

# Risk Factors and Sociodemographic Characteristics of Ischemic Stroke in Brazil – A Systematic Review

Cristianne Confessor Castilho Lopes, Eduardo Barbosa Lopes, Lucas Castilho Lopes, Vanessa da Silva Barros, Viviane Dorgievicz, Marivane Lemos, Daniela dos Santos, Paulo Sérgio Silva, Youssef Elias Ammar, Heliude de Quadros, Norberto Luiz Cabral (In Memoriam), Paulo Henrique Condeixa de França and Marcelo Pitombeira de Lacerda

Received: 07 Nov 2020; Received in revised form: 14 Dec 2020; Accepted: 21 Dec 2020; Available online: 31 Dec 2020

©2020 The Author(s). Published by AI Publications. This is an open access article under the CC BY license

(<https://creativecommons.org/licenses/by/4.0/>)

**Abstract—** *Introduction: Ischemic stroke corresponds to 80% of cases in Brazil, which demonstrates its epidemiological importance in Brazil. The magnitude of this fact reflects the reason why stroke is considered the second leading cause of death in the world, and the leading cause of death in Brazil, in addition to being the second leading cause of cognitive losses. The main causes that promote the occurrence of ischemic stroke determine the conjuncture of risk groups. Such factors can be classified into modifiable, non-modifiable and potential risk group. Objective: The objective of this study was to systematically review the public health literature on the risk factors and sociodemographic characteristics of ischemic stroke in Brazil, by analyzing epidemiological studies conducted in Brazil. Methods: Systematized literature review conducted by searching the US National Library of Medicine (Pub Med), Scientific Electronic Library online (SCIELO), Latin American Caribbean Health Sciences Information System (LILACS), Science Direct and Embase, using the descriptors: “Isquemic stroke”, “risk factors”, “sociodemographic characteristics” and “Brazil”. 852 articles were found, of which 11 were selected to build the review by six reviewers independently. Results: Chronic noncommunicable diseases (CNCD), such as stroke and ischemic heart disease, account for 63% or about 36 million of deaths worldwide, with emphasis on diseases of the circulatory system, diabetes, cancer and respiratory disease chronic. In Brazil, NCDs also present themselves as a health problem, corresponding to 54.0% of all deaths, in the year 2016. In the age group of 30-69 years, NCDs represented 56.1% of deaths. Conclusion: It is known today that stroke is one of the major causes of morbidity and mortality among patients, being the majority in the elderly. It is associated with CNCDs, among which we mention hypertension, diabetes and dyslipidemia. Such a disease is more common in men, blacks and those with low schooling, but in women it is more lethal, according to pre-existing data. Thus, new methodologies and analyzes need to be developed on the effects of the multiplicity of chronic diseases, which affect the elderly more intensely.*

**Keywords—** *Isquemic stroke, risk factors, sociodemographic characteristics and Brazil.*

## I. INTRODUCTION

Ischemic stroke is a disease resulting from an obstruction of a cerebral artery, usually resulting from fat deposits due to atherosclerosis and/or blood clotting. The decrease in neurological function occurs by blocking the

circulation in a certain brain area, causing ischemia, also known as stroke. These events promote the death of nervous tissue due to lack of blood supply to the obstructed area<sup>(1)</sup>.

Ischemic stroke is classified into three types: embolic, thrombotic and lacunar. The first is derived from small portions of matter that are released into the bloodstream and move to the cerebral arteries. The second is due to the development of a clot or thrombus inside the cerebral arteries or their branches. And finally, the third is caused by small infarcts that occur only where perforating arterioles branch directly from the great vessels. The neurological abnormalities of the stroke determine that the brain injury is opposite to the signs of motor deficit <sup>(2)</sup>.

In Brazil, 80% of cases of stroke are classified as ischemic stroke, demonstrating its epidemiological importance in the country, resulting in the first cause of death in Brazil, besides being the second cause of cognitive loss <sup>(1,3)</sup>.

Studies show that the individuals most affected are elderly, generally males from the black ethnic group. However, the most severe cases affect female patients, referring to a higher lethality rate than males. Other studies also show that stroke incidence and hospitalization rates emerge among young people, becoming a public health issue <sup>(4,5)</sup>.

The main associated risk factors that increase the occurrence of ischemic stroke can be classified as modifiable, non-modifiable and potential risk group. In the first classification, the greatest relationship arises from habits such as smoking and the control of pre-existing diseases such as hypertension and diabetes mellitus. The second classification, non-modifiable risk factors, presents characteristics such as advanced age, gender and ethnicity. The potential risk group lists factors resulting from bad life habits, such as sedentariness, obesity and alcoholism. Obesity is believed to be a triggering factor for cardiovascular diseases, transfiguring it as one of the key points for risk classification models <sup>(6)</sup>.

The stroke, usually resulting from the factors listed above, in addition to mortality, can generate after-effects that not only impact the individual, but also the social and economic sphere. These after-effects can compromise the individual's productivity and autonomy, and can be described and observed by the main signs and symptoms such as paresis, pain, visual deficits and motor attenuation <sup>(7)</sup>.

The extent and establishment of collateral flow is determined by the affected site, severity, signs and symptoms. The main indicative signs can be listed as loss of strength, sudden headache, loss of speech, imbalance, visual changes, immediate sensitivity changes, instability, dizziness, nausea or vomiting, fatigue, and personality and mood changes <sup>(8)</sup>.

As for the diagnosis, the ischemic stroke is detected by means of imaging tests that make it possible to identify the affected area of the brain, and some tests can be cited for their high degree of accuracy to confirm the mechanisms of the stroke. This set includes the following exams: computed tomography (CT), magnetic resonance imaging (MRI), electrocardiogram, echocardiogram and carotid Doppler ultrasound <sup>(9)</sup>.

The objective of the present study was to systematically review the public health literature on risk factors and sociodemographic characteristics of ischemic stroke in Brazil, through analysis of epidemiological studies conducted in Brazil.

## II. METHODS

This study is a systematic review, classified as exploratory and descriptive. The research was carried out in electronic databases on methods associated with RSL (Systematic Literature Review) and SMARTER (*Simple Multi-Attribute Rating Technique using Exploiting Rankings*) applications. The work performed is qualitative. The qualitative analysis of the data is carried out intuitively and inductively during the survey of the theoretical reference. It is also quantitative by using the multicriteria method. In addition, there is also a numerical experimental study in order to simulate a selection situation of articles based on the criteria observed. From the bibliographic search, located in the databases: *US National Library of Medicine* (Pub Med), *Scientific Electronic Library on-line* (SCIELO), *Latin American System of Health Sciences Information* (LILACS), *Science Direct* (Elsevier) and Embase.

The search in the databases was performed using the terminologies registered in the Health Sciences Descriptors created by the Virtual Health Library developed from the *Medical Subject Headings* of the *U.S. National Library of Medicine*, which allows the use of common terminology in Portuguese, English and Spanish. The keywords used in the Portuguese language for searching the databases were: Ischemic stroke, risk factors, sociodemographic characteristics and Brazil. As a tool to support decision making in the selection and prioritization of articles, a set of criteria were considered essential to represent the state of the art of the subject object of the research. This method has the following characteristics: (i) rigorous logic allows the acceptance of the method as a decision support tool; (ii) simple to be understood and applied with results that are easy to interpret. After all, the result obtained totaled 11 (eleven) articles that contemplated the desired characteristics for the study.

### III. THEORETICAL REFERENCE

According to the Brazilian Society of Cerebrovascular Diseases, the Cerebral Vascular Accident (CVA) presents great morbidity and mortality, being the main cause of death for Brazilians. All over the world, it is a disabling disease because, due to its after-effects, approximately 70% of people do not return to work and 50% become dependent on other people on the day they leave. Although it affects individuals over 60 more frequently, stroke can occur at any age, including children. *Stroke* has been increasing among young people, occurring in 10% of patients under 55 years and the *World Stroke Organization* predicts that one in six people in the world will have a stroke during their lifetime <sup>(10)</sup>.

According to the World Health Organization (WHO), stroke refers to the rapid development of clinical signs of focal and/or global disorders of brain function, with symptoms lasting 24 hours or more, of vascular origin, causing changes in the cognitive and sensory-motor planes, according to the area and extent of the injury. The most common sign of a stroke, which occurs more frequently in the adult phase, is sudden weakness or numbness of the face, arm and/or leg, usually on one side of the body. Other frequent signs include: mental confusion, cognitive change, difficulty speaking or understanding, swallowing, seeing with one or both eyes and walking; hearing disorders; dizziness, loss of balance and/or coordination; severe headache with no known cause; decreased or loss of consciousness. A very serious injury can cause sudden death <sup>(11)</sup>.

The classifications of strokes are: anoxic-ischemic (result of vasogenic failure to adequately supply the brain tissue with oxygen and substrates) and hemorrhagic (result of blood spillage into or around the structures of the central nervous system). Ischemic subtypes are lacunar, atherosclerotic and embolic, and hemorrhagic are intraparenchymal and subarachnoid <sup>(12)</sup>. Since the focus of this study is the ischemic stroke, the theoretical basis follows only this classification.

Ischemic stroke is a persistent focal neurological deficit, the result of ischemia followed by infarction. This event is caused by proximal obstruction of an artery by a thrombus, plunger or tumor compression. The clinical picture appears quickly due to the absence of glucose contribution to the neurons. After a few minutes of ischemia, an infarction occurs (death of the affected brain tissue). If the ischemia is reversed before the death of the neurons, the event is called transient ischemic attack <sup>(13)</sup>.

The stroke begins with a series of widespread events that occur with brain ischemia, defined as a cascade of

brain ischemia. The exact timing of each event depends on many variables, such as the size of the infarction, the onset and duration of the ischemia, and reperfusion efficiency <sup>(14)</sup>.

Acute occlusion of an intracranial vessel reduces blood flow to the brain region it supplies. The degree of reduced flow is a function of collateral blood flow, and this depends on the vascular anatomy (which can be altered by the disease), the site of occlusion, and the systemic blood pressure. A decrease in cerebral blood flow to zero causes brain tissue death in 4 to 10 minutes; values < 16 to 18 mL/100 g of tissue per minute cause infarction within 1 hour; and values < 20 mL/100 g of tissue per minute cause ischemia without infarction, except when prolonged for several hours or days <sup>(15)</sup>.

Ischemic events start with sudden or gradual brain hypoperfusion and include bioenergetic cell failure, excitotoxicity, oxidative stress, blood-brain barrier dysfunction, microvascular injury, homeostatic activation, inflammation and eventual neuronal, glial, and endothelial cell necrosis. The hematoencephalic barrier (BHE) disruption in stroke seems to depend on the aggressiveness and reperfusion response. Within the first 24 hours after a stroke, there is an increase in BHE permeability, and the greatest damage occurs between 48-72 hours after the event <sup>(14)</sup>.

The main risk factors for strokes are divided into three groups, being the modifiable (hypertension, smoking, diabetes mellitus), non-modifiable (age, gender, race) and the potential risk group that includes sedentariness, obesity, and alcoholism <sup>(16)</sup>.

Most of the care of stroke patients in Brazil is performed in secondary hospitals, which often do not have adequate infrastructure for full care of this type of patient <sup>(17)</sup>. As part of addressing this problem, the Ministry of Health, since April 2012, has had criteria for qualification of hospital facilities wishing to implement the Stroke Emergency Care Center (CAUAVC), under the Unified Health System (SUS), through Ordinance No. 665/2012. As a way of organizing a specialized service, with a role of reference to treat this disease and articulated between federal, state, and municipal governments, these Centers, also called Stroke Units, are classified into three types (type I, II, and III), which will depend on the size and capacity of the Hospital in which it is inserted <sup>(18)</sup>.

The Basic Health Care Network plays an important role in health promotion and disease prevention. For this, some measures are very relevant and need to be considered, such as permanent health education, people management action, formation of multiprofessional teams

through the Family Health Support Centers (NASF), training community health agents and other members of Family Health Strategies (ESF), referral to trained professionals, promotion of educational campaigns with accessible language allowing the population itself to identify groups at risk and seek assistance when necessary, and stimulation of health education for groups at risk<sup>(16)</sup>.

Prevention is the primary strategy to reduce stroke-related morbidity and mortality, adequate treatment, control of risk factors, and lifestyle changes can prevent up to 50% of stroke cases. However, there are no specific recommendations or guidelines for preventing stroke in young adults. In general, prevention strategies are similar for young and elderly patients<sup>(19)</sup>.

Epidemiological research makes it possible to sensitize, raise awareness and alert health managers and health professionals to develop appropriate strategies for preventing disease, and enable health professionals, especially those in primary care, to create actions to motivate and mobilize the population at risk to promote permanent changes in living habits, and thus reduce the mortality rate from stroke<sup>(20)</sup>.

In 2002, the Registration and Follow-up System for Hypertensive and Diabetic Patients (Registration and Monitoring System for Hypertensive and Diabetics), called Hiperdia, was implemented in Brazil, which consists of the continuous follow-up of such patients, together with the basic health units of the Unified Health System (SUS), with the supply of medications and the promotion of healthy living habits. Although it has existed for almost two decades, there are still no studies that estimate the effect of the implementation of Hypertension at the national level on the most common complication of cerebrovascular events, which is hospitalization for stroke. The estimation of this event is the main outcome indicator that directly evaluates the effects of preventive care for this morbidity. On the other hand, the proportion of hospital deaths from strokes after medical care represents an indicator of the quality of care in pre- and intrahospital emergency/emergency services<sup>(21)</sup>.

One of the measures usually used to compare the quality of care is hospital mortality from strokes up to 30 days, which represents its effectiveness. Care in the acute phase must be timely and effective to prevent brain tissue death. In order for the stroke care to be resolute, it is necessary to have a minimum set of technologies available at the correct time, such as the performance of computerized tomography ideally within four and a half hours after the onset of symptoms, in addition to other supports provided, in general, by specialized units. The use

of imaging exams for the care of the stroke is relevant for the differential diagnosis, definition and therapeutic prescription of appropriate care. As an indicator of quality of care, hospital mortality is a preliminary screening tool to discriminate hospitals potentially at risk of providing services of inadequate quality or below the expected standard. In this assessment, an adequate risk adjustment for clinical and demographic factors of the patient is essential, since the severity profile of the case interferes with care outcomes<sup>(22)</sup>.

#### IV. RESULTS

Eight hundred and fifty-two articles were identified in the stroke databases. From this the method *Simple Multi-Attribute Rating Technique using Exploiting Rankings* (SMARTER) was chosen. Of the 852 articles found by the combination of descriptors, 42 were selected for full text reading and only 11 articles were included for descriptive data analysis. In Figure 1, we describe the strategy for selecting articles on the subject in question.

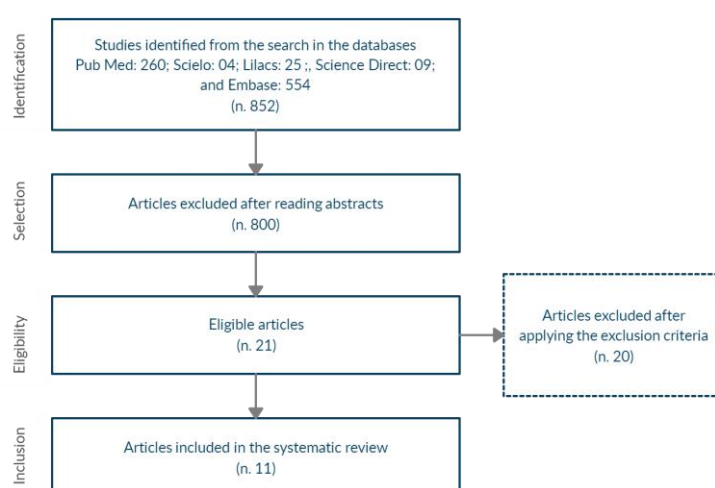


Fig.1: A search strategy for articles on interventions for caregivers of stroke survivors

Between the years 2010 and 2016, stroke mortality rates in women aged 30 to 69 decreased by 11%. This data was verified by the study Saúde Brasil 2018, conducted by the Ministry of Health. In this same period, the stroke rate decreased from 39.5 to 35.2 deaths per 100,000 female inhabitants, while Cardiac Diseases decreased from 55 to 51.6 deaths per 100,000<sup>(23)</sup>.

For the calculation of these figures, the study Saúde Brasil used the populations published by the Brazilian Institute of Geography and Statistics (IBGE); and for the standardized rate, the 2010 Brazilian Census.



The Strategic Action Plan for Chronic Noncommunicable Diseases (NCD) has shown a reduction in deaths from the two most deadly Chronic Noncommunicable Diseases (NCDs) in the country, which

are stroke and ischemic heart disease. This action has been developed by the Ministry of Health with states and municipalities in the population <sup>(24)</sup>.

Table 1. Description of the main study findings in the selected articles on stroke.

| Author/year<br>(reference) | Population      | Tools                                       | Results  |
|----------------------------|-----------------|---|--|
| Assis et al., 2013         | 120 patients    | Analysis of medical records<br>(database)   | Epileptic state, metabolic disorders and duration of disease were associated with hospital death. Epilepticus status was an independent risk factor for mortality. |
| Lamb; Martins, 201         | 385784 patients | Analysis of medical records<br>(database)   | higher mortality comorbidities; lower mortality with adequate hospital support   |
| Eisen et al. 201           | 15833 patients  | Analysis of exams<br>And records (database) | patients with atherosclerosis, increased risk of stroke and myocardial infarction  |
| Kuster et al.,<br>2015     | 206 patients    | Application of scales                       | the use of scales improves treatment and decreases the risk of mortality, especially the analysis of associated vascular damage                                    |
| Lange et al., 2018         | 359 patients    | Examination analysis                        | positive correlation of atherosclerosis and stroke   |
| Leitão et al., 2018        | 150 patients    | Quiz  | failure to know the risk of stroke in patients with atrial fibrillation; neglect   |
| Pedroso et al., 2017       | 60 patients     | Analysis of and<br>(database)               | exams positive correlation between stroke and records patients with psychiatric disorders  |
| Perera et al., 2016        | 2144 patients   | Analysis of medical records<br>(database)   | higher risk of stroke in patients with atrial fibrillation (women over 75 years)   |
| Rocha et al., 2014         | 120 patients    | Analysis of medical records<br>(database)   | epileptic seizures increase the risk of stroke, neoplasms and dementia   |

The Plan has the propagation of Basic Care as one of the main actions to confront NCD's, since in primary care one is able to solve up to 80% of health problems. The set of actions presents a result in increased access to health services, early diagnosis and treatment, as well as health promotion actions. Although there has been a fall, the two diseases remain at the top of those that kill the most women between 30 and 69 years of age <sup>(24)</sup>.

Chronic non-communicable diseases (NCD), such as stroke and ischemic heart disease, account for 63% or about 36 million of the world's deaths, especially circulatory diseases, diabetes, cancer and chronic respiratory disease. In Brazil, NCD also presents itself as a health problem, corresponding to 54.0% of all deaths in the

year 2016. In the 30-69 age group, NCD represented 56.1% of deaths.

Lifestyle and living conditions influence the occurrence of chronic non-communicable diseases. The World Health Organization (WHO) includes as important NCD the chronic respiratory diseases, circulatory system diseases (cerebrovascular, cardiovascular), diabetes mellitus and neoplasms. This disease has in common a number of risk factors, which may lead to a common approach to its prevention.

## V. DISCUSSION

According to Hobbs <sup>(25)</sup>, the worldwide incidence of AF (atrial fibrillation) is 1% to 2% of the total population.

Of the patients undergoing anticoagulant therapy, only 25.9% identified stroke as a risk of not adherence to treatment with AF anticoagulant. This alarming number shows us why AF patients continue to be seen frequently in stroke units, even in the face of a well known primary risk<sup>(26,27)</sup>. The crucial role of anticoagulation and adherence to AF therapy should be as evident to patients as to physicians.

The level of information should be as clear as possible. Considering the risks of anticoagulant therapy, education of patients about the disease and its risks is essential to improve compliance and reduce complications<sup>(28,29)</sup>. There is an alarming lack of knowledge about the basic concepts of AF and stroke. Studies have shown that 62.0% of patients with previous history of strokes had no knowledge about strokes as an AF complication. The lack of knowledge cannot be fully explained by the negligence of medical assistants. However, most of them did not mention the risk of strokes, so we can assume that there was a problem in communication.

Inadequate language and lack of effort in teaching patients may be interrelated. A low socioeconomic and educational level may also have contributed to low patient understanding.

Compared to other diseases, the stroke presented the highest gross hospital mortality rate (HBM) and highest *odds ratio* (OR), consistent with the severity of the diseases described in Brazilian studies. Regarding the comorbidities indexes, the highest chance of death when the congestive heart failure score (CHF score) was equal to or higher than two indicated greater severities, similar to previous studies<sup>(30,31)</sup>.

Of the Elixhauser comorbidities, the presence of low weight (OR = 1.82) stands out, as the other comorbidities had a protective effect. However, the quality of the information affects the accuracy of this type of index. In addition, pneumonia (OR = 1.49) presented a higher risk of death, but it is not possible to determine whether it was present at admission or whether it occurred during hospitalization, i.e., it was not possible to say whether it was a comorbidity or an avoidable complication. Moreover, as expected, they present a higher risk of death in elderly who used the ICU (OR = 4,095)<sup>(32)</sup>. This finding may express the greater severity of the case referred to the ICU. However, aspects related to access to these beds and the care process influence the use of this resource<sup>(32)</sup>. In general, studies report significant association and protective effect between ICU referrals and higher chances of survival in the adult population<sup>(33,34)</sup>.

At the hospital level, the MBT was higher in public hospitals (16.7%) than in private non-profit hospitals (11.6%) and in private for-profit hospitals (10.0%). The adjustment of this indicator decreased the TMHB only in public hospitals, highlighting the importance of risk adjustment. There is great variability in the MHAQ between hospitals, which raises the hypothesis of possible problems related to the quality of hospital care. However, we need to consider the limits of this study, especially regarding the robustness of hospital mortality as an indicator of the quality of care, mainly related to the causal validity between process and outcome and the accuracy of risk adjustment<sup>(35,36)</sup>. Separating variation because of the severity of the case, the care process and the clinical performance of professionals and the organization is an even more complex task in elderly patients, in which these elements can be more imbricated<sup>(36,37)</sup>. However, this type of approach is understood as a screening tool, i.e., a warning signal that requires subsequent analysis in order to improve the effectiveness of care and, consequently, its quality<sup>(35,38)</sup>.

In addition to the analysis of factors associated with the outcome of hospital care to elderly patients, it can be used as an indicator of the effectiveness of care<sup>(39)</sup>. Despite the limits, due to lack of information, the risk adjustment model presented reasonable discrimination capacity. Moreover, the analysis indicated that the length of hospital stay, predicted the risk of death. There was a clear improvement in comparing the predictive capacity of the models with the inclusion of length of stay. A protective effect was observed for hospitalizations longer than one day, possibly related to the seriousness of the case at the time of admission or the inadequacy of emergency care, which requires strictly timely and appropriate actions.

Another important limitation refers to the structure of hospital information system (HIS), which contained only one field for secondary diagnosis record in the period studied, in addition to underreporting, coverage and quality of available data. In this study, we observed low filling of the secondary diagnosis, that is, 13.8%. This value was lower than that described by Amaral<sup>(40)</sup>, who found registration in 19.5% of admissions in the state of Rio de Janeiro; however, our value was higher than that found by Martins<sup>(30)</sup> (5.4%) in admissions throughout Brazil. These deficiencies, mainly related to the description of comorbidities and complications, impact the analyses performed.

The use of these indices, together with the other variables, could predict in an acceptable way the hospital death of the elderly, and could be improved in the future to monitor the quality of care provided. On the other hand,

despite the contribution made, the development of new research is essential to increase knowledge about the profile of hospital interventions performed in elderly patients in Brazil and their effectiveness. We found that in Brazil the number of overweight patients with the first stroke was higher than the number with normal BMI and stroke. Most of the former had less than eight years of schooling, belonged to social class C and was significantly more physically inactive. Obesity is a worldwide pandemic<sup>(41-43)</sup>. In 2010, the *Global Burden of Disease Study* reported that overweight or obesity caused 3.4 million deaths, 3.9% of life years lost, and 3.8% of disability-adjusted life years worldwide<sup>(44)</sup>. According to this study, 7% of Brazilian men and 21% of women were obese in 2013<sup>(44)</sup>. As expected, these findings have an impact on stroke burden.

In a previous population study conducted in Joinville, it was found that 16% (CI95% 14-19) of 601 patients with first ischemic stroke were obese in the period 2005-2006. Six years later, (period from 2012 to 2013), the prevalence of obesity in 786 patients with ischemic stroke jumped significantly to 23% (95%CI, 20-27)<sup>(3)</sup>. This proportion is similar to our finding of 26% (95%CI, 24-29) in this study in five Brazilian cities.

Causality between obesity and stroke is debatable<sup>(44-46)</sup>. A meta-analysis of 21 cohort studies reported that the risk of ischemic stroke was 22% in overweight patients and 64% among obese. For "primary" intracerebral hemorrhage, the risk was not significant<sup>(47)</sup>. However, other studies demonstrated that the association with obesity was substantially reduced after the control of hypertension and diabetes variables for obesity<sup>(48)</sup>.

The main findings in another stroke study were high prevalence of hypertension and diabetes mellitus, some connectivity problems and problems related to the recording of PoIP (ambulatory monitoring system) signals and similar profile of cardiac arrhythmias among the study groups<sup>(49)</sup>.

The most frequent comorbidities were hypertension (84.6%) and diabetes mellitus (51.9%), with similar distribution between the groups studied and both comorbidities are also included in the CHADS2 and CHA2DS2-VASc scores. Although these scores provide simple methods to predict an individual risk of ischemic stroke, the risk estimated by these instruments represents only part of the overall risk (statistical concordance of 0.5). A recent meta-analysis showed that smoking is associated with a modest increase in AF and that quitting reduces, but does not eliminate, the risk associated with the

disease<sup>(50,51)</sup>. However, adding smoking to the score does not improve prediction of risk of stroke or TIA<sup>(52)</sup>.

The comparison between Holter and PoIP monitoring results showed a higher proportion of frequent HV and SVES detected by PoIP monitoring in the AVC / AIT and control groups, which was expected for their longer monitoring period. Studies suggested that an additional 24-hour monitoring period would increase the percentage of new paroxysmal AF diagnoses in 2-4% of stroke patients<sup>(53,54)</sup>. This confirms the efficacy of prolonged outpatient ECG in patients at risk for AF and may generate clinically significant diagnostic performance<sup>(55)</sup>.

In this study, all AF episodes lasted less than 30 seconds. Although an AF episode  $\geq 30$  seconds is used as a parameter for AF diagnosis, some authors have suggested that short AF episodes impact the risk of stroke / TIA or systemic thromboembolism<sup>(56,57)</sup>. An important finding was the lack of difference in the prevalence of atrial arrhythmias among patients with and without stroke or TIA, with similar risk for these conditions. This finding suggests that the atrial arrhythmias detected may be an epiphenomenon. Kottkamp<sup>(58)</sup> and other authors<sup>(59)</sup> suggested the presence of thrombogenic fibrotic atrial cardiomyopathy, with risk of embolic events without causal connections with atrial arrhythmias. Contractile alterations would be responsible for the increased thrombogenic risk during sinus rhythm, in addition to interatrial block and sinus node dysfunction. Even AF ablation would not be able to impede the progression of the fibrotic process<sup>(58)</sup>. Factors such as diabetes, hypertension, age, among others, would be involved in myocardial damage. In this sample, more than 80% of patients had hypertension and more than 50% were diabetics. The paradigm used in most studies is that the detection of AF would be only a matter of time, but even in one year of follow-up, AF is detected in less than half of the patients with stroke. This pioneering study monitored patients at similar risk of stroke and TIA, including a stroke group and a control group without the disease. The finding that the incidence of atrial arrhythmias was not different between the two groups is consistent with the hypothesis that a different factor from arrhythmia may be involved in the risk of stroke; one possibility is fibrotic atrial cardiomyopathy.

Ischemic stroke associated with AF is common: The differences in prevalence between sites and regions are mainly due to variation in the mean ages of the stroke populations. There was a strong and significant correlation between the mean age of the stroke cohort and the frequency of AF between sites. Compared to other regions,

Latin America had the lowest frequency of AF-related strokes; this probably reflects the lower mean age of the stroke population in Latin America, which was on average a decade lower than the stroke population in other regions. The assigned risk of AF for ischemic stroke in a given population is expected to be influenced by the life expectancy of the population<sup>(60)</sup>, and this may partially explain the regional variations in the frequency of AF between high- and high-income countries in this study. This regional variability can also be partially explained by the variability in access to diagnostic tests in each center; at least hypothetically, we can assume that access to prolonged monitoring for AF is easier in high-income regions compared to upper middle-income regions.

Recent studies published since the record show that prolonged heart rate monitoring (> 1 month) identifies additional patients with strokes that present episodes of paroxysmal AF, <sup>(61,62)</sup> that are generally brief and have uncertain pathogen relevance<sup>(63)</sup>. The increase in frequency of AF-associated strokes compared to other ischemic strokes occurred despite the more widespread use of oral anticoagulants in AF patients<sup>(60)</sup>. More than half of the strokes related to AF occurred in patients with known history of AF. Although no data on antithrombotic or anticoagulant therapy are available, this finding emphasizes the importance of optimizing stroke prevention in patients with known AF. It should be recognized that precise subtyping of stroke may not be possible in all cases, even with advanced neuroimaging and vascular imaging techniques, and that some lacunar strokes may have cardioembolic or atheroembolic sources. However, previously published data on treatment with anticoagulation in AF patients with lacunar strokes show no benefit in the use of anticoagulants when compared to treatment with antiplatelet in reducing the risk of recurrent stroke<sup>(64,65)</sup>.

In a study cohort, mortality at 30 days was significantly higher in AF patients compared to nonAF patients in global regions. The findings are consistent and according to the largest randomized trials, and show a significant correlation between the mean age of stroke patients and the frequency of AF, which is statistically significant and according to several recent observational data<sup>(60,66,67)</sup>. However, the study sites represented many global regions, allowing a unique comparison of AF-associated strokes around the world.

In summary, these studies provide a unique insight into the global burden of FA-related stroke. Stroke associated with AF comprises an important subset (28%; 95% CI, 25.6-29.5) of ischemic stroke patients worldwide

and is the most frequent cause of ischemic stroke in older women. These traits are potentially preventable.

The analysis of the socio-demographic characteristics of the sample allows the profile of the patients attended by a public hospital, considered the local reference center for the treatment of stroke. Thus, it was observed that the sample consisted of elderly patients, predominantly unemployed, with low income and low education and socially vulnerable. The patients presented high rates of clinical comorbidities, mainly hypertension, obesity, dyslipidemia, diabetes and smoking.

A similar profile of medical comorbidity was found in a previous study, conducted at the same hospital, which investigated the role of Chagas' disease as an independent risk factor for the occurrence of stroke<sup>(68)</sup>. Observations of mean BMI values above 25 kg / m<sup>2</sup> and high mean blood pressure values, despite the use of drugs, draw attention to the unsatisfactory clinical management of patients before admission. Framingham's score for the sample was calculated from the clinical variables recorded. This score was developed based on information collected from population epidemiological studies conducted over 36 years and estimates the probability of stroke from clinical information<sup>(69)</sup>. The mean score observed was 21.27. This value indicates that the probability of stroke in 10 years is higher than 30% for men and 14% for women, and this value confirms the high risk profile for the development of stroke in this sample<sup>(70)</sup>.

Most of the individuals observed had lacunar strokes, with predominance of lesions in the middle cerebral artery topography of the right hemisphere. NIHSS, mRS and MIF Scales were used to measure the initial severity of the ischemic event and its resulting disability. Mean results were below 5 for NIHSS and below 3 for mRS, indicating a slight stroke impact on the sample. This fact is reflected in the measurement of patient dysfunction obtained by MIF, a scale ranging from 18 (worst result) to 126 (best result) points. The mean value, 113.67, found in the sample was compatible with a mild functional deficit<sup>(71)</sup>.

Despite the slight functional impact, the evaluation through structured psychiatric interview revealed the presence of mental disorders, mainly depressive and anxiety disorders, in approximately 55% of the cases. According to other studies, depression was the most frequent psychiatric disorder<sup>(72,73)</sup>. Chemerinski and Robinson<sup>(74)</sup> observed that the frequency of depression among patients hospitalized during the acute phase of the stroke is approximately 22% for major depression and 17% for minor depression. In outpatient samples (ranging from



3 months to 10 years after the stroke), the frequency is approximately 23% for major depression and 35% for minor depression, while community samples exhibit mean prevalence of 13% and 10%, respectively.

Through meta-analysis the prevalence of depression at any time after the stroke was 29%. In this sense, a systematic review of Brazilian studies that evaluated the prevalence of depression after stroke in different contexts found prevalence rates ranging from 20 to 59%<sup>(75)</sup>. Anxiety disorders are also common after stroke. Between 25% and 50% of patients develop generalized anxiety disorder (TAG) in the first months after the stroke, with a small reduction in incidence in the following three years<sup>(76)</sup>. Burton<sup>(77)</sup> reported that anxiety disorders affected 20% to 25% of patients at any time after the stroke. According to Burton<sup>(77)</sup>, phobic disorders and TAG are the most common types of anxiety disorders after a stroke.

Considering that mental disorders negatively influence the recovery of patients after strokes and that factors associated with social vulnerability are risk factors that complicate treatment, the high frequency of depression and anxiety disorders draws attention to possible consequences that may result if patients are not identified and adequately treated, even when the functional impact of the stroke in patients is mild<sup>(78,79)</sup>. The relationship between depression after stroke and functional impairment is complex. Depressed patients have a significantly greater disability in daily life activities than eutymic individuals with equivalent neurological diseases<sup>(74)</sup>.

## VI. CONCLUSION

It is now known that stroke is one of the major causes of morbidity and mortality among patients, most of them in the elderly. It is associated with NCD, among which we mention hypertension, diabetes and dyslipidemia. This disease is more common in men, blacks and with low schooling, but in women it is more lethal, according to pre-existing data.

In Brazil, the evaluation of hospital care by means of administrative data and risk adjusted performance indicators is a little developed subject. There is also a lack of studies specifically on hospital care for the elderly.

The survey showed that the population between 30 and 69 years of age and over 70 years of age, ischemic heart disease presented the highest mortality rates in all regions of the country, both in women and men. Stroke, on the other hand, occupied the second place of the main causes of deaths among women from all regions and men

from the South and Southeast, aged between 30 to 69 years.

Our data brings to light important information, from causes, motor and emotional after-effects, and the lack of information on quality of care data (both clinical and diagnostic) and hospitalization of these patients with stroke. This shows the importance of this systematic review, and of new studies that can elucidate and bring more data about this gap within the stroke studies.

Thus, new methodologies and analyses need to be developed on the effects of the multiplicity of chronic diseases, which affect the elderly more intensely. Considering this context, this work contributes to the Brazilian production, since it has analyzed the studies that deal with strokes in Brazil, gathering the available information.

## REFERENCES

- [1] Oliveira-Filho J, Martins SCO, Pontes-Neto OM, Longo A, Evaristo EF, de Carvalho JF, et al. Diretrizes para tratamento do acidente vascular isquêmico - parte I. *Arq Neuropsiquiatr*. 2012;70(8):621–9.
- [2] Kernan WN, Viscoli CM, Furie KL, Young LH, Inzucchi SE, Gorman M, et al. Pioglitazone after Ischemic Stroke or Transient Ischemic Attack. *N Engl J Med* [Internet]. 2016 Apr 7;374(14):1321–31. Available from: <http://www.nejm.org/doi/10.1056/NEJMoa1506930>
- [3] Vicente VS, Cabral NL, Nagel V, Guesser V V, Safanelli J. Prevalence of obesity among stroke patients in five Brazilian cities: a cross-sectional study. *Arq Neuropsiquiatr* [Internet]. 2018 Jun;76(6):367–72. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0004-282X2018000600367&lng=en&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2018000600367&lng=en&tlng=en)
- [4] Assis TR de, Bacellar A, Costa G, Nascimento OJM. Etiological prevalence of epilepsy and epileptic seizures in hospitalized elderly in a Brazilian tertiary center – Salvador - Brazil. *Arq Neuropsiquiatr* [Internet]. 2015 Feb;73(2):83–9. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0004-282X2015000200083&lng=en&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2015000200083&lng=en&tlng=en)
- [5] Eisen A, Bonaca MP, Jarolim P, Scirica BM, White HD, Tendera M, et al. High-Sensitivity Troponin I in Stable Patients with Atherosclerotic Disease in the TRA 2°P - TIMI 50 Trial. *Clin Chem* [Internet]. 2017 Jan 1;63(1):307–15. Available from: <https://academic.oup.com/clinchem/article/63/1/307/5612779>
- [6] Lange MC, Ribas G, Scavasine V, Ducci RD-P, Mendes DC, Zétola V de HF, et al. Stroke recurrence in the different subtypes of ischemic stroke. The importance of the intracranial disease. *Arq Neuropsiquiatr* [Internet]. 2018 Oct;76(10):649–53. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0004-282X2018001000649&lng=en&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2018001000649&lng=en&tlng=en)

- 004-282X2018001000649&lng=en&tlng=en
- [7] Kuster GW, Dutra LA, Brasil IP, Pacheco EP, Arruda MJC, Volcov C, et al. Performance of four ischemic stroke prognostic scores in a Brazilian population. *Arq Neuropsiquiatr* [Internet]. 2016 Feb;74(2):133–7. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0004-282X2016000200010&lng=en&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2016000200010&lng=en&tlng=en)
  - [8] Morgan JA, Brewer RJ, Nemeh HW, Gerlach B, Lanfear DE, Williams CT, et al. Stroke while on long-term left ventricular assist device support: incidence, outcome, and predictors. *ASAIO J*. 2014;60(3):284–9.
  - [9] Who WHO. 10 facts on obesity. Available from: <https://www.who.int/features/factfiles/obesity/en/>
  - [10] Sociedade Brasileira de Doenças Cerebrovasculares. Acidente vascular cerebral. Available from: [http://www.sbdcv.org.br/publica\\_avc.asp](http://www.sbdcv.org.br/publica_avc.asp)
  - [11] Brasil. Ministério da Saúde. Secretaria de Atenção à Saúde. Departamento de Ações Programáticas Estratégicas. Diretrizes de Atenção à Reabilitação da Pessoa com Acidente Vascular Cerebral [Internet]. Brasília,DF. 2013. 72 p. Available from: [www.saude.gov.br/bvs](http://www.saude.gov.br/bvs)
  - [12] Chaves ML. Acidente vascular encefálico: conceituação e fatores de risco. *Rev Bras Hipertens*. 2000;7.
  - [13] Rodrigues MDS, Santana LF e, Galvão IM. Fatores de risco modificáveis e não modificáveis do AVC isquêmico: uma abordagem descritiva. *Rev Med*. 2017;96(3):187.
  - [14] Saenger AK, Christenson RH. Stroke biomarkers: progress and challenges for diagnosis, prognosis, differentiation, and treatment. *Clin Chem*. 2010 Jan;56(1):21–33.
  - [15] Dennis L, Kasper ... [ et al. ]. Manual de medicina de Harrison [recurso eletrônico]. 2017; Available from: [arquivo60017773/manual-de-medicina-de-harrison-kasper-dennis](http://arquivo60017773/manual-de-medicina-de-harrison-kasper-dennis)
  - [16] MINISTÉRIO DA SAÚDE. Manual Instrutivo da Rede de Atenção às Urgências e Emergências no Sistema Único de Saúde (SUS) [Internet]. 2013. 86 p. Available from: [http://bvsms.saude.gov.br/bvs/publicacoes/manual\\_instrutivo\\_rede\\_atencao\\_urgencias.pdf](http://bvsms.saude.gov.br/bvs/publicacoes/manual_instrutivo_rede_atencao_urgencias.pdf)
  - [17] Barella RP, Duran V de AA, Pires AJ, Duarte R de O. Perfil Do Atendimento De Pacientes Com Acidente Vascular Cerebral Em Um Hospital Filantrópico Do Sul De Santa Catarina E Estudo De Viabilidade Para Implantação Da Unidade De Avc. *Arq Catarinenses Med* [Internet]. 2019;48(1):131–43. Available from: <http://www.acm.org.br/acm/seer/index.php/arquivos/article/view/432/334>
  - [18] BRASIL M da S. Dispõe sobre os critérios de habilitação dos estabelecimentos hospitalares como Centro de Atendimento de Urgência aos Pacientes com Acidente Vascular Cerebral (AVC), no âmbito do Sistema Único de Saúde (SUS). 2012; Available from: [https://bvsms.saude.gov.br/bvs/saudelegis/gm/2012/PRT0665\\_12\\_04\\_2012.html](https://bvsms.saude.gov.br/bvs/saudelegis/gm/2012/PRT0665_12_04_2012.html)
  - [19] Smajlović D. Strokes in young adults: epidemiology and prevention. *Vasc Health Risk Manag*. 2015;11:157–64.
  - [20] Em PDEP, Coletiva S. Criciúma 2017.
  - [21] Lopes JM, Sanchis GJB, Medeiros JLA de, Dantas FG. Hospitalização por acidente vascular encefálico isquêmico no Brasil: estudo ecológico sobre possível impacto do Hiperdia. *Rev Bras Epidemiol* [Internet]. 2016 Mar;19(1):122–34. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S1415-790X2016000100122&lng=pt&tlng=pt](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1415-790X2016000100122&lng=pt&tlng=pt)
  - [22] Rolim CLRC, Martins M. Qualidade do cuidado ao acidente vascular cerebral isquêmico no SUS. *Cad Saude Publica* [Internet]. 2011 Nov;27(11):2106–16. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0102-311X2011001100004&lng=pt&tlng=pt](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-311X2011001100004&lng=pt&tlng=pt)
  - [23] Brasil M da S. Taxas de óbito por AVC e doenças cardíacas caem entre as mulheres. 2019; Available from: <https://www.saude.gov.br/noticias/agencia-saude/45282-taxas-de-obito-por-avc-e-doencas-cardiacas-caem-entre-as-mulheres>
  - [24] Saúde M Da. Ministério da Saúde Brasília-DF 2011. 2011. 160 p.
  - [25] Hobbs FR, Taylor CJ, Jan Geersing G, Rutten FH, Brouwer JR. European Primary Care Cardiovascular Society (EPCCS) consensus guidance on stroke prevention in atrial fibrillation (SPAF) in primary care. *Eur J Prev Cardiol* [Internet]. 2016 Mar 20;23(5):460–73. Available from: <http://journals.sagepub.com/doi/10.1177/2047487315571890>
  - [26] Cabral NL, Volpato D, Ogata TR, Ramirez T, Moro C, Gouveia S. Fibrilação atrial crônica, AVC e anticoagulação: sub-uso de warfarina? *Arq Neuropsiquiatr* [Internet]. 2004 Dec;62(4):1016–21. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0004-282X2004000600016&lng=pt&tlng=pt](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2004000600016&lng=pt&tlng=pt)
  - [27] Amaral CH do, Amaral AR, Nagel V, Venancio V, Garcia AC, Magalhaes PS, et al. Incidence and functional outcome of atrial fibrillation and non-atrial fibrillation-related cardioembolic stroke in Joinville, Brazil: a population-based study. *Arq Neuropsiquiatr* [Internet]. 2017 May;75(5):288–94. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0004-282X2017000500288&lng=en&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2017000500288&lng=en&tlng=en)
  - [28] Hernández Madrid A, Potpara TS, Dagres N, Chen J, Larsen TB, Estner H, et al. Differences in attitude, education, and knowledge about oral anticoagulation therapy among patients with atrial fibrillation in Europe: result of a self-assessment patient survey conducted by the European Heart Rhythm Association. *Europace* [Internet]. 2016 Mar;18(3):463–7. Available from: <https://academic.oup.com/europace/article-lookup/doi/10.1093/europace/euv448>
  - [29] Potpara TS, Pison L, Larsen TB, Estner H, Madrid A, Blomstrom-Lundqvist C, et al. How are patients with atrial fibrillation approached and informed about their risk profile and available therapies in Europe? Results of the European Heart Rhythm Association Survey. *Europace* [Internet]. 2015 Mar 1;17(3):468–72. Available from: <https://academic.oup.com/europace/article->

- lookup/doi/10.1093/europace/euv025
- [30] Martins M. Uso de medidas de comorbidades para predição de risco de óbito em pacientes brasileiros hospitalizados. *Rev Saude Publica* [Internet]. 2010 Jun;44(3):448–56. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0034-89102010000300008&lng=pt&tlng=pt](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-89102010000300008&lng=pt&tlng=pt)
- [31] Miyata H, Hashimoto H, Horiguchi H, Matsuda S, Motomura N, Takamoto S. Performance of in-hospital mortality prediction models for acute hospitalization: Hospital Standardized Mortality Ratio in Japan. *BMC Health Serv Res* [Internet]. 2008 Dec 7;8(1):229. Available from: <https://bmchealthservres.biomedcentral.com/articles/10.1186/1472-6963-8-229>
- [32] Machado JP, Martins M, Leite I da C. Public-private settlement and hospital mortality per sources of payment. *Rev Saude Publica* [Internet]. 2016;50. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0034-89102016000100405&lng=en&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-89102016000100405&lng=en&tlng=en)
- [33] Simchen E, Sprung CL, Galai N, Zitser-Gurevich Y, Bar-Lavi Y, Gurman G, et al. Survival of critically ill patients hospitalized in and out of intensive care units under paucity of intensive care unit beds\*. *Crit Care Med* [Internet]. 2004 Aug;32(8):1654–61. Available from: <http://journals.lww.com/00003246-200408000-00004>
- [34] Cardoso LT, Grion CM, Matsuo T, Anami EH, Kauss IA, Seko L, et al. Impact of delayed admission to intensive care units on mortality of critically ill patients: a cohort study. *Crit Care* [Internet]. 2011;15(1):R28. Available from: <http://ccforum.biomedcentral.com/articles/10.1186/cc9975>
- [35] Leatherman S. Performance measurement for health system improvement [Internet]. Smith PC, Mossialos E, Papanicolas I, editors. Cambridge: Cambridge University Press; 2010. Available from: <http://ebooks.cambridge.org/ref/id/CBO9780511711800>
- [36] McCormick B, Pearson M, White J. Hospital mortality rates and place of death. *J Public Health (Bangkok)* [Internet]. 2015 Dec 24;fdv188. Available from: <https://academic.oup.com/jpubhealth/article-lookup/doi/10.1093/pubmed/fdv188>
- [37] van Doorn C, Bogardus ST, Williams CS, Concato J, Towle VR, Inouye SK. Risk adjustment for older hospitalized persons. *J Clin Epidemiol* [Internet]. 2001 Jul;54(7):694–701. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S089543560000367X>
- [38] Martins M, Blais R, Leite I da C. Mortalidade hospitalar e tempo de permanência: comparação entre hospitais públicos e privados na região de Ribeirão Preto, São Paulo, Brasil. *Cad Saude Publica* [Internet]. 2004;20(suppl 2):S268–82. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0102-311X2004000800021&lng=pt&tlng=pt](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-311X2004000800021&lng=pt&tlng=pt)
- [39] Weber R, Kraywinkel K, Diener H-C, Weimar C. Symptomatic Intracranial Atherosclerotic Stenoses: Prevalence and Prognosis in Patients with Acute Cerebral Ischemia. *Cerebrovasc Dis* [Internet]. 2010;30(2):188–93. Available from: <https://www.karger.com/Article/FullText/317107>
- [40] Amaral ACS, Coeli CM, Costa M do CE da, Cardoso V da S, Toledo ALA de, Fernandes CR. Perfil de morbidade e de mortalidade de pacientes idosos hospitalizados. *Cad Saude Publica* [Internet]. 2004 Dec;20(6):1617–26. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0102-311X2004000600020&lng=pt&tlng=pt](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-311X2004000600020&lng=pt&tlng=pt)
- [41] Colombo PJ, Crawley ME, East BS, Hill AR. Aging and the Brain. *Encycl Hum Behav Second Ed*. 2012;53–9.
- [42] Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi J-C, et al. Coding Algorithms for Defining Comorbidities in ICD-9-CM and ICD-10 Administrative Data. *Med Care* [Internet]. 2005 Nov;43(11):1130–9. Available from: <http://journals.lww.com/00005650-200511000-00010>
- [43] Aylin P, Bottle A, Majeed A. Use of administrative data or clinical databases as predictors of risk of death in hospital: comparison of models. *BMJ* [Internet]. 2007 May 19;334(7602):1044. Available from: <http://www.bmj.com/lookup/doi/10.1136/bmj.39168.49636.6.55>
- [44] Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* [Internet]. 2014 Aug;384(9945):766–81. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0140673614604608>
- [45] Dehlendorff C, Andersen KK, Olsen TS. Body Mass Index and Death by Stroke. *JAMA Neurol* [Internet]. 2014 Aug 1;71(8):978. Available from: <http://archneur.jamanetwork.com/article.aspx?doi=10.1001/jamaneurol.2014.1017>
- [46] George MG, Tong X, Bowman BA. Prevalence of Cardiovascular Risk Factors and Strokes in Younger Adults. *JAMA Neurol* [Internet]. 2017 Jun 1;74(6):695. Available from: <http://archneur.jamanetwork.com/article.aspx?doi=10.1001/jamaneurol.2017.0020>
- [47] Strazzullo P, D'Elia L, Cairella G, Garbagnati F, Cappuccio FP, Scalfi L. Excess Body Weight and Incidence of Stroke. *Stroke* [Internet]. 2010 May;41(5). Available from: <https://www.ahajournals.org/doi/10.1161/STROKEAHA.109.576967>
- [48] Mitchell AB, Cole JW, McArdle PF, Cheng Y-C, Ryan KA, Sparks MJ, et al. Obesity Increases Risk of Ischemic Stroke in Young Adults. *Stroke* [Internet]. 2015 Jun;46(6):1690–2. Available from: <https://www.ahajournals.org/doi/10.1161/STROKEAHA.115.008940>
- [49] Sampaio RF, Gomes IC, Sternick EB. Cryptogenic Acute Ischemic Stroke: Assessment of the Performance of a New Continuous Long-Term Monitoring System in the

- Detection of Atrial Fibrillation. *Arq Bras Cardiol* [Internet]. 2018; Available from: <http://www.gnresearch.org/doi/10.5935/abc.20180112>
- [50] Ritter MA, Kochhäuser S, Duning T, Reinke F, Pott C, Dechering DG, et al. Occult atrial fibrillation in cryptogenic stroke: detection by 7-day electrocardiogram versus implantable cardiac monitors. *Stroke*. 2013 May;44(5):1449–52.
- [51] Zhu W, Yuan P, Shen Y, Wan R, Hong K. Association of smoking with the risk of incident atrial fibrillation: A meta-analysis of prospective studies. *Int J Cardiol*. 2016 Sep;218:259–66.
- [52] Kwon Y, Norby FL, Jensen PN, Agarwal SK, Soliman EZ, Lip GYH, et al. Association of Smoking, Alcohol, and Obesity with Cardiovascular Death and Ischemic Stroke in Atrial Fibrillation: The Atherosclerosis Risk in Communities (ARIC) Study and Cardiovascular Health Study (CHS). *PLoS One*. 2016;11(1):e0147065.
- [53] Lazzaro MA, Krishnan K, Prabhakaran S. Detection of atrial fibrillation with concurrent holter monitoring and continuous cardiac telemetry following ischemic stroke and transient ischemic attack. *J stroke Cerebrovasc Dis Off J Natl Stroke Assoc*. 2012 Feb;21(2):89–93.
- [54] Shafqat S, Kelly PJ, Furie KL. Holter monitoring in the diagnosis of stroke mechanism. *Intern Med J*. 2004 Jun;34(6):305–9.
- [55] Turakhia MP, Ullal AJ, Hoang DD, Than CT, Miller JD, Friday KJ, et al. Feasibility of Extended Ambulatory Electrocardiogram Monitoring to Identify Silent Atrial Fibrillation in High-risk Patients: The Screening Study for Undiagnosed Atrial Fibrillation (STUDY-AF). *Clin Cardiol* [Internet]. 2015 May;38(5):285–92. Available from: <http://doi.wiley.com/10.1002/clc.22387>
- [56] Hart RG, Diener H-C, Coutts SB, Easton JD, Granger CB, O'Donnell MJ, et al. Embolic strokes of undetermined source: the case for a new clinical construct. *Lancet Neurol*. 2014 Apr;13(4):429–38.
- [57] Higgins P, Dawson J, MacFarlane PW, McArthur K, Langhorne P, Lees KR. Predictive value of newly detected atrial fibrillation paroxysms in patients with acute ischemic stroke, for atrial fibrillation after 90 days. *Stroke*. 2014 Jul;45(7):2134–6.
- [58] Kottkamp H. Fibrotic atrial cardiomyopathy: a specific disease/syndrome supplying substrates for atrial fibrillation, atrial tachycardia, sinus node disease, AV node disease, and thromboembolic complications. *J Cardiovasc Electrophysiol*. 2012 Jul;23(7):797–9.
- [59] Hirsh BJ, Copeland-Halperin RS, Halperin JL. Fibrotic atrial cardiomyopathy, atrial fibrillation, and thromboembolism: mechanistic links and clinical inferences. *J Am Coll Cardiol*. 2015 May;65(20):2239–51.
- [60] Lakshminarayan K, Solid CA, Collins AJ, Anderson DC, Herzog CA. Atrial Fibrillation and Stroke in the General Medicare Population. *Stroke* [Internet]. 2006 Aug;37(8):1969–74. Available from: <https://www.ahajournals.org/doi/10.1161/01.STR.0000230607.07928.17>
- [61] Gladstone DJ, Spring M, Dorian P, Panzov V, Thorpe KE, Hall J, et al. Atrial Fibrillation in Patients with Cryptogenic Stroke. *N Engl J Med* [Internet]. 2014 Jun 26;370(26):2467–77. Available from: <http://www.nejm.org/doi/10.1056/NEJMoa1311376>
- [62] Sanna T, Diener H-C, Passman RS, Di Lazzaro V, Bernstein RA, Morillo CA, et al. Cryptogenic Stroke and Underlying Atrial Fibrillation. *N Engl J Med* [Internet]. 2014 Jun 26;370(26):2478–86. Available from: <http://www.nejm.org/doi/10.1056/NEJMoa1313600>
- [63] Arsava EM, Bas DF, Atalar E, Has AC, Oguz KK, Topcuoglu MA. Ischemic Stroke Phenotype in Patients With Nonsustained Atrial Fibrillation. *Stroke* [Internet]. 2015 Mar;46(3):634–40. Available from: <https://www.ahajournals.org/doi/10.1161/STROKEAHA.114.006396>
- [64] Hart RG, Pearce LA, Miller VT, Anderson DC, Rothrock JF, Albers GW, et al. Cardioembolic vs. noncardioembolic strokes in atrial fibrillation: frequency and effect of antithrombotic agents in the stroke prevention in atrial fibrillation studies. *Cerebrovasc Dis*. 2000;10(1):39–43.
- [65] Evans A, Perez I, Yu G, Kalra L. Should Stroke Subtype Influence Anticoagulation Decisions to Prevent Recurrence in Stroke Patients With Atrial Fibrillation? *Stroke* [Internet]. 2001 Dec;32(12):2828–32. Available from: <https://www.ahajournals.org/doi/10.1161/hs1201.099520>
- [66] Shroff GR, Solid CA, Herzog CA. Atrial Fibrillation, Stroke, and Anticoagulation in Medicare Beneficiaries: Trends by Age, Sex, and Race, 1992–2010. *J Am Heart Assoc* [Internet]. 2014 May 22;3(3). Available from: <https://www.ahajournals.org/doi/10.1161/JAHA.113.000756>
- [67] Heeringa J, van der Kuip DAM, Hofman A, Kors JA, van Herpen G, Stricker BHC, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: the Rotterdam study. *Eur Heart J* [Internet]. 2006 Apr 1;27(8):949–53. Available from: <https://academic.oup.com/eurheartj/article/27/8/949/2887153>
- [68] Paixão LC, Ribeiro AL, Valacio RA, Teixeira AL. Chagas Disease. *Stroke* [Internet]. 2009 Dec;40(12):3691–4. Available from: <https://www.ahajournals.org/doi/10.1161/STROKEAHA.109.560854>
- [69] D'Agostino RB, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General Cardiovascular Risk Profile for Use in Primary Care. *Circulation* [Internet]. 2008 Feb 12;117(6):743–53. Available from: <https://www.ahajournals.org/doi/10.1161/CIRCULATIONAHA.107.699579>
- [70] Pires SL, Gagliardi RJ, Gorzoni ML. Estudo das frequências dos principais fatores de risco para acidente vascular cerebral isquêmico em idosos. *Arq Neuropsiquiatr* [Internet]. 2004 Sep;62(3b):844–51. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0004-282X2004000500020&lng=pt&tlng=pt](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2004000500020&lng=pt&tlng=pt)
- [71] Itaquy RB, Favero SR, Ribeiro M de C, Barea LM,



- Almeida ST de, Mancopes R. Disfagia e acidente vascular cerebral: relação entre o grau de severidade e o nível de comprometimento neurológico. *J Soc Bras Fonoaudiol* [Internet]. 2011 Dec;23(4):385–9. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S2179-64912011000400016&lng=pt&tlng=pt](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S2179-64912011000400016&lng=pt&tlng=pt)
- [72] Angelelli P, Paolucci S, Bivona U, Piccardi L, Ciurli P, Cantagallo A, et al. Development of neuropsychiatric symptoms in poststroke patients: a cross-sectional study. *Acta Psychiatr Scand* [Internet]. 2004 Jul;110(1):55–63. Available from: <http://doi.wiley.com/10.1111/j.1600-0447.2004.00297.x>
- [73] Buijck BI, Zuidema SU, Eijk M, Geurts AC, Koopmans RT. Neuropsychiatric symptoms in geriatric patients admitted to skilled nursing facilities in nursing homes for rehabilitation after stroke: a longitudinal multicenter study. *Int J Geriatr Psychiatry* [Internet]. 2012 Jul;27(7):734–41. Available from: <http://doi.wiley.com/10.1002/gps.2781>
- [74] Chemerinski E, Robinson RG. The Neuropsychiatry of Stroke. *Psychosomatics* [Internet]. 2000 Jan;41(1):5–14. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0033318200711686>
- [75] PEDROSO VSP, SOUZA LC, BRUNONI AR, TEIXEIRA AL. Post stroke depression: clinics, etiopathogenesis and therapeutics. *Arch Clin Psychiatry (São Paulo)* [Internet]. 2015 Feb;42(1):18–24. Available from: [http://www.scielo.br/scielo.php?script=sci\\_arttext&pid=S0101-60832015000100018&lng=en&nrm=iso&tlng=en](http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0101-60832015000100018&lng=en&nrm=iso&tlng=en)
- [76] Åström M. Generalized Anxiety Disorder in Stroke Patients. *Stroke* [Internet]. 1996 Feb;27(2):270–5. Available from: <https://www.ahajournals.org/doi/10.1161/01.STR.27.2.270>
- [77] Burton JL, Xiong Y, Solomon MJ. Mechanisms of pseudosubstrate inhibition of the anaphase promoting complex by Acm1. *EMBO J*. 2011 May;30(9):1818–29.
- [78] Oldehinkel AJ, Ormel J, Brilman EI, van den Berg MD. Psychosocial and vascular risk factors of depression in later life. *J Affect Disord* [Internet]. 2003 May;74(3):237–46. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S0165032702000149>
- [79] Paolucci S, Gandolfo C, Provinciali L, Torta R, Toso V. The Italian multicenter observational study on post-stroke depression (DESTRO). *J Neurol* [Internet]. 2006 May 18;253(5):556–62. Available from: <http://link.springer.com/10.1007/s00415-006-0058-6>