-volume centers in different parts of the world, and assess the effects of these complications on patient-reported outcomes.

CONCLUSION

Our treatment result of CAS seemed to be acceptable compared with previously published articles regarding CAS in developed countries. In addition, these findings reinforce the safety of CAS in a high-volume reference center.

AUTHORS' CONTRIBUTIONS

ISM: Data curation, Formal Analysis, Writing – original draft. **RAA:** Conceptualization, Data curation. **LSV:** Conceptualization, Data curation. **PPJ**: Supervision, Validation. **ABC:** Conceptualization, Methodology, Project administration, Supervision, Validation, Writing – review & editing.

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