

Association between Mapuche Ethnicity and Stroke: A Case-Control Study

Álvaro Soto, MD, MSc,*†‡ Gladys Morales, MSc, PhD,‡§ Rosa Provoste,§
Fernando Lanas, MD, MSc, PhD,¶# Isabel Aliaga,|| Daniela Pacheco,|| and
Sergio Muñoz, PhD‡§¶

Background: There is evidence of a greater incidence of stroke in native populations and minorities. A total of 34% of the population in the Araucanía Region is indigenous. The association between Mapuche ethnicity and stroke is unknown. The aim of the study was to estimate the magnitude of the association between Mapuche ethnicity and stroke occurrence in patients admitted to the Dr. Hernán Henríquez Aravena Hospital (HHHA) in Temuco, Chile. **Methods:** We performed an incident case–control-paired study with patients hospitalized with an acute stroke in the internal medicine service and controls from other medical services at the HHHA. One control was selected for each case, matched by gender and age (± 5 years). **Results:** A total of 104 nonconsecutive cases of stroke were included. The proportion of Mapuche individuals was similar between cases and controls (27.9% and 32.7%, respectively, $P = .45$). Hypertension and overweight-obesity were associated with stroke. Low socioeconomic status, rurality, diabetes, and smoking were associated with Mapuche ethnicity. In the conditional logistic regression model, Mapuche ethnicity was not associated with stroke. The odds ratio was .75 ($P = .47$, 95% confidence intervals: .35-1.62). **Conclusions:** There is no statistically significant evidence in the study to support the hypothesis of an association between Mapuche ethnicity and stroke. None of the control variables modified the effect of ethnicity on stroke.

Key Words: Stroke—risk factors—ethnic groups—case-control studies

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Introduction

Stroke is the leading cause of disability and the second cause of death worldwide.¹ The total incidence adjusted

for age for a first stroke in Chile is 140.1 per 100,000 population.² According to the 2016-2017 National Health Survey, the prevalence of cerebrovascular diseases is 2.6% in the general population and rises to 8.2% in 65 years old or older.³ In Chile, cerebrovascular diseases are the leading cause of death, with a rate of 50.6 deaths per 100,000 population in 2011. In addition, they are the primary specific cause of disability-adjusted life years (DALYs) in people over 74 years and the fifth between 60 and 74 years.^{4,5}

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.⁶ According to the National Socioeconomic Characterization Survey (2015), the indigenous population in Chile has worst socioeconomic indicators than nonindigenous.⁷ 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 versus 3.3%, respectively. A total of 87% of the indigenous population is served in the public health system

From the *Department of Medical Specialties, Faculty of Medicine, Universidad de La Frontera, Temuco, Chile; †Unit of Neurology, Dr. Hernán Henríquez Aravena Hospital, Temuco, Chile; ‡Center for Research in Cardiovascular and Nutritional Epidemiology (EPICYN), Universidad de La Frontera, Temuco, Chile; §Department of Public Health, Faculty of Medicine, Universidad de La Frontera, Temuco, Chile; ¶Center of Excellence CIGES, Faculty of Medicine, Universidad de La Frontera, Temuco, Chile; #Department of Internal Medicine, Faculty of Medicine, Universidad de La Frontera, Temuco, Chile; and ||Universidad de La Frontera, Temuco, Chile.

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Address correspondence to Álvaro Soto, MD, MSc, Department of Medical Specialties, Faculty of Medicine, Universidad de La Frontera, Francisco Salazar # 01145, Temuco, Chile. E-mail: alvaro.soto@ufrontera.cl. 1052-3057/\$ - see front matter

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compared to 76.3% of the nonindigenous population.⁷ The Araucanía Region has twice the mortality rate due to stroke compared to other regions in the country.⁸

Ten risk factors are associated with 90% of the risk of stroke: hypertension, smoking, overweight-obesity, unhealthy diet, physical inactivity, diabetes mellitus, alcohol intake, psychological stress and depression, cardiac issues, and dyslipidemia.⁹ Globally, 90.5% of the stroke burden as measured in DALYs is attributable to modifiable risk factors, including 74.2% due to behavioral factors (smoking, poor diet and low physical activity). Clusters of metabolic factors (high systolic blood pressure, high body mass index, high fasting plasma glucose, high total cholesterol, and low glomerular filtration rate; 72.4%) and environmental factors (air pollution and lead exposure; 33.4%) are the second and third largest contributors to DALYs.¹⁰

There is evidence of a higher incidence of stroke among native populations and minorities.^{11,12} Mapuche subjects have a 40% higher mortality rate from stroke than non-Mapuche in the Province of Malleco in the Araucanía Region. The association between Mapuche ethnicity and stroke incidence is unknown.

Dr. Hernán Henríquez Aravena Hospital (HHHA) has 730 beds, is the only high complexity hospital in the Araucanía Region, and serves a beneficiary population of approximately 800,000 inhabitants.¹³ The HHHA Neurology Unit does not have its own service and is part of the Internal Medicine Service.¹⁴ Our hospital lacks a stroke unit. Both ischemic stroke (IS) and intracerebral hemorrhage (ICH) are frequent reasons for neurological consultation in the Adult Emergency Service of the HHHA, accounting for 30.7% and 7% of neurology consultations, respectively.¹⁵

The aim of this study was to estimate the magnitude of the association between Mapuche ethnicity and stroke incidence.

Patients and Methods

A paired, incident case-control study was conducted. Patients were over 18 years of age, hospitalized in the Internal Medicine Service of the HHHA with a first stroke (IS or ICH). Gender- and age-matched (± 5 years) controls, without stroke, were obtained from the surgery, traumatology, urology, gynecology, and internal medicine departments (diagnosis unrelated to stroke). The exclusion criteria considered for cases and controls were shared conditions of atherogenesis mechanism and stroke: a known prior history of coronary heart disease, peripheral arterial occlusive disease, diabetic foot, and cancer.

The outcome variable was incident stroke. The exposure variable was Mapuche ethnicity defined by self-recognition, dichotomized as Mapuche, and non-Mapuche.¹⁶ Ethnicity is a concept of the social sciences that includes biological and sociocultural aspects.¹⁷ Given that there are

no biological determinants specific enough to distinguish between Mapuche and non-Mapuche Chilean populations,¹⁸ we opted for a previously validated anthropological criterion.¹⁹

The sample size was calculated with a 95% significance level and a power of 80%. Thirty-five percent of Mapuche subjects in the cases and 21% of Mapuche subjects in the controls were estimated, with an expected odds ratio (OR) of 2.0.¹³ The sample calculation was 164 cases. An interim analysis was carried out when the first 100 cases were included. The interim analysis concluded that approximately 1400 cases with their respective controls had to be included to determine whether Mapuche ethnicity constitutes a protective factor for stroke. As reaching this sample size was not considered feasible, it was determined that the analysis would be performed with the subjects recruited up to that moment.

Data Analysis

The association between Mapuche ethnicity, control variables, and stroke was estimated using conditional logistic regression. A chi-square test was used to estimate the association of the control variables with the exposure variable (Mapuche ethnicity). Finally, to estimate the effect of Mapuche ethnicity on stroke adjusted for the control variables, a conditional logistic regression was used. The STATA 14.0 software was used for the data analysis.

Statement of Ethics

This research project was approved by the Scientific Ethics Committee of the Araucanía Sur Health Service on May 13, 2015, and conforms to the ethical norms of the Helsinki Declaration.

Results

Between February 2017 and February 2018, 104 nonconsecutive cases of stroke were included 88 with IS and 16 with ICH. In turn, 104 gender- and age-matched (± 5 years) hospital controls were incorporated. Among the cases, 54.8% were male and the average age was 68.6 years (± 12.2). [Table 1](#) summarizes the prevalence of exposure and control variables in cases and controls. There were a similar proportion of Mapuche individuals between cases and controls (27.9 versus 32.7%). The prevalence of exposure and control variables and clinical characteristics of the cases are detailed in [Table 2](#). No relation between Mapuche ethnicity and stroke subtypes was found. A total of 27.3% of the subjects with IS and 31.3% of the patients with ICH were Mapuche ($P = .74$).

The crude association between Mapuche ethnicity and stroke was estimated using conditional logistic regression; the result was an OR of .84 (confidence intervals [CI]: 95% .46-1.51), which was not statistically significant ($P = .55$).

Table 1. Prevalence of exposure and control variables by stroke occurrence

Variables	Cases N = 104	Controls N = 104	P value
Mapuche (%)	29 (27.9)	34 (32.7)	.451
Rurality (%)	38 (36.5)	31 (29.8)	.303
Low SES* (%)	71 (68.3)	70 (67.3)	.882
Hypertension (%)	80 (76.9)	63 (60.6)	.011
Diabetes (%)	31 (29.8)	26 (25)	.437
Dyslipidemia (%)	41 (39.4)	39 (37.5)	.776
Smoking (%)	24 (23.1)	13 (12.5)	.046
Atrial fibrillation (%)	10 (9.6)	8 (7.7)	.622
Heart failure (%)	7 (6.7)	9 (8.7)	.603
Alcoholism (%)	11 (10.6)	9 (8.7)	.638
Exercise (%)	18 (17.3)	19 (18,3)	.856
Body mass index (SD [†])	28.5 (±4.6)	25.9 (±4.9)	.0002
Overweight-obesity (%, SD [†])	70 (67.3)	52 (50)	.011
Glycemia (SD [†])	136.0 (±70.8)	123.2 (±52.7)	.142
Creatininemia (SD [†])	.96 (±.39)	1.0 (±.58)	.503
LDL [‡] Cholesterol (SD [†])	98.5 (±36.9)	95.0 (±31.1)	.612
Glycosylated hemoglobin (%, SD [†])	6.7 (±2.5)	7.4 (±2.7)	.339
Admission systolic BP [§] (SD [†])	146.5 (±29.1)	132.2 (±25.7)	.0003
Admission diastolic BP [§] (SD [†])	79.2 (±16.6)	73.4 (±14.6)	.008

*Socioeconomic status.
[†]Standard deviation.
[‡]Low density lipoprotein.
[§]Blood pressure.

Conditional logistic regression was used to study the association of control variables with stroke. Only the association with hypertension and overweight-obesity was statistically significant ($P = .08$ and $P = .01$, respectively). A chi-square test was used to estimate the association of the control variables with the exposure variable (Mapuche ethnicity). A statistically significant association was found with the following variables: low socioeconomic status (SES), rurality, diabetes, and smoking. These results justified the

inclusion of hypertension, overweight-obesity, low SES, rurality, diabetes, and smoking in the statistical model, given that they were associated with stroke or ethnicity.

The nonsimultaneous hypothesis test was used to evaluate the hypothesis that some of the control variables were modifiers of the effect of ethnicity on stroke. The result was not significant ($P = .62$). The final model that responds to the research question is detailed in Table 3.

Table 2. Bio demographic characteristics, risk factors and stroke severity by stroke type

Variables	Ischemic stroke 88 (84.6%)	Intracerebral hemorrhage 16 (15.4%)	P value
Men (%)	48 (54.6)	9 (56.3)	.900
Age (SD*)	68.6 (±12)	68.9 (±13.8)	.930
Mapuche (%)	24 (27.3)	5 (31.3)	.744
Rurality (%)	30 (34.1)	8 (50)	.224
Hypertensión (%)	67 (76.1)	13 (81.3)	.655
Diabetes (%)	28 (32.6)	3 (20)	.331
Dyslipidemia (%)	35 (42.2)	6 (40)	.896
Smoking (%)	22 (25.9)	2 (13.3)	.294
Atrial fibrillation (%)	9 (10.7)	1 (6.7)	.632
Heart failure (%)	7 (8.4)	0 (0)	.243
Alcoholism (%)	10 (12.1)	1 (6.7)	.543
Exercise (%)	16 (18.6)	2 (13.3)	.623
Admission NIHSS [†] (median, IQR [‡])	5 (8-2)	8 (10.5-3.5)	.117
Discharge NIHSS [†] (median, IQR [‡])	2 (6-0)	7 (11.5-3)	.007

*Standard deviation.
[†]National Institute of Health Stroke Scale.
[‡]Interquartile range.

Table 3. Final conditional logistic regression model. Effect of Mapuche ethnicity on stroke occurrence adjusted by control variables

Variables	Odds ratio	P value	CI 95%
Mapuche ethnicity	.75	.470	.35-1.62
Hypertension	2.55	.023	1.14-5.69
Overweight-obesity	2.08	.042	1.03-4.19
Low socioeconomic status	1.15	.686	.58-2.31
Rurality	1.45	.324	.70-3.06
Diabetes	.93	.841	.46-1.90
Smoking	2.80	.027	1.13-6.94

According to the final conditional logistic regression model used, we can conclude that ethnicity is not a factor associated with stroke adjusted for hypertension, overweight-obesity, low SES, rurality, diabetes, and smoking. However, overweight/obesity, hypertension, and smoking are risk factors for stroke. The risk of stroke in overweight/obese is 2.1, in hypertensive patients 2.5 and in smokers 2.8; when these 3 risk factors are combined, the risk increases to 7.4.

Discussion

In our study, we found no association between Mapuche ethnicity and stroke occurrence. Although we found that the control variables hypertension, overweight/obesity, low SES, rurality, diabetes, and smoking were linked to the outcome variable (stroke) or the exposure variable (ethnicity), none of them modified the effect of ethnicity on stroke.

Our results are unlike those reported in the literature concerning the effect of race/ethnicity on the occurrence of a stroke. For example, a hospital study in South Auckland, New Zealand reported double the frequency of IS in young adults for Maori and Pacific Islanders compared to other ethnic groups; however, no control group was used.²⁰ In a cohort study conducted in the United States, it was shown that at 45 years of age, the relative risk of incident stroke was 2.9 (95% CI: 1.72-4.89) when comparing Afro-Americans with whites, and 1.66 (95% CI: 1.34-2.07) at age 65.²¹ These different results in comparison with our study can be explained by the study design and the age of the patients.

Our results also differ from a study conducted in New Zealand in which Maori/Pacific and Asian subjects had a higher risk of IS and ICH than those of New Zealand/European ethnicity.²² The differences found in our study may be due to the study design and because our population is more ethnically/racially homogeneous.

We also found no relation between Mapuche ethnicity and stroke subtypes. This is in contrast to the report by Howard et al, who estimated an ICH risk more than 5 times higher in Afro-Americans than in whites at the age of 45, but only one third greater at 85 years according to a

recent longitudinal study.²³ The differences found can be explained by the methodology used (longitudinal study versus cases and controls) and by sample size (27,760 versus 208 subjects).

The strengths of our study include that it constitutes, to the best of our knowledge, the first time the effect of Mapuche ethnicity on the occurrence of stroke has been investigated. It also seems to us that the design chosen was the most appropriate to answer the research question. In addition, the evaluation of patients was exhaustive. All patients underwent neuroimaging and were assessed clinically upon admission and at discharge with scales widely used in vascular neurology: National Institute of Health Stroke Scale, modified Rankin scale, etc. Moreover, both the cases and the controls were examined with a comprehensive nutritional survey and assessment.

Our work, as with all case-control studies, is not free of bias. With respect to recall bias, we consider that self-recognition as Mapuche is not affected by this type of bias. We recognize a possible sampling bias given that the cases were not included consecutively. On the other hand, all the IS and ICH cases were of mild to moderate severity with a National Institute of Health Stroke Scale median score of 5 and 8 points, respectively, upon admission. This bias can affect mainly subjects with ICH who tend to present more severe conditions, with high mortality in the first hours of evolution, and who may be under-represented during hospitalization in an internal medicine service. As this is a hospital-based case-control study, there is the possibility of selection bias due to differential hospitalization rates between ethnicities.

We are aware that there are other exposures that could interact with ethnicity, such as indoor air pollution, chronic stress, and periodontal disease. Unfortunately, we did not evaluate these exposures in our study. Indoor air pollution is a known risk factor for stroke.²⁴ For example, in a cohort study performed in China, coal fumes were found to be an independent risk factor for stroke in addition to diastolic blood pressure, age, and cigarette smoking.²⁵ We suppose that Mapuche people use more coal and wood fumes but there are no data in Chile regarding a resulting increased risk of stroke. The Interstroke study has shown psychosocial stress as a risk factor for stroke

(OR 1.30, 99% CI 1.06-1.60); therefore, we decided not to explore psychological issues.⁹ In terms of the link between periodontal disease and stroke, according to a meta-analysis of cohort studies, the risk of stroke was significantly increased by the presence of periodontitis [relative risk 1.63 (1.25-2.00)]. Tooth loss was also a risk factor for stroke [relative risk 1.39 (1.13, 1.65)]. The risk of stroke did not vary significantly with the presence of gingivitis.²⁶ A high degree of damage to their oral health has been reported among the Mapuche population, particularly due to tooth loss, which could be explained by their limited access to preventive and restorative dental care.²⁷ However, dental status was not measured in our study.

In conclusion, Mapuche ethnicity does not seem to be either a risk factor or a protective factor. New epidemiological studies must be conducted to identify factors related to Mapuche ethnicity that explain this null effect on stroke. Nevertheless, our study validates the importance of traditional vascular risk factors such as hypertension, overweight-obesity, diabetes, and smoking in addition to the social determinants of low SES and rurality that account for the high incidence and mortality of stroke in the Araucanía.^{9,10}

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