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# Epidemiology and Management of Intracerebral Hemorrhage in Chile

*Álvaro Soto, Marcelo Peldoza and Debora Pollak*

## Abstract

Intracerebral hemorrhage (ICH) is the second cause of stroke in Chile (23% of all strokes). The Araucanía Region has double the mortality rate by stroke compared with most regions in Chile. In developing countries like Chile, it is difficult to admit patients with ICH to the intensive care unit (ICU) for general neuroprotection and an aggressive lowering of blood pressure. The aim is to report the experience in the treatment of patients with ICH in a regional public hospital in Temuco, Chile. A convenience sample of the ICH consultations made during shift # 1 in the emergency room (ER) of the Hospital Dr. Hernán Henríquez Aravena between January 2016 and December 2018 was analyzed. There were 108 consultations for ICH in the period. The average age of the patients was 66.0 years (SD = 14.1). About 56.5% of the patients were male. Regarding the etiology, 70.4% were hypertensive, 18.5% were due to amyloid angiopathy, and 11.1% were for other causes. The implementation of 24/7 neurology shifts in the ER allowed us to reduce the evaluation time and improve the management of ICH patients. On the other hand, our hospital lacks a stroke unit, so ICH patients do not receive the standard care.

**Keywords:** intracerebral hemorrhage, stroke, epidemiology, management, Chile, hypertension, developing countries

## 1. Introduction

Stroke is the leading cause of disability and the second cause of death worldwide [1]. More than two thirds of the global burden of stroke occurs in developing countries, where the average age of patients is 15 years younger than in developed countries [2]. In the period 2000–2008, the total incidence rates in low- and middle-income countries exceeded the level of stroke incidence in high-income countries by 20% for the first time [3]. Latin America is experiencing an epidemiological transition toward older urban-dwelling adults that has led to a rise in cardiovascular risk factors and an increase in morbidity and mortality rates related to both stroke and myocardial infarction [4, 5]. According to the Global Burden of Disease 2013 Study (GBD 2013), stroke is the second cause of death in Latin America [6].

Stroke is also a serious public health problem in Chile. It is the leading cause of death in Chile, with a rate of 50.6 deaths per 100,000 inhabitants in 2011 [7]. Stroke accounted for 9% of all deaths in 2010 (8888 people) [8]. In addition, stroke is the first specific cause of disability-adjusted life years (DALY) in people older than 74 years and the fifth in those between 60 and 74 years [7]. 26,072 were hospitalized with the diagnosis of stroke in Chile in 2009 [8].

The prevalence of stroke in Chile, according to the National Health Survey (NHS) 2016–2017, is 2.6% in the general population and rises to 8.2% in  $\geq 65$  years [9]. A slight increase was observed when comparing the prevalence estimated in the 2009–2010 NHS, with 2.2 and 8.1%, respectively [10].

Intracerebral hemorrhage (ICH) is the second cause of stroke in Chile and represents approximately 23% of all strokes [11]. According to the Global Burden of Disease 2010 Study, the incidence of ICH in Chile is 46.9 per 100,000 person-years; the mortality is 22.36 per 100,000 person-years, and DALYs lost are 443.9 [12]. The comparison of the incidence, mortality, and DALYs between 1990 and 2010 is shown in **Table 1**.

The main source of information about the epidemiology of stroke comes from the Proyecto Investigación de Stroke en Chile: Iquique Stroke (PISCIS) Study conducted in Iquique in the north of Chile in 2000–2002 [11]. This study included 69 cases of first-ever ICH. Of these, 64 (92.7%) had spontaneous ICH. The mean age was  $57.3 \pm 17$  years, and 62.3% of the subjects were male. The age-adjusted incidence rates were 13.8 (non-lobar) and 4.9 (lobar) per 100,000 person-years. Non-lobar ICH was more frequent in young men and lobar ICH in older women. The non-lobar-to-lobar ratio was similar to previous findings in Hispanics. Hypertension was more frequent in non-lobar ICH and in diabetes, while heavy drinking and antithrombotic use were more frequent in lobar ICH, but in none significantly. There was no association between location and prognosis [13]. In the PISCIS Study, the incidence rate per 100,000 was 27.6 for ICH. The case-fatality rate for incident ICH was 28.9 (17.7–44.8). The outcome at 6 months after the first-ever ICH was 33% of patients at mRankin 0–2, 28% at mRS 3–5, and 39% dead [11].

The INTERSTROKE (risk factors for ischemic and intracerebral hemorrhagic stroke in 22 countries) Study showed that hypertension, smoking, waist-to-hip ratio, diet, and alcohol intake were significant risk factors for ICH [14]. According to the National Health Survey (NHS) 2016–2017, 27.6% of the population in Chile has hypertension; 73.3% in the subgroup  $\geq 65$  years old; 12.3% with diabetes (30.6% in  $\geq 65$ ); 74.2% with overweight-obesity; 86.7% with physical inactivity; 11.7% with alcoholism; and 33.3% who smoke [9].

In relation to the in-hospital management of ICH in Chile, the percentage of patients admitted with ICH varies from 14% in a private neurological intermediate care unit to 34% of stroke cases in a public hospital in Santiago [15, 16].

The most important risk factor for ICH is age. Each advancing decade from 50 years of age is associated with a twofold increase in ICH incidence [17]. In other words, ICH is more common in the elderly (1.97 x for each 10-year increase) [18]. This is a very important issue because according to the 2017 Chilean National Census, 11.4% of the population is 65+ years old [19]. On the other hand, in the Araucanía Region, 12.6% of population is 65+ years old; this region is the second oldest after the Valparaíso Region (13.6% 65+ years old) [19].

| Year | Incidence           | Mortality           | DALYs <sup>a</sup>     |
|------|---------------------|---------------------|------------------------|
| 1990 | 58.26 (42.38–76.24) | 43.21 (38.58–48.77) | 884.19 (787.41–996.20) |
| 2010 | 46.93 (35.24–61.38) | 22.36 (19.41–26.57) | 443.90 (385.72–519.42) |

<sup>a</sup>Disability-adjusted life-years.

**Table 1.**

Age-standardized incidence and mortality per 100,000 person-years and DALYs lost per 100,000 people, for hemorrhagic stroke, in Chile in 1990–2010.

## **1.1 Intracerebral hemorrhage in the Araucanía region**

The Araucanía Region has an area of 31,842.3 km<sup>2</sup>, which represents 4.2% of the American and insular territory [20]. The region has a 17.2% poverty by income, twice the national rate (8.6%) [21]. It also has 9.9 years average schooling (11.1% national) and 29.1% rurality that it is the second at the national level [19]. The Temuco-Padre Las Casas (PLC) conurbation has approximately 360,000 inhabitants [19].

According to the 2017 Chilean National Census, 34.0% of those surveyed in the Araucanía Region stated they belonged to an indigenous or native group, a proportion significantly higher than the 12.8% registered nationally [19]. According to the National Socioeconomic Characterization Survey (CASEN) 2015, the indigenous population in Chile has worse socioeconomic indicators than nonindigenous [22]. For example, 18.3% of the indigenous population lives in poverty by income compared to 11% of the nonindigenous population; extreme poverty by income was 6.6 vs. 3.3%, respectively. Eighty-seven percent of the indigenous population is served in the public health system compared to 76.3% of the nonindigenous population [22]. There is evidence of a higher incidence of stroke among native populations and minorities [23, 24]. However, in a recent case-control study, we found no association between Mapuche ethnicity and stroke incidence. This study only included 16 patients with ICH [25].

The Araucanía Region, along with the Valparaíso, Maule, and Bío Bío regions, has double the mortality rate by stroke compared with the rest of the regions in Chile. Most of the increased risk is due to the prevalence of poverty, diabetes, sedentary lifestyle, and overweight [26]. Furthermore, according to the 2009–2010 NHS, the Araucanía Region has the highest prevalence of high systolic blood pressure compared to the other regions [10].

On the other hand, the incidence rate of stroke, calculated as a diagnosis of hospital discharge, in the period 2001–2010 in the Araucanía Sur Health Service, was 961.3 per 100,000 inhabitants/year [27].

## **1.2 Management of intracerebral hemorrhage in the HHHA**

ICH is the fourth most frequent reason for neurological consultation in the emergency room (ER) of the Hospital Dr. Hernán Henríquez Aravena (HHHA) in Temuco, Chile, accounting for 4.5–7% of the care provided by the neurologist and 13.5–18.1% of stroke cases [28, 29].

The HHHA is located in the heart of the Temuco-PLC conurbation (360,000 inhabitants), about 670 kilometers south of Santiago de Chile. The HHHA has 730 beds, is the only hospital of high complexity in the Araucanía Region, and serves a beneficiary population of approximately 800,000 inhabitants [30]. The Araucanía Sur Health Service also has four medium-complexity hospitals (nodes) and eight low-complexity hospitals. The HHHA is also a referral center for neurological emergencies from the Araucanía Norte Health Service.

The HHHA neurology unit does not have its own service and depends on the internal medicine service. Our hospital lacks a stroke unit [30]. The hospital has two CT scanners and a MRI. There is an interventional neuroradiologist (MP) during daytime hours.

The HHHA has face-to-face neurologists 24/7 in the ER since July 2013 [29]. Patients with mild ICH (ICH score 0–1) are admitted to the internal medicine service [31]. Patients with severe ICH (ICH score 2–3) are admitted to the ICU. The ICU has 54 beds (18 with mechanical ventilation) for a population of about 800,000

inhabitants. Most patients with ICH stay a long time (24–48 h) in the ER waiting for a bed in the ICU. In these conditions it is very difficult to provide the standard care to these patients, including intensive blood pressure management and general neuroprotection. Based on the results of INTERACT2 and ATACH-2 studies, our target for systolic blood pressure in the first 48 h is less than 140 mmHg [32, 33]. Intravenous labetalol and nitroglycerin are the drugs more frequently used.

Another issue is the delay for the presentation of ICH patients. In a recent study, we estimated a median of 4 h and 45 mins ( $P_{25}$ – $P_{75}$  = 3 h 13'–14 h 16') for arrival to the ER. Just 17.4% of patients with ICH arrived in less than 3 h. In a chi-square test, the variables associated with a presentation in under 3 h were living in Temuco-PLC ( $p < 0.01$ ), urban origin ( $p = 0.02$ ), arrival by own car ( $p = 0.032$ ), and severity (NIHSS  $\geq 7$ ) ( $p < 0.01$ ). In a logistic regression model, only living in Temuco-PLC and severity were statistically significant with a combined odds ratio of 5.97 (95% CI = 3.23–11.04) [34].

The objective of this chapter is to report the experience in the treatment of patients with ICH in a regional public hospital in Temuco, Chile.

## 2. Material and methods

We performed a descriptive study of ICH in our hospital. A convenience sample of the consultations for ICH made during shift # 1 at the ER between January 2016 and December 2018 was analyzed. All patients were evaluated and diagnosed by AS in the ER. Due to the huge number of stroke patients diagnosed in the ER of the HCHA (about 220 cases of ICH per year), it was not possible to access to the clinical data of all patients with ICH in the period. We collected clinical, biodemographic, and imaging data. The radiological data were reviewed in all cases by a neuroradiologist (MP) unblinded to the clinical data. The cases were allocated to either spontaneous ICH or secondary to vascular malformation (arteriovenous malformation, cerebral saccular aneurysm, or cavernous angioma), tumor, or anticoagulants. On the other hand, the cases were classified according to one of two possible locations: supra- or infratentorial. Supratentorial hemorrhages included lobar, basal ganglia, and thalami locations. Infratentorial hemorrhages included the brainstem or cerebellum. The volume of the hematoma was calculated using the formula  $ABC/2$ , where A is the greatest diameter of the hematoma on the slice with the largest diameter, B is the diameter of the hematoma on the axis perpendicular to A, and C is the number of axial slices in which the hematoma is visible, multiplied by the slice thickness [35].

The continuous variables were described with measures of central tendency and dispersion, mean  $\pm$  standard deviation (SD), and/or medians with percentiles 25–75 ( $P_{25}$ – $P_{75}$ ). The STATA 14.2 software was used for the data analysis.

## 3. Results

There were 108 consultations for ICH in the period. The average age of the patients was 66.0 years (SD = 14.1). 56.5% of the patients were male. The median NIHSS was 14 points. The median time to arrival to the ER was 4 h and 45 min. The median ICH score at admission was 1 point. Only 39.8% of patients were admitted in the ICU. The mortality at 30 days was 30.6%. This value was equivalent with in-hospital mortality. The clinical and biodemographic characteristics of the ICH patients are shown in **Table 2**. The radiological characteristics of patients are shown in **Table 3**.

| Characteristics  | Patients (N = 108)  |
|--|---|
| Age (SD <sup>a</sup> )   | 66.0 (14.1)   |
| ≥65 years (%)  | 55.6  |
| ≥80 years (%)  | 17.6  |
| Male sex (%)   | 56.5  |
| Mapuche ethnicity (%)  | 27.8  |
| Rurality (%)   | 38.0  |
| Temuco (%)   | 35.2  |
| NIHSS <sup>b</sup> (median, P <sub>25</sub> -P <sub>75</sub> )     | 14.0 (5-20)   |
| Time to arrival (median, P <sub>25</sub> -P <sub>75</sub> ) [min]  | 4 h 45' (3 h-14 h 21')  |
| Time to triage (median, P <sub>25</sub> -P <sub>75</sub> )         | 8 min (5-15)  |
| Time to evaluation (median, P <sub>25</sub> -P <sub>75</sub> )     | 34 min (17-78)  |
| ICH <sup>c</sup> score (median, P <sub>25</sub> -P <sub>75</sub> ) | 1 (1-3)   |
| ICH score (%)  | 0 = 23.1<br>1 = 32.7<br>2 = 15.4<br>3 = 14.4<br>4 = 12.5<br>5 = 1.9   |
| Surgical hematoma evacuation (%)                                   | 3.1   |
| EVD <sup>d</sup> placement (%)                                     | 2.1   |
| Mortality (%)  |   |
| 30-day   | 30.6  |
| 90-day   | 32.4  |
| 180-day  | 37.0  |
| Destination (%)  | Intensive care unit = 39.8<br>Internal medicine service = 32.4<br>Other hospital = 24.1<br>Dye = 2.8<br>Discharge = 0.9 |

<sup>a</sup>Standard deviation.

<sup>b</sup>National Institute of Health Stroke Scale.

<sup>c</sup>Intracerebral hemorrhage.

<sup>d</sup>External ventricular drain.

**Table 2.**

*Clinical and biodemographic characteristics of patients with intracerebral hemorrhage Hospital Dr. Hernán Henríquez Aravena, Temuco, Chile, in 2016–2018.*

## 4. Discussion

In our study we found several similarities with many papers about ICH. In our series the mean age of the patients was 66 years old. The same was reported by Hemphill et al. (66 ± 15 years) but is higher than the age reported by Lavados et al. in the PISCIS Study (57.3 ± 17 years) [13, 31]. This difference could be explained because we used a convenience sample with cases that were not included consecutively. In our series we included about 1/6 of the ICH cases diagnosed in the ER of HHHA (about 220 cases/year). On the other hand, the locations found were similar to the findings of Hemphill et al.: 81.5%

| Characteristics                             | Patients (N = 108)   |
|---|--|
| Location 1                                  |  |
| Supratentorial                              | 81.5   |
| Infratentorial                              | 18.5   |
| Location 2                                  |  |
| Basal ganglia                               | 32.4   |
| Lobar                                       | 25.0   |
| Thalamus                                    | 24.1   |
| Cerebellum                                  | 10.2   |
| Pons  | 8.3  |
| Volume (cm <sup>3</sup> , SD <sup>a</sup> ) | 29.1 (37.6)  |
| Intraventricular hemorrhage (%)             | 52.6   |
| Etiology (%)                                | Hypertension = 70.4<br>Amyloid angiopathy = 18.5<br>Other = 11.1 |

<sup>a</sup>Standard deviation.

**Table 3.**

*Radiological characteristics of patients with intracerebral hemorrhage Hospital Dr. Hernán Henríquez Aravena, Temuco, Chile, in 2016–2018.*

supratentorial and 15.5% infratentorial [31]. We also found a 70.4% of the cases due to hypertension as the presumed cause. This is similar to the Hemphill study but higher than what was reported in the PISCIS Study [13, 31]. This difference in the results in comparison with our study can be explained because in the PISCIS Study, the patients were younger.

We found a 30-day mortality of 30.6% which is lower than the mortality reported by Hemphill in 2001 (45%) and similar to the 28.9% reported in Iquique, Chile [11, 31]. We also found a 6-month mortality of 37.0% which is similar to the 39% found in the PISCIS Study [11].

Unlike what was reported by Hemphill who found an association between mortality and age over 80 years, we found an association with age 65+ years ( $p = 0.091$ ) [31]. In this sense we consider useful the modification in the ICH score proposed by Hegde et al. by reducing the age criteria by 10 years to prognosticate the disease better in populations belonging to developing countries like Chile [36].

Only 39.8% of our patients were admitted in the ICU. This reality is completely contrary to the clinical recommendations in developed countries. For instance, the American guideline for ICH management states that the initial monitoring and management of ICH patients should take place in an intensive care unit or dedicated stroke unit with physician and nursing neuroscience acute care expertise (Class I; Level of Evidence B) [37]. We can suppose that many patients die because they do not receive the care that the severity of their illness requires.

When presenting our results, we must emphasize that the HCHA does not have a specific infrastructure to attend to neurological patients, that is, a stroke unit. These units have demonstrated their cost-effectiveness in decreasing mortality and disability due to stroke [38]. In our situation, not all ICH patients are admitted to the ICU and complete 24–48 h of observation in the ER, being later hospitalized at the internal medicine service.

About 80% of the population in Chile is treated in the public health system [21]. Users of the public system have worse health indicators than users of the private health system [9]. On the other hand, it is expected that the incidence of ICH will

increase significantly in our country due to the aging of the population and the poor control of cerebrovascular risk factors. This is why we see the need to have a stroke unit and/or a neurologic intermediate care unit in our hospital for the adequate management of patients with ICH. We also hope to set a Telestroke system with the future primary stroke centers in our region (Nueva Imperial, Pitrufrquén, Lautaro, Villarrica, Victoria, and Angol hospitals). In short, we hope that the HHA will become a comprehensive stroke center [39]. We also consider a priority to develop a better access in the detection and treatment of all the vascular risk factors mainly the control of hypertension. In the NHS 2003 in Chile, only 60% of the hypertensive knew their condition, 33% were being treated, and only 30% had normal values [40].

## **5. Conclusion**

ICH is a common cause of consultation in our hospital, especially in older people. The implementation of 24/7 neurology shifts in the emergency room allowed us to reduce the evaluation time and to improve the management of ICH patients; however, it is still difficult to admit ICH patients to the ICU. We are aiming for a soon implementation of a stroke unit, so ICH patients receive a standardized care. It's a main priority to have better access to primary care prevention, diagnosis, and treatment in developing countries like ours.

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## **Conflict of interest**

None.

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