

Epidemiological Profile of Intracerebral Hemorrhage during a 10-Year Period in a Southern Brazilian Region

Perfil epidemiológico da hemorragia cerebral espontânea no período de 10 anos em uma região do sul do Brasil

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Abstract

Objective Spontaneous intracerebral hemorrhage is responsible for 20% of all cases of cerebrovascular accidents, which might lead to functional disabilities and death. There are few epidemiological data on spontaneous intracerebral hemorrhage in Brazil, and more specifically in the southern region of the country.

Methods We reviewed data of 221 patients with intracerebral hemorrhage who attended our department between January of 2004 and December of 2013 and were registered as I61 and I62 according to the 10th edition of the International Classification of Diseases and Related Health Problems (ICD-10).

Results From the 221 cases, 53.8% were male, and the median age was 63 years old. Arterial hypertension was reported in 62.4% of the patients. Surgical treatment was performed in 28.9% of all cases and pneumonia affected 19.9%. In 73.4% of the cases, the patients died or were severely disabled at discharge. We found an association of heart disease, coagulopathies, chronic kidney disease, anticoagulant drugs use, surgical treatment, and pneumonia with a poorer outcome.

Conclusion The present study describes the epidemiological profile of intracerebral hemorrhage in a southern Brazilian population during a 10-year period.

Keywords

- ▶ intracerebral hemorrhage
- ▶ epidemiology
- ▶ Brazil
- ▶ cerebrovascular accident/stroke

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Resumo

Introdução A hemorragia cerebral espontânea é responsável por 20% de todos os acidentes vasculares cerebrais e acarreta grande número de óbitos e incapacidade funcional. Poucos são os dados epidemiológicos da hemorragia cerebral espontânea no Brasil, e especificamente no Sul do Brasil.

Metodologia Foram revisados 221 casos de hemorragia cerebral espontânea atendidos entre janeiro de 2004 e dezembro de 2013, selecionados aleatoriamente dentre os casos registrados como I61 e I62 de acordo com a 10ª revisão da Classificação Estatística Internacional de Doenças e Problemas Relacionados à Saúde (CID-10) nesse período.

Resultados Dos 221 casos, 53,8% eram do sexo masculino. A idade média foi de 63 anos e a distância média do local de residência até o centro de tratamento foi de 78,7 Km. Hipertensão arterial sistêmica foi relatada em 62,4% dos casos, *diabetes mellitus* em 20,4% e tabagismo em 15,4%. Tratamento cirúrgico foi realizado em 28,9% dos casos; pneumonia ocorreu em 19,9%, e 73,4% evoluíram com óbito ou incapacidade grave. Encontramos uma associação entre cardiopatia, coagulopatias, insuficiência renal crônica, uso de anticoagulantes, tratamento cirúrgico, pneumonia e sepse com um pior desfecho.

Conclusão O presente estudo descreve o perfil epidemiológico da hemorragia cerebral espontânea de uma população do Sul do Brasil e os fatores prognósticos encontrados no período de 10 anos.

Palavras chave

- ▶ hemorragia cerebral
- ▶ epidemiologia
- ▶ Brasil
- ▶ acidente vascular cerebral

Introduction

Stroke is the second leading cause of death and one of the most important causes of functional disability in the world. Spontaneous or primary intracerebral hemorrhage is the most common reason for hemorrhagic stroke and refers to the intraparenchymal hemorrhage without an identifiable cause.¹ Despite some studies demonstrating a reduction of stroke incidence in developed countries,² the incidence of stroke is likely to rise due to the increased life expectancy and to the precariousness of medical assistance and preventive strategies.³

Pathophysiology, epidemiology, risk factors and preventative measures of intracerebral hemorrhage are well known, but there is a lack of effective treatment for intracerebral hemorrhage, which is of fundamental importance to reduce the damage and improve the clinical outcome.⁴

Our study took place at a reference center for neurological and neurosurgical care located in the South of Brazil, which covers an area of 260,000 Km² and attends a population of ~ 650,000 people. The aims of our study were to present the epidemiological profile of patients with intracerebral hemorrhage who attended our clinical department during a 10-year period, and to describe the prognostic factors observed in this population.

Methods

We performed a random search of medical records that were registered as I61 or I62 according to the 10th edition of the International Disease Classification (ICD-10) between January

of 2004 and December of 2013 at a hospital in the city of Passo Fundo, Brazil. The medical records were reviewed to select spontaneous intracerebral hemorrhage cases. Erroneous classifications of ICD-10 I61 or I62 and other hemorrhage types, such as subarachnoid hemorrhage, post-traumatic hemorrhage, and postoperative hemorrhage, were excluded.

The SPSS software version 22.0 (IBM Corp., Armonk, NY, USA) was used for data analysis. The qualitative variables were evaluated by frequency analysis, and the Fisher exact test (for 2 × 2 tabs) or chi-square was performed for their proportions. Numerical variables were analyzed by using the Student *t*-test or analysis of variance (ANOVA), according to their characteristics, as well as with Pearson correlation. When necessary, the Tukey test for post-hoc analysis was applied. Differences were considered significant when the *p*-values were lower than 0.05. The study was approved by the local ethics committee (CAAE 52246914.0.0000.5342).

Results

A total of 221 patients with intracerebral hemorrhage between January of 2004 and December of 2013 were included. The majority of the patients were male (53.8%) (▶**Fig. 1**) and the mean age was 63 years (SD 14.6). ▶**Fig. 2** describes the distribution by age. Most of our study population was insured by the Brazilian public health system (SUS) (82.4%), 14.9% was insured by complementary health insurances, and 2.7% by private care companies. The mean distance from residency to the treatment center was 78.7 km (SD 69.3). For imaging, a computer tomography was performed in all patients.

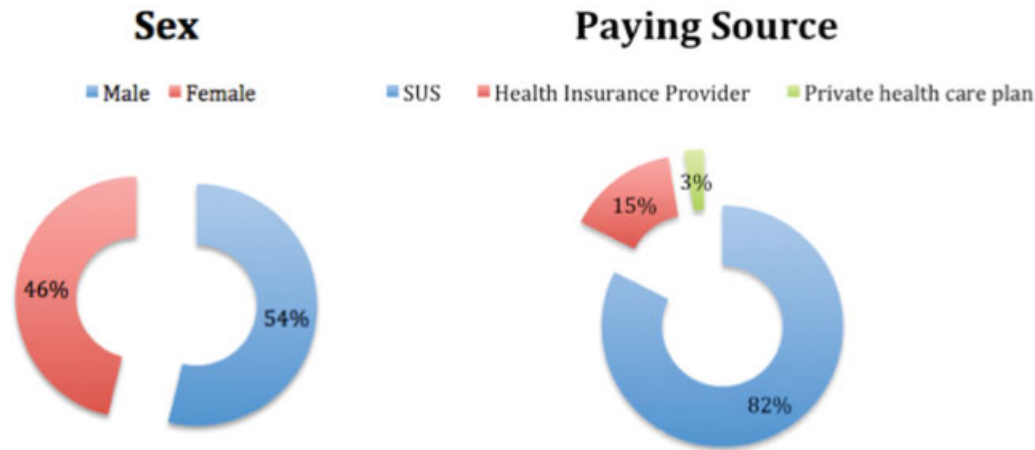


Fig. 1 Distribution by sex and paying source. Abbreviations: SUS, Brazilian National Health Care System (*Sistema Único de Saúde*, in Portuguese).

Among the reported comorbidities, arterial hypertension was present in 62.4% of the patients, diabetes mellitus in 20.4%, and 15.4% of the patients had history of smoking. Of all patients, 46.6% had at least one of those risk factors, 20.4% had an association of two of them, and 3.6% had a combination of all three.

Antihypertensives were used by 31.7% of the patients, platelet antiaggregant drugs by 11.3%, anticoagulants by 11.3%, cardiotoxic or antiarrhythmic drugs by 6.3%, hypoglycemic agents by 4.5%, and anticonvulsants by 2.3%. Surprisingly, only 45.7% of the 138 patients who had already been diagnosed with arterial hypertension used anti-hypertensives, and only 22.2% of the 45 diabetic patients used hypoglycemic agents regularly.

The Glasgow Coma Scale (GCS) score was described in 95.9% of the records. In 36.3% of the cases, the GCS score was between 14 and 15, 29.2% between 9 and 13, and 34.4% between 3 and 8. During the hospitalization, pneumonia was reported in 19.9% of the cases and sepsis in 5%. Surgical treatment was performed in 28.9% of the cases, and the average length of hospitalization was 11.9 days (standard deviation [SD] 12.3). The overall mortality was 57%, and the Glasgow Outcome Scale (GOS) score was between 1 and 3 in 73.4% of the cases.

The mortality rate was higher among women (62.7% versus 52.1%, $p = 0.134$), and the functional result was

also worse among them (GOS score 1 to 3 in 80.9% versus 67.3%, $p = 0.039$). Patients with a previous diagnosis of heart disease had a higher mortality rate (74.5% versus 51.2%, $p = 0.003$), as well as those with coagulopathies (100% versus 55.6%, $p = 0.021$) or chronic kidney disease (100% versus 55%, $p = 0.006$). Arterial hypertension, diabetes, or smoking individually did not reach a statistical difference in mortality or in functional outcome, but the association of these 3 risk factors raised the mortality to 87.5% and resulted in a worse functional outcome (100% with GOS score 1 to 3, $p = 0.09$).

The worse the level of consciousness at arrival, according to the GCS score, the higher was the mortality rate (90.4% for GCS score 3 to 8, 40.3% for GCS score 9 to 13 and 39% for GCS score 14 to 15, $p < 0.001$), and the worse was the functional outcome at the discharge (GOS 1 to 3 in 100% for GCSs 3 to 8, 67.9% for GCSs 9 to 13 and 50.7% for GCS score 14 to 15, $p < 0.001$).

There was no significant difference in mortality between patients who were submitted to surgery or not, but patients submitted to surgical treatment had a worse functional outcome (GOS score 1 to 3 in 86.4% versus 66.9%, $p = 0.005$). Moreover, there was no statistical difference in mortality between patients with or without pneumonia, but patients who developed pneumonia during hospitalization showed a worse functional outcome at discharge (GOS score 1 to 3 in 90.5% versus 69.1%, $p = 0.005$). Sepsis was associated with increased mortality (100% vs 54.8%, $p = 0.003$) and a worse functional outcome (GOS score 1 to 3 in 100% vs 71.9%, $p = 0.039$).

The mortality rate increased progressively with advancing age (36.4% until 40 years old, 57.3% from 40 to 65 years old, 59.5% from 65 to 80 years old, and 60% above 80 years old, $p = 0.53$), and there were worse functional outcomes (GOS score 1 to 3 in 45.5% until 40 years old, 71.1% from 40 to 65 years old, 77.9% from 65 to 80 years old, and 84.2% above 80 years old, $p = 0.08$). There was no significant difference in the mortality for patients admitted on weekends or holidays compared with those who were admitted during the weekdays ($p = 1$).

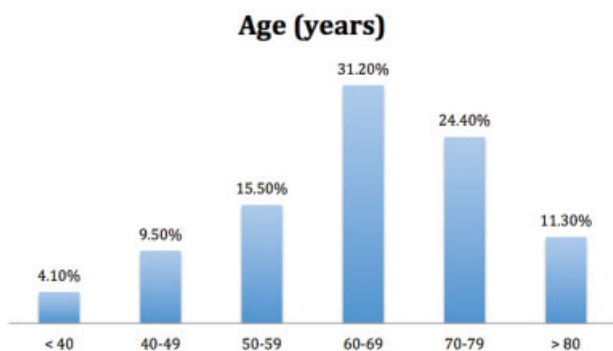


Fig. 2 Distribution by age.

Patients with arterial hypertension who had been using platelet antiaggregant agents showed better functional outcome at discharge (GOS score 1 to 3 in 55% versus 75.9%, $p = 0.05$), while those who had been using antihypertensive drugs showed lower mortality (47.6% versus 61.3%, $p = 0.12$) and better functional outcome (GOS score 1 to 3 in 65.5% versus 78.6%, $p = 0.11$). Use of platelet antiaggregant agents, independently of a previous diagnosis of systemic arterial hypertension, resulted in a better functional outcome (GOS score 4 to 5 in 41.7% versus 24.6%, $p = 0.09$). Use of anticoagulant drugs, by its time, was associated with higher mortality (84% versus 53.6%, $p = 0.005$) and worse functional outcome (GOS score 1 to 3 in 92% versus 70.9%, $p = 0.028$), as well as the mortality rate was higher in diabetic patients (68.9% versus 54%, $p = 0.09$).

The length of hospitalization was longer for patients who developed pneumonia during the hospitalization (22.4 days versus 9.2 days, $p < 0.001$), and those submitted to surgical treatment (17.5 days versus 9.4 days, $p < 0.001$). A weakly positive correlation was established between the length of hospitalization and the GCS score at arrival ($p = 0.039$), and there was also a weakly negative correlation between the length of hospitalization and year of hospitalization ($p = 0.01$). There was no association between age, sex, arterial hypertension, smoking, alcoholism or coagulopathies and the length of hospitalization (→ Fig. 3). → Fig. 4 resumes the relative risk for mortality from the major prognostic factors evaluated.

Mortality vs Prognostic factors

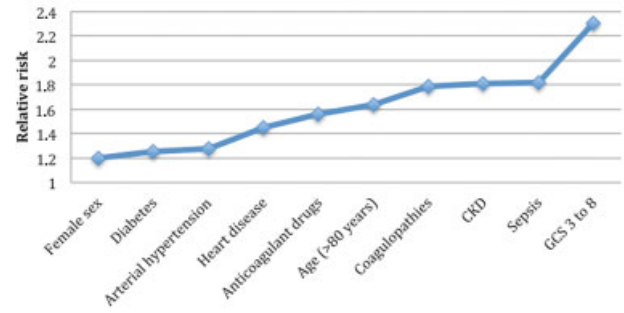


Fig. 4 Relative risk for mortality between prognostic factors studied. * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.01$.

Discussion

In contrast to other studies from Latin America,⁵⁻⁷ we found a slight predominance of the male gender among the studied cases. The mean age was 63 years old, which is in accordance with the literature.^{5,6}

Arterial hypertension is the most frequently described risk factor for intracerebral hemorrhage in the literature, reaching up to 87 to 89% prevalence in several studies.^{8,9} In the current study, we found a prevalence of 62.4% for arterial hypertension and 20.4% for diabetes mellitus in the population studied, agreeing with the international literature.^{5,6,10}

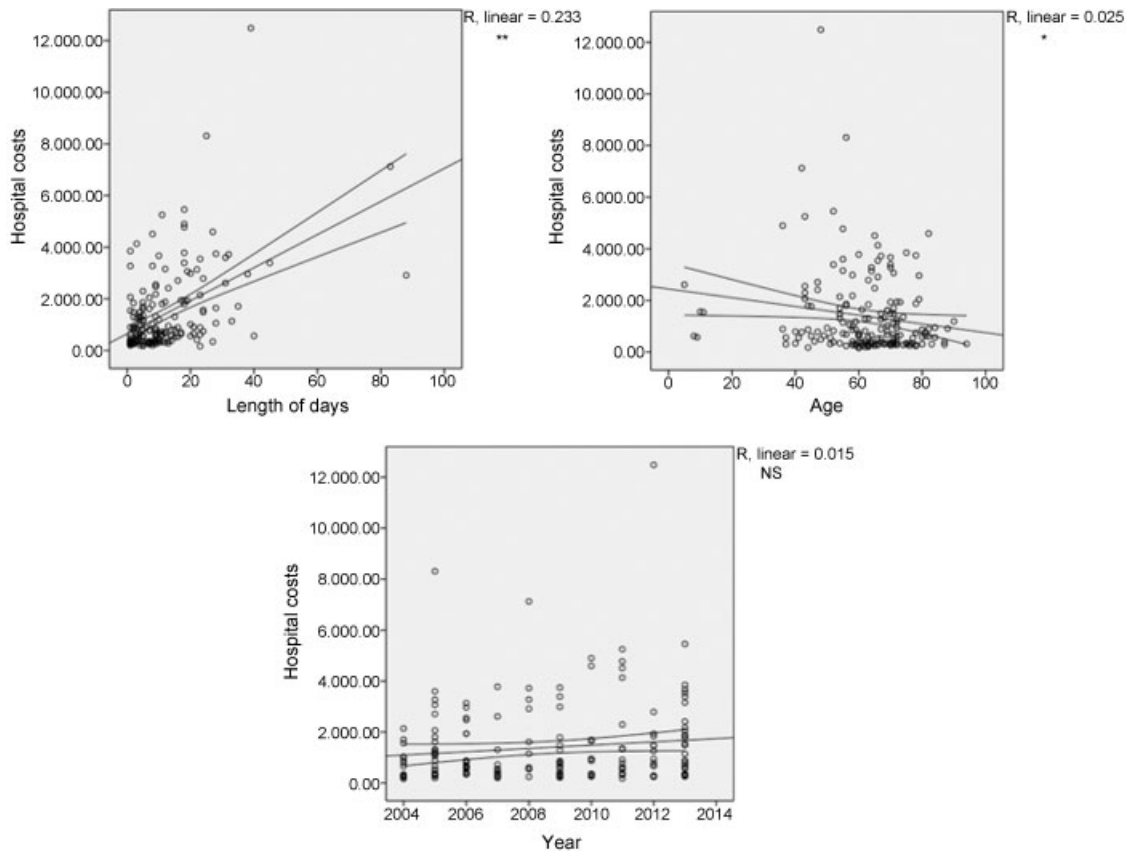


Fig. 3 Pearson correlation coefficient between hospital cost and length of stay, age, and year. * = $p < 0.05$; ** = $p < 0.01$; NS = not significant (US Dollars).

We noticed a low adherence to the treatment of chronic comorbidities before the hemorrhagic ictus, which was represented by the regular medication of only 45.7% of all hypertensive patients and 22.2% of all diabetic patients. The small percentage of treatment adherence for chronic disease is a well-known and greatly revised issue in medical literature. The percentage might even be lower than the value we found because this study was only based on statements given during hospital admission, and sometimes, not even performed by the patients themselves. According to Wong et al,¹¹ only 32.4% of the hypertensive patients were adherent to the prescribed optimal treatment by the end of the year, while 73% of patients discontinued the medical prescription within 29 days. Other authors confirmed the low adherence rate to the proposed treatment of chronic diseases and suspect that the adherence failure rises with increasing age, lower education, insufficient explanation of the treatment by the medical team, and those patients who are not followed-up by a private doctor.^{12,13} Public health and preventive medicine strategies, a greater adherence to treatment and a better arterial pressure and glycemic level control are essential to reduce the incidence of the intracerebral hemorrhage. This study shows that there might be a cumulative effect of the cardiovascular risk factors with the intracerebral hemorrhage prognosis.

Ruiz-Sandoval et al,⁶ studying 564 intracerebral hemorrhage cases in Mexico, found severe consciousness level reduction (GCS score 3 to 8) in 26.7% of the cases, which is lower than the value described in the current paper (34.4%). We assume that this can partially justify the discreetly higher mortality found, since the mortality in this group was significantly higher, compared with the other group with GCS score 9 to 15.^{5,6,10,14,15} In addition to this, a higher percentage of patients submitted to surgical treatment was found (28.9%) compared with the literature from other Latin America countries,^{6,10} which showed values of ~ 10%. This could be explained by the fact that our hospital is a reference center for neurosurgical treatment in this region. Moreover, the distance from the residency place to the treatment center may contribute to the worse outcome.

Van Asch et al¹⁶ reported, in a recent meta-analysis, an overall mortality of 40.4%, showing that, in Australian studies, there was a higher case fatality in women than in men, in contrast to data from other countries. Although we could not find a significant increase in mortality among women, we could show a worse functional outcome in this group. The previous diagnosis of heart disease, coagulopathies, chronic kidney disease, or the use of anticoagulant drugs also resulted in increased mortality rate and worse functional outcome.

Patients with intracerebral hemorrhage have a high incidence of hospital infections, according to literature, mostly pneumonia, which was reported in ~ 30% of cases, and urosepsis, in ~ 12%.^{6,10} In our study population, pneumonia was also the most frequently reported hospital morbidity, present in 19.9% of the patients during hospitalization, and being evidenced as an important prognostic factor, resulting in a worse functional outcome, while sepsis

was associated with worse functional outcome and increased mortality.

Conclusion

Intracerebral hemorrhage represents a severe public health problem with a high prevalence. It is responsible for a significant number of deaths and functional disability. As the life expectancy increases, a rise in the cerebral hemorrhage incidence is likely to occur, which could result in higher health expenses and productivity loss secondary to illness or death.

We found a similar distribution of sex, with a slightly higher frequency of males, and a median age of 63 years. The mortality in the study occurred in 57% of the cases, which was significantly more frequent in patients with coagulopathies, heart disease, chronic renal failure, and in patients who developed sepsis during hospitalization. The incidence of disabilities after a hemorrhagic event was significantly higher in female patients, in comatose patients on arrival, in patients who developed pneumonia during hospitalization, and in those treated surgically.

The primary treatment strategy for intracerebral hemorrhage continues to be preventive with early identification of risk factors and adequate treatment, as well as health education campaigns for a better treatment adherence in cases of chronic diseases.

Beside epidemiological knowledge and understanding of the risk and prognostic factors of the disease are of fundamental importance for establishing the condition to public health programs, aiming to decrease its incidence and morbimortality. Epidemiological studies will continually be important to reach this goal in the management of intracerebral hemorrhage, especially in developing countries, where these data are still deficient.

Disclosure/Conflict of Interest Statement

The authors have no financial disclosures to report and declare that there is no conflict of interest.

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