Annales Africaines de Médecine
Article original

Results of conservative treatment of malignant sylvian infarction: a prospective cohort study from the Conakry University Hospital Center

Résultats du traitement conservateur de l'infarctus sylvian malin : étude de suivi longitudinal réalisée au Centre hospitalier universitaire de Conakry

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Résumé

Contexte et objectif. L'impact réel du traitement conservateur de l'infarctus sylvien malin (ISM), type spécifique d'accident ischémique cérébral du territoire de l'artère cérébrale moyenne (ACM) n'est pas clairement déterminé. L'étude visait à en évaluer le résultat chez 25 patients (âge moyen : 59,1 ±17,7 ans) admis pour cette affection. ***Méthodes***. Cette enquête descriptive et prospective a analysé les données des patients consécutifs, admis au service de Neurologie pour un ISM confirmé par TDM cérébrale, pendant la période d'étude. Résulta***ats***. Sur un total de 329 cas d'AVC, l'ISM a constitué 11,7%, avec une prépondérance féminine.Le trouble de conscience était présent chez tous , avec un délai moyen d'admission de 77,1 ± 73,8 heures. L'hypertension artérielle, le diabète et le tabagisme étaient les principaux facteurs de risque cardiovasculaires retrouvés. Le score de Glasgow (GCS) était ≤ 8 chez un patient et ≥ 8 chez les 24 autres. Le score de National institutes of health stroke scale (NIHSS) moyen est de 17,5 (extrêmes de 15 – 20) ; et presque tous les patients (96%) avaient un score compris entre 16 – 20. La TDM cérébrale a montré un infarctus hémisphérique avec un œdème et effet de masse sur les structures médianes. Les complications les plus fréquentes étaient respectivement : la pneumonie d'inhalation, l'escarre fessier et/ou talonnier, et l'embolie pulmonaire. Le taux de mortalité a été de 68% dans la série. un score NIHSS ≥ 17 et/ou GCS ≤ 8 endéans les trois premiers jours d'admission et l'hypoxémie étaient des prédicteurs d'un mauvais pronostic. ***Conclusion***. Le pronostic vital réservé et le taux élevé de mortalité de ce traitement justifient le renforcement du plateau technique neurochirurgical dans cette institution.

Mots-clés : Infarctus sylvien malin, traitement conservateur, pronostic, Conakry
Reçu le 24 septembre 2020 ; Accepté le 13 février 2021

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Summary

Context and objective. Little is known about the impact of conservative treatment of malignant sylvian infarction (MSI), a specific type of ischemic stroke that generally affects the entire territory of the middle cerebral artery (MCA). This study aimed to evaluate the effect of conservative treatment of patients suffering from MSI. ***Methods***. This was a prospective cohort and descriptive study including consecutive patients who were hospitalized in the Neurology Department for MSI confirmed by brain imaging, over a period of six 6 months from October 24, 2019 to April 24, 2020. ***Results***. The MSI represented 25 cases (11.7 %) of 329 strokes recorded. Their average age was 59.1 ± 17.7 year with a female preponderance. Disorder of consciousness was found in all patients. The mean time of admission in hours was 77.1 ± 73.8 hours (extreme of 7 - 360 hours). Hypertension, diabetes and smoking were found as vascular risk factors in our patients. The Glasgow coma scale (GCS) was ≤ 8 in one patient and ≥ 8 in 24 other patients. The average National Institutes of Health Stroke Scale (NIHSS) score was 17.5 (extremes of 15 – 20); and 96 % of patients had a score between 16 and 20. The brain CT scan revealed a hemispheric infarction with edema and mass effect on the median structures. Inhalation pneumopathy, buttock and/or heel pressure ulcer, and pulmonary embolism were the most common complications. With the conservative treatment, the mortality rate was 68 %. The NIHSS ≥ 17 and/or GCS ≤ 8 score within three days of the vascular event and hypoxemia was a poor prognostic factor in 86.6 % of cases. ***Conclusion***. Conservative treatment of MSI is associated with poor prognosis with a high mortality rate especially in the absence of surgery.

Keywords: malignant sylvian infarction; conservative treatment; prognosis; Conakry
Received: September 24th, 2020
Accepted: February 13th, 2021

Introduction

The malignant sylvian infarction (MSI) corresponds to a specific type of Ischemic Stroke that generally affects the entire middle cerebral artery (MCA) or sylvian artery and may extend to other arterial territories, due to a complete or almost complete occlusion of the MCA, associated with significant cerebral edema (1-2). The conservative treatment of anti-epidematous drugs has so far not proven to be effective. MSI accounts for less than 10 % of all supratentorial Ischemic Stroke with an annual incidence of 10-20 cases per 100,000 population (1, 3). The usual clinical presentation of MSI is complete hemiplegia, severe hemibody sensory deficit, impaired alertness, combined deviation of the eyes and head, hemi-neglect and total aphasia (2). Cerebral computed tomography (CT) scans often indicate cerebral edema occupying more than 50 % of the MCA territory. The volume of the infarction is greater than 145 cubic centimeters measured on scattered magnetic resonance imaging (MRI) during the first 24 hours (4-5). Surgical management by decompressive hemi craniectomy (DHC) with durotomy/duroplasty is an approach that rapidly reduces intracranial pressure (ICP) and may therefore have a beneficial effect on patient outcome (6). However, rigorous medical treatment with mechanical ventilation, osmotic diuretics, hypothermia, sedation and hyperventilation have been ineffective to date (7). The prognosis for MSI is extremely severe regardless of the choice of treatment, with a mortality rate close to 80 % (8). The main cause of death is post-ischemic cerebral edema, followed by increased ICP, mass effect and cerebral involvement (9). This almost high mortality rate and the increase in the number of patients suffering from MSI in a context with such limited resources, leads us to constantly adapt the recommendations established by the learned societies to the constraints of our medical environment. The aim of this study is to evaluate the impact of conservative treatment of patients suffering from MSI, by studying the mortality rate and prognostic aspects.

Methods

Design, setting and period of study

This was a prospective cohort and descriptive study enrolling consecutive all patients who were hospitalized in the Neurology Department at the CHU of Conakry for an MSI confirmed by brain imaging, over a six (6) month period from October 24, 2019 to April 24, 2020.

Parameters of interest, outcome and operational definitions

The parameters collected were: frequency, age, gender, reason for visit, time to admission, vascular risk factors, vital signs, neurological examination, NIHSS score, modified Rankin score, stroke severity, Glasgow score (neurological deterioration), complications, imaging data and medical management modalities were analyzed. Ischemic Stroke cases with an NIHSS score ≥ 15 with less than 50% of the MCA arterial territory affected or without MCA territory affected were not included in the study. A urinary and nasogastric catheter followed by hydration with isotonic solutes were put in place. Monitoring of the water balance was mandatory. Mannitol; platelet anti-aggregants; antihypertensives; anticoagulants; insulin therapy; statins; antipyretics; antibiotics were introduced as indicated. Oxygen therapy with an oxygen extractor was performed in patients who experienced hypoxemia with pulsed oxygen saturation below 95%.

The outcome was defined as favorable for patients in whom we noted an improvement in clinical status at discharge compared to their status at admission (modified Rankin score < 3). However, it was defined as unfavorable for patients in whom we recorded death or persistence of severe disability (modified Rankin score ≥ 3; NIHSS ≥ 11) after hospital discharge. Mortality, on the other hand, represents all cases of death of patients hospitalized for MSI as well as the causes of death.

Statistical analysis

All these data and their correlations were analyzed on Excel and EPI Info tables in version 7.2.3.1. For the comparison of our proportions

we used the chi-square test and the Fisher exact test, and all p-values below 5% ($p < 0.05$) were considered statistically significant. We performed a univariate analysis including poor prognostic factors and patient prognosis.

Ethical considerations

The study was previously submitted to the Ethics Committee for approval and confidentiality was maintained throughout the study period. Informed consent of patients and/or responsible persons was obtained for all patients.

Results

Incidence of malignant sylvian infarctus

During the study period, 329 stroke patients were admitted to the department, including 213 (64.6 %) with ischemic stroke. After applying our criteria, 25 patients were selected for the study.

General characteristics of study population

The mean age of the patients was 59.12 ± 17.70 years, and they were divided into age groups with a range of 15 years, with extremes of 29 - 94 years. There was a strong predominance of females (sex ratio =0.92); 100% of the patients consulted for altered consciousness, aphasia, 56 % for left hemiplegia, altered consciousness, aphasia and 44% for right hemiplegia, altered consciousness plus aphasia. The mean time of admission in hours was 77.1 ± 73.8 h with extremes of 7 h and 360 h, 72 % of patients were admitted beyond 48 hours and only 20% within the first 24 hours (figure 1).

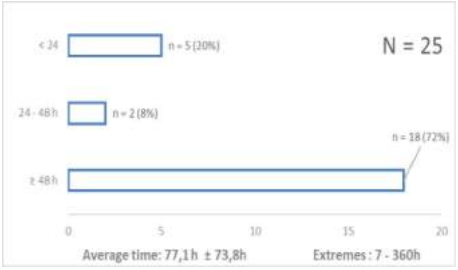

Figure 1. Distribution of Patients by Time to Consult

Four patients (16%) and 4 others (16%) had diabetes and smoking as comorbidities, respectively. Neurological examination on admission found a disorder of consciousness and body hemiplegia in all patients; 14 or 56% of patients had an intracranial hypertension syndrome and 9 (36%) had pulsed oxygen saturation below 95%. The GCS score was ≤ 8 in one patient (4%) and ≥ 8 in 24 patients or 83.3% of cases. However, the mean NIHSS score was 17.5 with extremes of 15 and 20, and 96% of patients or 24 patients had a score between 16 - 20 on admission. After 3 days of hospitalization, 11 patients or 44% had a GCS of 3 - 8; 12 patients or 48% had a GCS of 9 - 14 and only 2 patients or 8% had a GCS of 15. In addition, 72 % of our patients had an NIHSS score above 17 versus 28 % with an NIHSS score below 17. The cerebral CT found a right MSI with ipsilateral ventricular mass effect in 14 (56%) of the patients versus a left MSI with ipsilateral ventricular mass effect (Figures 2 and 3) in 11 (44%) (figures 4 and 5).

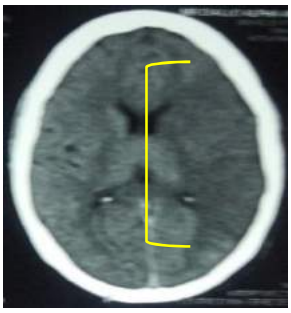

Figure 2. Brain scan without injection of contrast agent in axial section revealed a subacute hypodensity of the superficial and deep areas of the left MCA with a discrete mass effect on the ipsilateral ventricle.

Figure 3. Spontaneous hyperdensity in the left sylvian valley in relation to fresh thrombus at the M1 segment of the left MCA.

Figure 4. Cerebral scanner without injection of contrast agent in axial section revealed a hypodensity of the superficial and deep territories of the right MCA

Figure 5. Mass effect on the ipsilateral lateral ventricle.

Cerebral edema was found in 23 (92%), mass effect on median structures in 20 (80%) and cerebral involvement in 12 (48%) (table 1).

Table 1. Brain CT scan results for the 25 patients

Brain CT Scan result	n/25	%
Cerebral hemisphere affected		
Right	14	56
Left	11	44
Cerebral edema		
Yes	23	92
No	2	8
Mass effect on median structures		
Yes	20	80
No	5	20
Cerebral herniation (subfalcine and/or central)		
Yes	12	48
No	13	52

The most common secondary cerebral attacks of systemic origin were fever and hypoxemia in 15 (60%) of our patients.

Outcome

During hospitalization, many complications are encountered, the most common being inhalation pneumopathies 13 (52%); buttock and/or heel sores 8 (32%); pulmonary embolism in 3 (12%). Seventeen cases of death (68%) were recorded during hospitalization and 32% of patients had a favorable outcome. Of the 10 patients discharged directly to home, 7 (70%) had an NIHSS score between 11 - 15 and 2 (20%) had an NIHSS score between 16 and 20. Of the 8 patients living 1 month after hospital discharge, only 4 had an improvement with an NIHSS between 5 - 10 and 3 remained stationary with an NIHSS between 11 - 15 (table 2).

Table 2. Distribution of Patients by NIHSS Score at discharge and at 1 month

NIHSS Scores	Output n (%)	At 1 month n (%)
0 – 5	0	1 (12,5)
5 - 10	1 (10)	4 (50)
11 - 15	7 (70)	3 (37,5)
16 - 20	2 (20)	0
Total	**10 (100)**	**8 (100)**

The modified Rankin score was 4 in 9 patients at discharge and 6 were stable at 1 month from discharge. The NIHSS ≥ 17 and/or GCS ≤ score 8 at 3 days of the vascular event and hypoxemia was a poor prognostic factor in 86.6 % of cases (table 3).

Table 3. Results of univariate analysis on association between mortality and socio-demographic, clinical and neuroradiological characteristics

Variables	Death		P value
	Yes n (%)	No n (%)	
Sex			
Female	8 (61,5)	5 (38,4)	0,470
Male	9 (75)	3 (35)	
Age ≥ 65 years old	7 (70)	3 (30)	0,860
Admission deadline ≥ 24h	12 (60)	8 (40)	0,086
Hypertension	15 (71,4)	6 (28,5)	0,399
Diabetes	3 (75)	1 (25)	0,743
NIHSS on admission ≥ 17	13 (68,4)	6 (31,5)	0,935
NIHSS at J3 ≥ 17	15 (83,3)	3 (16,67)	0,008
Glasgow to J3 ≤ 8	11 (100)	0 (00)	0,002
Hyperglycemia on admission	5 (83,3)	1 (16,6)	0,355

Variables	Death		P value
	Yes n (%)	No n (%)	
Hyperthermia on admission	11 (73,3)	4 (26,6)	0,483
Affected Hemisphere			
Right	10 (71,4)	4 (28,5)	0,678
Left	7 (63,6)	4 (36,3)	
Cerebral edema	15 (65,2)	8 (34,7)	0,311
Brain engagement	7 (58,3)	4 (41,6)	0,319
Hypoxemia	13 (86,6)	2 (13,3)	0,014
Inhalation pneumopathy	11 (84,6)	2 (15,3)	0,063

Discussion

Ischemic Stroke was the main reason for admission to intensive care units, 25 of which (11.7 %) were MSI cases, with data lower than those found in the literature: 13 % for Dharmasaroja PA *et al.* in Thailand (10). This difference could be explained by the duration of the study and the size of our sample. Contrary to our experience, which shows a predominance of females, the higher frequency in males is well established in underdeveloped countries (Otiobanda GF *et al.* in Congo in 2012) and in the Arabian Peninsula (Kamal A *et al.* in Pakistan in 2016) (2, 11). There was a delay in consultation, i.e. an average admission time of 77.1 ± 73.8 hours, which is much higher than that found in the African literature: 24 ± 4.2 hours for Lompo DL et al. in Burkina Faso; 26.3 ± 27.3 hours for Otiobanda GF *et al.* in Congo (2,12). These high figures compared to neighboring countries sharing the same socio-economic difficulties as Guinea reflect the magnitude of this pathology and the need to measure its specific epidemiological, clinical and prognostic aspects in a country where there is no SAMU; no neurovascular unit; and no possibility of artificial ventilation. The most frequently reported risk factors in Africa and Asia are: hypertension, diabetes mellitus, smoking and obesity (2,9, 13-14). In Guinea, hypertension is the most common vascular risk factor, followed by diabetes mellitus and smoking. Our result would thus be justified by poor diet, physical inactivity, dyslipidemia, heart disease, stress; depression and alcohol consumption for a resource-limited population. The mean Glasgow and NIHSS scores at 3 days in hospital were 8.9 ± 3.2 and 17.8 ± 2.4 respectively. Albert AF *et al.* and Kamran S *et al.* report results comparable to ours, with mean Glasgow Score of 9.1 ± 2.8 and 7.5 ± 2.3 respectively (13-14). In agreement with data from the literature, we say that this neurological deterioration is explained by the evolution of malignant cerebral edema, which is maximal between the first and third day after the onset of symptoms during an MSI (1). It has been clearly established that the complications that are most rapidly identified include bronchopneumopathy and hyperthermia (9-10, 12, 15). In this study, complications were dominated by: hypoxemia and hyperthermia in 60% of cases each, followed by inhalation pneumopathy in 52% of cases. Some originality in the medical management of our patients deserves particular attention: Elevation of the head of the bed at 30°, known to have a rapid effect on the reduction of intracranial pressure without affecting the cerebral perfusion rate (16). All patients in our series benefited from this. Prevention of any drop in arterial pressure below 100 mm Hg by vascular filling with 0.9 percent saline is recommended and was applied to all our patients. Twenty-one patients or 84 % benefited from hyperosmolar therapy. In this regard, Li J *et al.* (9) reported the use of antiedematous therapy in 80.6% of their patients and decompressive hemi-craniectomy in 9.48% (9). The osmotherapy practiced in our study allowed us to attract water to the vascular area following the osmolar gradient. Mannitol and Hypertonic Saline have the additional advantage of lowering blood viscosity, rigidity and red blood cell volume. Mannitol as a first-line treatment reduces ICP at doses of 0.25 to 1g/kg under blood pressure monitoring, which should not be < 90 mm Hg (Level II recommendation) (17), and Hypertonic Saline Serum (HSS) can be used for high ICPs refractory to Mannitol use (18). In practice we have used intravenous Mannitol

boluses and salt-concentrated mineral water solutions administered nasogastrically with a target natremia of 145-155 mmol per liter. Although hypertonic saline and its forms of central administration were not available, we justified this aggressive hyperosmolar attitude by the major gravitational state of our patients. The lower ranking of HSS in the literature compared to mannitol in the recommendations is not related to a lower efficacy, but to the fact that mannitol remains the most studied historical treatment. All patients received antiplatelet therapy and 64 % benefited from oxygen therapy at 5 liters per minute, however, none of our patients benefited from decompressive hemi-craniectomy. This corresponds to the work of Otiobanda GF et al. who reported in their series the exclusive use of antiplatelet agents and mannitol (2). In contrast to the study by Hofmeijer J *et al.* (19), who reported a mortality rate of 40.6 %, our study found a mortality rate of 68 %. Thus we can deduce that this high mortality rate in our series is justified by the absence of emergency decompressive hemi-craniectomy given the lack of technical facilities and the often late consultation time. Among the patients hospitalized for MSI, ten (32 %), were discharged from the hospital under the advice of medical staff. The modified Rankin score at 1 month was 4 for 6 patients, i.e. 75 %, and 2 for 2 patients, i.e. 25 %. The severity of the neurological deficit and the extent of brain damage during MSI may explain this result.

Conclusion

MSI is an extremely serious ischemic stroke, it is associated with a poor prognosis for life with a high mortality rate. The NIHSS score ≥ 17 and or GCS ≤ 8, and oxygen desaturation during hospitalization were the poor prognostic factors in our study. Decompressive hemi-craniectomy is the most productive treatment option during this condition. However, due to the lack of technical facilities in a country with limited resources, medical therapy in a neurovascular and resuscitation unit with regular care at fixed times may have some beneficial effects as anti-oedematous drugs (Mannitol 20 %) have proven effective.

Funding
The authors did not receive any funded support for research, writing and publication of this article.

Declaration of interest
The authors declare that they have no conflicts of interest.

Authors' contributions
All authors contributed equally to this work.

Acknowledgements
The authors would like to thank the patients and their parents and the ethics committee for consenting to this study.

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Cite this article as:Atakla HG, Souare IS, Noudohounsi MMUD, Barry LF, Sulemana S, Noudohounsi ACW, *et al*. Results of conservative treatment of malignant sylvian infarction: a prospective cohort study from the Conakry University Hospital Center. *Ann Afr Med* 2021; **14** (2): e4117-e4123.