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ARTICLE

Does the side of middle cerebral artery compromise matters in the mortality after thrombolysis in ischemic stroke?

O lado acometido da artéria cerebral média interfere na mortalidade do acidente vascular isquêmico pós trombólise?

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ABSTRACT

The impact of the side in middle cerebral artery (MCA) ischemic stroke is not well established. Our aim was to analyze the differences between right (RMCA) and left middle cerebral artery (LMCA) stroke in patients submitted to intravenous thrombolysis and the influence of the affected side in the patient's mortality after 3 months. **Method:** Patients with MCA ischemic stroke submitted to intravenous thrombolysis from March 2010 to December 2011 at two Brazilian Stroke Centers were included. Differences between patients with RMCA and LMCA stroke were identified by univariate analysis. **Results:** Forty-five patients with RMCA stroke and 67 with LMCA stroke were analyzed. Patients with LMCA had a higher incidence of atrial fibrillation (p = 0.031), although patients with RMCA more often had a previous ischemic stroke (p = 0.034). The mortality over 3 months was similar for either side (OR = 1.20 ;0.37 - 4.29, p = 0.772). **Conclusion:** The side of the MCA ischemic stroke did not influence the patients mortality.

Keywords: stroke, middle cerebral artery stroke, thrombolytic therapy, prognosis, mortality.

RESUMO

O impacto do lado de acometimento da artéria cerebral média (ACM) não é bem estabelecido. Nosso objetivo é analisar as diferenças entre pacientes com acidente vascular isquêmico (AVCi) de ACM direita (ACMD) e esquerda (ACME) submetidos à trombólise endovenosa e a influência do lado acometido na mortalidade em 3 meses. **Método:** Pacientes com AVCi ACMD e ACME submetidos à trombólise endovenosa entre Março de 2010 a Dezembro de 2012 em duas Unidades de AVC brasileiras foram incluídos. Diferenças entre AVCi ACMD e ACME foram identificadas pela análise univariada. **Resultados:** Quarenta e cinco pacientes com AVCi de ACMD e 67 de ACME foram analisados. Pacientes com AVCi de ACME tiveram maior incidência de fibrilação atrial (p = 0,031), enquanto de ACMD maior de AVCi prévio (p = 0,034). A mortalidade em 3 meses foi similar em ambos os grupos (OR = 1,20; 0,37 -4,29, p = 0,772). **Conclusão:** O lado de acometimento da ACM no AVCi não influencia na mortalidade.

Palavras-chaves: acidente vascular isquêmico, artéria cerebral média, terapia trombolítica, prognóstico, mortalidade.

The influence of the side of the ischemic stroke (IS) and the outcome remains controversial; with some studies demonstrating a worse prognosis in those patients with right MCA (RMCA) as compared to left MCA (LMCA) IS, thus suggesting a possible laterality effect[1,2,3,4,5,6,7,8]. This could be related to a delay in treatment time, as well as a result of the fact that the National Institute of Health Stroke Scale (NIHSS) tends to favour the evaluation of the dominant (usually left) hemisphere over the non-dominant one[1,2,3,4,5,6,7]. However, most recent studies could not find any differences in the outcomes comparing either side of MCA IS[7,8,9]. The aim of the present study was to evaluate if there was a relation between the affected side and the mortality in the first 3 months in patients with MCA IS submitted to intravenous thrombolysis (IVTT).

METHOD

This is a cross-sectional and retrospective study with prospective data collection from medical records in a

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computerized date registry. The study group consisted of patients with stroke in the MCA territory, including cortical, subcortical and deep lesions, who underwent IVTT from 1st March 2010 to 31st December 2011 at two Brazilian Stroke Centres (Hospital de Clínicas, Universidade Federal do Paraná in Curitiba, Paraná; and the Hospital Municipal São José in Joinville, Santa Catarina). Stroke management, including the standardized IVTT, was based on current guidelines[10,11,12,13]. Exclusion criteria were the following: the presence of bilateral MCA stroke during the same admission, the presence of an infarction outside of the MCA territory during the same admission, intra-arterial rescue therapy, and incomplete data about the territory of infarction and the modified Rankin score (mRS) at 3 months. Although, among all ischemic stroke subtypes, lacunar strokes have been considered the most benign, this subtype was not excluded because reviewed studies show that thrombolysis is an effective treatment in those cases and the prognosis can be better or without significant trend for better or worse outcome compared with others etiologies[10,14,15,16,17,18]. The ethics committees of both hospitals had previously evaluated and authorized the study.

Neurologists certified in the use of the NIHSS examination evaluated all of the patients at both centres using the validated Portuguese version of the NIHSS[19]. The NIHSS was stratified in three different severity groups based on total punctuation: mild ranging from 0 to 3; moderate: 4 - 19; and severe: 20 - 42[9].

The main outcome measure was mortality during the three months after stroke onset. The other outcome variables evaluated were hemorrhagic transformation (HT), symptomatic HT (SHT), functional independency as defined as a mRS ≤ 2 on discharge, mRS ≤ 2 after three months and death during admission.

HT was defined as a hemorrhagic infarction (HI) in which a petechial bleeding inside the infarcted area was demonstrated on control neuroimaging, but without a space-occupying effect. A parenchymal haemorrhage (PH) was defined as a haemorrhage with a space-occupying effect[20,21]. A SHT was defined as brain imaging evidence of HT with clinical worsening, which was indicated by an increase of at least four points in the NIHSS score[15].

The statistical analyses were performed with the Statistica 8.0 software: statistical significance was assessed by either the Student's t-test or the Mann-Whitney's test for continuous variables and the χ^2-test or Fisher's exact test for categorical variables. Statistical significance was set at a $p < 0.05$ value with a 95% confidence interval.

RESULTS

During the study period, 112 MCA IS patients were analysed: 45 (40.2%) RMCAs and 67 (59.8%) LMCAs. Table 1 shows the demographic and admission variables of both groups. On the one hand patients with LMCA IS had atrial fibrillation more often when compared to the RMCA IS group (34.3% vs. 15.6%, p = 0.031), while on the other hand patients with RMCA IS were more prone to have had a history of previous IS as compared to the LMCA IS ones (6% vs. 20%, p = 0.034). Regardless of laterality, patients with a history of previous IS on admission had a lower punctuation in the NIHSS scale if compared to those without (7 ± 7 vs. 15 ± 5.8, p = 0.027).

In LMCA IS, the etiological distribution was: 14 (20.9%) had an atherothrombotic cause, 26 (38.8%) were cardioembolic, two (3%) had lacunar strokes and the remaining 25 (37.3%) had an undetermined mechanism. In RMCA IS, the etiological classification was: 14 (31.1%) were atherothrombotic, 17 (37.8%) cardioembolic, two (4.4%) lacunar and 12 (26.7%) had an undetermined cause (p = 0.529).

Both sides of unilateral MCA compromise had similar median NIHSS on admission (14 vs. 14, p = 0.456). Nevertheless, those patients that had a more severe compromise, the severe NIHSS subgroup, were more frequent in the LMCA IS group than in the RMCA IS (20 vs. 4, p = 0.009) (Table 1).

The outcome findings of each group are presented in Table 2. There was no statistically significant difference between the RMCA IS and LMCA IS groups for any of the outcome measures.

DISCUSSION

The present study failed to demonstrate that there was a difference in the mortality after 3 months between RMCA IS and LMCA IS. However, there is still some controversy in the literature regarding whether the side of the MCA IS can have any influence in its prognosis. Some authors suggested that patients with RMCA IS could have a longer symptom-to-needle time and a lower score in neurological scales because these scores are predominantly focused on language items, therefore favouring LMCA IS, and thus having a negative impact in the treatment and a worse outcome when compared to LMCA IS[1,2,4,5,6]. In the present study, the symptom-to-needle time and the median NIHSS were similar in both groups. Additionally, the LMCA IS group had a greater number of severely compromised patients as compared to the RMCA IS group, and this could have influenced the results obtained. Previous studies have shown that the influence of the dominant hemisphere occurs predominantly in those patients within the lower total punctuation of NIHSS score subgroup, because the lateralization of hemispheric compromise has a significant influence on the cortical items, mostly on those related to assessment of language and comprehension, an effect which disappears in patients with greater compromise and higher scores, becoming similar for either side[2].

It was observed that in the RMCA stroke patients with HT (n = 5), most of them had SHT (n = 4), but this did not change the patients outcome and also it was not

Table 1. Demographic and admission variables comparing LMCA and RMCA stroke patients.

	LMCA n (%)	RMCA n (%)	p
	67 (59.8)	45 (40.2)	
Age (in years) mean ± SD	65.6 ± 14.4	65.6 ± 14.4	0.986
Female gender n (%)	38 (56.7)	22 (48.9)	0.445
Arterial hypertension n (%)	47 (70.2)	34 (75.6)	0.667
Diabetes mellitus n (%)	10 (14.9)	11 (24.4)	0.225
Coronary heart disease n (%)	9 (13.4)	8 (17.8)	0.596
Hypercholesterolemia n (%)	51 (76.1)	35 (77.8)	1
Smoking n (%)	19 (28.4)	11 (24.4)	0.840
Previous ischemic stroke n (%)	4 (6)	9 (20)	0.034
Cardiac heart failure n (%)	8 (11.9)	7 (15.6)	0.585
Previous TIA n (%)	1 (1.5)	1 (2.2)	1
Atrial fibrillation n (%)	23 (34.3)	7 (15.6)	0.031
mRS med (min-max)	0 (0 – 3)	0 (0 – 2)	0.353
SNT mean ± SD	168.4 ± 56.2	177.5 ± 57.2	0.986
NIHSS on admission med (min-max)	14 (4 – 29)	14 (4 – 23)	0.456
Stratification NIHSS:			0.009
Mild NIHSS (%)	0	0	
Moderate NIHSS (%)	47 (70.2)	41 (91.1)	
Severe NIHSS (%)	20 (29.9)	4 (8.9)	
Glycemic levels (mg/dL) mean ± SD	119.8 ± 39.4	123 ± 51.1	0.708
Creatinine levels (mg/dL) mean ± SD	0.92 ± 0.38	1.1 ± 0.78	0.168
Systolic blood pressure (mmHg) mean ± SD	154.6 ± 27.2	148.7 ± 24.5	0.242
Diastolic blood pressure (mmHg) mean ± SD	89.4 ± 16	85.1 ± 14.8	0.160

LMCA: left middle cerebral artery ischemic stroke; RMCA: right middle cerebral artery ischemic stroke; TIA: transient ischemic attack; mRS: modified Rankin score; SNT: symptoms-to-needle time; NIHSS: National Institutes of Health Stroke Scale; MCA: middle cerebral artery; CT: computed axial tomography; IV: intravenous; IVTT: intravenous thrombolytic therapy; SD: standard deviation.

Table 2. Outcomes comparing LMCA and RMCA patients.

	LMCA n (%)	RMCA n (%)	p
	67 (59.8)	45 (40.2)	
Any hemorrhagic transformation n (%)	14 (20.9)	5 (11.1)	0.208
Symptomatic hemorrhagic transformation n (%)	6 (8.9)	4 (8.8)	0.303
Death during admission n (%)	15 (22.4)	9 (20)	0.818
mRS < 3 on discharge n (%)	24 (35.8)	16 (35.6)	1.00
Mortality in 3 months n (%)	19 (28.4)	12 (26.7)	1.00
mRS < 3 in 3 months n (%)	30 (44.8)	19 (42.2)	0.847

LMCA: left middle cerebral artery ischemic stroke; RMCA: right middle cerebral artery ischemic stroke; mRS: modified Rankin score.

statistically significant when compared to LMCA stroke patients (HT = 14, SHT = 6). When analyzed all SHT in the current study (n = 10, 8.9%), this was similar when compared to previous large trials[10,20] and real world studies[13].

There are some limitations in the present study. First, only those patients with MCA strokes that underwent intravenous thrombolysis were analysed; this restricted the validation of the current data with other topographies and with non-thrombolysis treated patients. The retrospective method excluded patients without complete data and this could also have influenced the observed results. In addition to the previous validation of NIHSS in the Portuguese-speaking Brazilian population[19], patients included in this study could have different cultural and educational levels, predominantly in regards to the language items, and this could have affected the observed results. Language dominance with neuropsychological testing was not evaluated in the present model. Finally, this study did not access the mortality in the different severity groups based on NIHSS. Nevertheless, some studies suggest that the influence of the dominant hemisphere occurs predominantly when there is lower total punctuation of NIHSS score[2] and in our study there is no patient with mild NIHSS in any of the groups. However, this is the first study that includes only patients who underwent IVTT and uses a differentiated analysis of NIHSS.

In conclusion, the side of MCA IS did not influence the patient's outcome in the present study and therefore should not be used as a prognostic marker. Future studies should emphasize other factors that could be used to establish the prognosis of MCA IS in a more reliable manner.

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