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Biomarkers in a Post-Stroke Population: Allied to Health Care in Brazil

M. Ricardo Lang, A. Costa, I. Iesbik, K. Haag, L. Trindade Buffara, O. Reimann Junior, C. Auswaldt Steclan

***Abstract*—**Stroke affects not only the individual, but has significant impacts on the social and family context. Therefore, it is necessary to know the peculiarities of each region, in order to contribute to regional public health policies effectively. Thus, the present study discusses biomarkers in a post-stroke population, admitted to a stroke unit (U-stroke) of reference in the southern region of Brazil. Biomarkers were analyzed, such as age, length of stay, mortality rate, survival time, risk factors and family history of stroke in patients after ischemic stroke. In this studied population, comparing men and women, it was identified that men were more affected than women, and the average age of women affected was higher, as they also had the highest mortality rate and the shortest hospital stay. The risk factors identified here were according to the global scenario; with systemic arterial hypertension (SAH) being the most frequent and those associated with sedentary lifestyle in women the most frequent (dyslipidemia, heart disease and obesity). In view of this, the importance of studies that characterize populations regionally is evident, strengthening the strategic planning of policies in favor of health care.

***Keywords*—**Biomarkers, population, stroke, sex, stroke unit.

I. Introduction

STROKE affects not only the individual, but also their family and society as a whole [1]. In Brazil - a country still in development - we have around 610,000 cases of acute stroke each year [2]-[5]. This scenario causes us to have catastrophic economic reflexes in relation to the Unified Health System (SUS), with an average cost of R$ 6000 per patient, R$ 640 per day in cases of mild sequelae to R$ 32000 for patients with severe sequelae and hospitalization periods of one month [6]. In addition, there are significant impacts on the social and family context [7].

More than 80% of strokes are ischemic diseases. In this type of event, damage to the brain - due to the sharp reduction in blood supply - makes stroke a major cause of long-term mortality and disability worldwide. Bearing this in mind, in the care of stroke patients, the window between the beginning of the event and clinical care is essential for a possible reduction in the involvement of the area that is being affected/injured. There is an estimate that 1.8 million neurons are lost every minute that proper treatment is not given ("time is brain") [8], [9]. Thus, it is clear that care in the acute phase of stroke must be timely and effective [10].

Among the treatment approaches for stroke, stroke units (U-stroke) have enabled exceptional advances in the prognosis of affected individuals. This resulted in an 18% reduction in mortality, 25% in institutionalization and 29% in functional dependence. To this end, they must have the availability of technology to perform diagnostic tests, thrombolytic therapy, mechanical thrombectomy, etiological investigation and a multidisciplinary team specialized in the care of acute stroke [11]. However, it is known that in addition to the appropriate care process, other factors influence the outcome of treatment in stroke, as it is also necessary to consider that the epidemiological and clinical characteristics vary according to regional factors and access to health conditions [12]. Therefore, it is necessary to know the peculiarities of each region, in order to contribute to public regional health policies. Furthermore, there is evidence of the scarcity of information on the epidemiological and functional data of individuals treated for stroke in Brazilian hospitals [13]. Being perceived the inexistence of data about the region of North Plateau of Santa Catarina state, this study aimed to characterize, in a sample form, post-stroke individuals hospitalized in a U-stroke reference in the southern region of the Brazil.

Michael Lang is with HSVP and Neuromax, Brazil (e-mail: steclan.consultoria@gmail.com).

II. Materials and Methods

This is a prospective, observational and longitudinal study carried out from November 2019 to December 2020 with 44 post-stroke individuals, who were hospitalized at the stroke unit (U-AVC) of Hospital São Vicente de Paulo (HSVP), located in the municipality of Mafra-SC. The U-AVC is a reference in the North Plateau of Santa Catarina state, with an estimated population of 341,403 inhabitants [14], with an estimate for 2020 year of 367,521 inhabitants, this population is spread over a territorial area of approximately 10,000 km^2. There is an average attendance of 45 ± 2.5 individuals with stroke events per month, with an average of 10% of these being computed in this study according to the inclusion and exclusion criteria of this study. For this purpose, this study included adult individuals (≥ 18 years old) of both sexes, after ischemic stroke (stroke) and whose diagnosis was confirmed by Computed Tomography (CT) or Nuclear Magnetic Resonance (NMR). The stroke subtypes were classified according to TOAST [15] and determined by the medical team. Individuals diagnosed with Transient Ischemic Accident (AIT) were excluded; history of previous stroke that generated sequelae (ERm ≥ 1); hemorrhagic stroke or stroke with hemorrhagic transformation, the last one verified by control CT between 24 and 36 hours after admission; or other neurological and orthopedic diseases that could lead to motor deficits or functional changes in addition to those caused by stroke (Parkinson; Amputations). Thus, sociodemographic data and biomarkers were analyzed, for example, age and risk

factors which were obtained from medical records and a questionnaire for the patient or caregiver on the day of hospital discharge. The mortality rate and length of stay of these patients were also computed.

This study was approved by the Research Ethics Committee of partner institutions and the proposing institution (CEP nº 3609943). All participants signed a Free and Informed Consent Form as provided by the ethics committee on research with human beings.

Statistical analysis: For the characterization of the sample, descriptive statistics were performed by means of absolute and relative frequency (categorical variables) and by measures of position and dispersion (numerical variables), using GraphPadPrism 9.0.1. The differences in sociodemographic and clinical variables between the different post-stroke groups were analyzed using the Wilcoxon test for numerical variables, used due to the non-parametric distribution of the data (Kolmogorov-Smirnov).

III. Results

The sample computed here had a total number of individuals equal to 44, of which 43.2% were female and 56.8% were male, with an average age between 72 ± 14 years. Within the sample studied, it can be identified that women remain in hospital longer than men, in addition to conferring a mortality rate three times higher than men (Table I). These results demonstrate evident discrepancies between these two populations, and it can be interpreted that there are in fact differences regarding the age at risk and clinical evolution after the stroke, since there was also a significant difference regarding the period of survival between these two populations, with women shorter average time. In addition, on the sample studied, through questions and answers indexed to the medical record, risk factors and their qualifications were identified, whether treated or not. In this scenario, seven risk factors were found, some of which with specific descriptions, when reported by family members. Table II shows the percentages for the two populations defined according to inclusion and exclusion criteria (men and women). Having this in mind, it can be identified that the main most frequent risk factors in men were SAH, diabetes and smoking. Differently when the population of women in the sample was analyzed, where the most frequent risk factors were dyslipidemia, heart disease, obesity and physical inactivity (Table II).

TABLE I
Percentage Values of the Population When Analyzing Age, Length of Hospital Stay, Mortality Rate and Survival Time after Stroke

	Men	Woman	General
Middle Ages	69 ± 13 year	76 ± 13,8 year	72 ± 14 year
Length of hospital stay	6 ± 3,9 days	7 ± 4,7 days	7 ± 4 days
Mortality rate	12%	26,32%	18,18%
Survival time after stroke	54 ± 42,9 year	22 ± 16,2 days	33,88 ± 30,8 days

Data computed by descriptive statistics.

When the descriptive variables of the population were analyzed for Pearson's correlation, the value for analysis between men and women was r = 0.87, thus indicating a strong perfect negative correlation between the groups analyzed. When the distribution of means is visualized, it easily retains attention as to treatment adherence for SAH, diabetes and dyslipidemia, with worrying information regarding the latter here, as women have a higher incidence of this risk factor and less adherence treatment (Fig. 2, yellow arrow). Associated with this result, it is also important to note that, in addition to the higher percentage of dyslipidemia in women, they also have higher rates for the factors of heart disease, obesity and physical inactivity (Fig. 2, delimited by the quadrant). Regarding the two groups analyzed - men and women - they were significantly different and with the same distribution of the analyzed population ($p < 0.05$, according to Wilcoxon test).

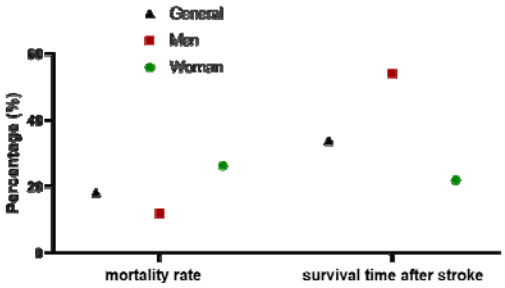

Fig. 1 Distribution of the averages of the mortality rate and survival time after stroke, comparing the averages of the population of men and women in relation to the average of the general population. Survival time calculated for the indices that made up the mortality rate

TABLE II
Percentage Values of the Population When Analyzing the Found Risk Factors

Risk Factor	Men		Woman		General	
SAH	80	%	73,7	%	77,27	%
Treated SAH	80	%	92,9	%	85,29	%
Diabetes	32	%	31,6	%	31,82	%
Treated Diabetes	87,5	%	66,7	%	78,57	%
Smoking	28	%	15,8	%	22,73	%
Dyslipidemia	16	%	36,8	%	25	%
Treated dyslipidemia	75	%	57,1	%	63,64	%
Cardiopathy	32	%	42,1	%	36,33	%
Obesity	16	%	31,6	%	22,73	%
Sedentary lifestyle	80	%	89,5	%	75	%

Data computed by descriptive statistics.

Within the studied male population, interestingly, there was a significant percentage of individuals who had already suffered a stroke or more (48%), and of these, 50% had a family history (parents and close relatives) for stroke. Of those individuals who had the second stroke event, the window between the first and last event was an average of 7.29 years. In the female population studied, it was found that only 31.58% of women had already suffered a stroke or more, and of these, 50% also had a family history (parents and close relatives) for stroke. Of the women with a previous history of stroke, a window was found between the first and last event,

on average 4.58 years. Having this in mind, it appears that in this population studied there is a higher percentage of second stroke events in men, however, both men and women with more than one stroke event have the same percentage when analyzing the presence of a family history for stroke. However, an information worth mentioning is the interval between one event and another, demonstrating that for women this window of time was shorter (Table III).

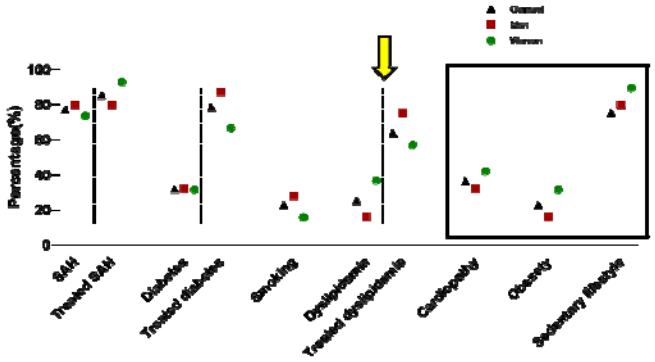

Fig. 2 Distribution of the percentage of incidence of risk factors: hypertension (SAH) (if under treatment); diabetes (if at all); smoking; dyslipidemia (if at all); heart disease; obesity and physical inactivity in post-stroke individuals. The values presented compare averages of the population of men and women in relation to the average of the total sample. The groups, men and women, behave independently and were selected from populations that have the same distribution ($p < 0.05$ - Wilcoxon test)

TABLE III
PERCENTAGE VALUES OF HISTORY OF STROKE IN THE STUDIED POPULATION

	Men	Woman	General
Previous stroke event	48%	31,58%	40,9%
Family history for stroke	50%	50%	25%
Time interval between the first and second stroke events	7,29 average/years	7,29 average/years	7,29 average/years

Data computed by descriptive statistics.

Within the descriptive analyzes considering discrimination by sex, it is already visible that this sample corresponds to the characteristics of world studies, in which the tendency of certain risk factors related to sex is also verified. It was also confirmed the occurrence of more than two stroke events in a large part of the population and the presence of a family history of stroke. However, when analyzing the population that suffered stroke as a whole, it is clear that women remained below the general average when analyzing the presence of a previous stroke event. However, it is also below when the average number of years of interval between the first and the second stroke events is analyzed (Table III).

IV. DISCUSSION

Several areas of medicine proposed promising results when approached in a personalized way, whether by age, presence/absence of associated comorbidities and even by particularities in relation to sex. Stroke - besides being a major global health problem - is the fourth and fifth leading cause of death in women and men, respectively. In addition, survivors commonly remain with neurological deficiency, mood disorders, increased likelihood of rehospitalization, infections and co-infections, venous thromboembolism, and high risk of falls and fractures [16]. In this study, just as the literature exposes [17]-[19], there was a higher percentage of male affected individuals. Bearing in mind that the average age of the general population was 72 ± 14 years, with a higher average age of women. In the population studied here, there was a higher percentage of clinical evolution to death in the affected women, which may perhaps be associated with a larger age group. In this context, there are several studies in the literature that support and bring the perception of the existence of differences in the incidence and clinical evolution of cerebrovascular diseases when analyzed separately in the population of men and women. Jiang et al. [20] portray in their study that men have a high risk of mortality from cerebrovascular diseases in relation to women, and this study also analyzed characteristics regarding the race of patients, being white individuals associated with the highest mortality rate. Recently, Boot et al. [21] demonstrated that there are differences in relation to epidemiological markers with age groups in the population, with differences in mortality rates between genders remaining in young adulthood.

When populations are subdivided according to some characteristics, there is a tendency to identify variables that will support differential measures and strategies in health for each subpopulation. Thus, these results promote an increase in the resolution and effectiveness of health systems. When comparing some indexes on the flow and stroke care systems between Brazil and France, Nugem et al. [22] found a significantly different index in the period of hospitalization of post-stroke patients, with Brazil having an average of 7.6 days and France 12.6 days. In our results, we found findings that were in accordance with the study cited, with an average of 7 ± 4 days of hospitalization until hospital discharge. Also, according to Nugem et al. [22], this index is directly related to the double mortality rate that France has compared to Brazil. Having this in mind, the results presented here are in accordance with other international and Brazilian studies, with the length of hospital stay ranging from 5 to 8 days [23], [24].

When addressing the stroke context/scenario, there are many biomarkers used as predictors, associated with the diagnosis and clinical course of stroke [19]. As for these, there are biomarkers that comprised the three perceptions, which can accelerate and/or aggravate any of these, for these they are called risk factors [25], [26]. In the present study, a significant presence of the following risk factors was identified in the population affected by stroke: SAH (77.27%); diabetes (31.82%); dyslipidemia (25%); heart disease (36.33%) and obesity (22.73%); the findings here are in line with what the literature already predicts and describes. In a study with 32 countries, 10 risk factors associated with stroke in all regions of the world can be computed, with hypertension, dyslipidemia, diabetes, heart disease and smoking being the main associated risk factors [27]. Gallacher et al. [28] discuss and show that in stroke survivors, the number of comorbidities

can be a more useful predictor of mortality than the condition itself. Having this in mind, in the present study, it was observed not only the percentage of individuals with risk factors, but also whether the situation considered was treated or not. In this sense, it was noticed, through the collection of information from medical records and interviews with the patient or his family, that in both sexes there was no complete adherence of the population to the treatment, with a worrying quarter of the population of women with dyslipidemia did not treat the condition, which may be associated with a higher mortality rate in this population. However, in this study, attention was paid to sedentary lifestyle (75%), which in recent decades has gained prominence among the risk factors associated with stroke. Interestingly, a sedentary lifestyle is the risk factor with the greatest power of modification among the others, unlike the others that have a direct and/or indirect relationship with the individual's genetic individuality. Recent studies demonstrate that lifestyle has become a strong biomarker for chronic non-communicable diseases, sparing no age group [29], [24], [30]. In order to rethink, the population of women analyzed here presented a higher percentage for four associated risk factors, namely: sedentary lifestyle, dyslipidemia, heart disease and obesity, these are usually present together and/or as a result. In fact, it is known that the absolute number of women living with cardio and cerebrovascular diseases, as well as the number of hospital discharges for heart failure and stroke, significantly exceeds that of men [31]. Thus, in this scenario presented here, on a specific population of the northern plateau of Santa Catarina, in the southern region of Brazil, the retrospective and prospective need for policies and actions aimed at health care would be evident considering these biomarkers, especially in the interventionist actions of factors modifiable. Thus, multi and interprofessional approaches tend to circumvent challenges to better meet the demand of stroke risk groups and stroke survivors. This requires coordination and collaboration of basic, clinical, legislators, community and industry research, all of which are efficiently linked together to reduce the socioeconomic impacts of this disease.

V. Conclusion

Stroke affects more men than women. However, the highest mortality rate in this computed study was for post-stroke women. The resulting risk factors accompany the world scenario, including modifiable ones. Differences in relation to sex exist and coexist, therefore, need to be considered in the different levels of health care, because if there are differences in relation to the affected population, there will also be differences in relation to the side effects of stroke survivors and their families, already that women mainly take care of the family. Therefore, it is exposed here, through these results, the importance of knowledge of these biomarkers for regionally different population, since among the risk factors, the modifiable ones are significant and can be changed with health policies directed at them. However, this study is pioneering for the region in question, and the need for further studies on biomarkers in the population is exacerbated, as they support strategic health planning in favor of improving the quality of services provided to the population and in favor of improving the quality of life of stroke survivors and their families.

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M.R. Lang graduated in Medicine from the Regional University Foundation of Blumenau, Brazil (2002-2008). Medical residency in neurosurgery by MEC and SBN held at Santa Isabel Hospital in Blumenau, Brazil (2009-2014). Fellowship in neuroradiology interventionist by SILAN at the ENERI institute in Buenos Aires, Argentina (2014-2015).

Observership in vascular neurosurgery and skull base at Barrow Neurological Institute in Phoenix, United States (2015). Fellowship on skull base at the Hospital Evangelical University of Curitiba and Hospital Nossa Senhora das Graças (2015-2016). Full Member of the Brazilian Society of Neurosurgery (2016). Title of Interventional Neuroradiology by the Brazilian Society of Neuroradiology Diagnosis and Therapeutics (2018). Titular Member of the Brazilian Society of Diagnostic and Therapeutic Neuroradiology (2021). Service Coordinator Neurology and Neurosurgery at Hospital Universitário Santa Terezinha. Coordinator of Neurology and Neurosurgery Service of Hospital São Vicente de Paulo. Technical director Hospital São Vicente de Paulo. Medical coordinator of Neuroclinica Joinville. Full professor of the neuroanatomy discipline of the medical course at the University of Disputed. Works with research in neurosurgery and neurosurgery.