Social and health determinants related to adverse short-term outcomes after a first-ever stroke in adults younger than 65 years

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Background: Stroke-related mortality and disability-adjusted life years in adults younger than 65 have increased over the last decade. However, geographical differences in distributing these outcomes could reflect dissimilarity in determinants. Therefore, this cross-sectional study of secondary data from Chilean hospitals aims to analyze the association of sociodemographic and clinical factors with in-hospital case-fatality risk or acquired neurologic deficits (adverse outcomes) in inpatients aged 18 to 64 who experienced their first-ever stroke. *Methodology:* Adjusted multivariable logistic regression models and interaction analysis using multiple imputation for missing data (4.99%) for 1,043 hospital discharge records from the UC-CHRISTUS Health Network International Refined Diagnosis Related Groups (IR-DRG) system database (2010−2021) were conducted. *Results:* Mean age: 51.47 years (SD, 10.79); female: 39.60%. Stroke types: subarachnoid hemorrhage (SAH): 5.66%, intracerebral hemorrhage (ICH): 11.98%, and ischemic: 82.45%. Adverse outcomes: 25.22% (neurological deficit: 23.59%; in-hospital case-fatality risk: 1.63%). After adjusting for confounders, adverse outcomes were associated with stroke type (patients with ICH and ischemic stroke had higher odds than those with SAH), sociodemographic characteristics (age ≥ 40 years, residence in an area of the capital city other than the center-east, and coverage by public health insurance), and discharge diagnoses (obesity, coronary artery and chronic kidney diseases, and mood and anxiety disorders). For hypertension, women had higher odds of adverse outcomes. *Conclusions:* In this predominantly Hispanic sample, modifiable social and health determinants are related to adverse short-term outcomes after a first-ever stroke. Longitudinal studies are needed to investigate the causal role of these factors.

Keywords: Cerebrovascular disease—Risk factors—Young adult—Neurological sequelae

Introduction

Although the Global Burden Disease (GBD) study concluded that age-standardized stroke incidence and mortality rates considerably decreased throughout the last 3 decades, age strata data analysis revealed an emergent increase in stroke occurrence among individuals younger than 70 years.[1] Additionally, data from the Centers for Disease Control and Prevention (CDC) showed an increase in stroke-adjusted annual mortality rate between 2010 and 2016 for US adults aged 35 to 64 years.[2]

Stroke in young people is known to increase the risk of neurological disability substantially. Following a mean follow-up of 13.9 years in a European stroke population, the FUTURE study determined that the prevalence of functional impairment in adults aged 18 to 50 years is around 45%.[3] Furthermore, previous research has indicated a considerable occupational and socioeconomic impact on young individuals even years after the acute cerebrovascular episode.[4,5]

In addition to the well-known health-related determinants, current literature accepts that several social factors

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are associated with a higher risk of adverse vital and functional outcomes after a stroke.[6] In brief, patients who are older, women, or belong to racial and ethnic minorities and those who have lower incomes, adverse work conditions, and less social support have displayed higher short- and long-term case fatality or neurological disability.[5,7–12] Moreover, mortality and disability-adjusted life-years (DALYs) age-standardized rates have noticeable differences between countries,[1] underscoring the need to explore risk factors for adverse post-stroke consequences in populations of different geographic distributions.

Little is known about the association between demographic, socioeconomic, and clinical variables and vital and neurological outcomes following a stroke in adults younger than 65 from predominantly Hispanic populations.[13] Therefore, this study aims to analyze the relation between in-hospital case-fatality risk and neurological deficits at discharge and social and health-related factors in individuals aged 18 to 64 years consecutively admitted for a first-ever stroke over a period of 12 years in a Chilean healthcare network.

Methodology

Design and patients

This observational study of secondary data from the International Refined Diagnosis-Related Groups (IR-DRG) system of two high-complexity hospitals of the UC-CHRISTUS Health Network in Santiago, Chile, from January 2010 to December 2021 analyzed extensive and temporally associated clinical and sociodemographic data registered by the attending physician at hospital discharge following the Chilean Ministry of Health regulations.[14,15] The institutional ethics committee (CEC-Salud UC) approved the protocol of this study (ID 220608003) and the informed consent waiver.

The studied sample includes all patients aged 18 to 64 admitted consecutively throughout the study period with cerebrovascular disease as their primary or secondary discharge diagnosis in the IR-DRG system. Individuals with a history of a prior stroke or diagnosis of transient ischemic attack (ICD-10 code: G45.X), occlusion and stenosis of precerebral or cerebral arteries not resulting in cerebral infarction (ICD-10 codes: I65.X and I66.X), and other cerebrovascular diseases (ICD-10 code: I67.X) were excluded. Likewise, re-hospitalization episodes for stroke recurrence or programmed complementary studies were excluded to avoid the overrepresentation of some factors of interest.

Studied variables

The IR-DRG lists of primary and secondary diagnoses were reviewed, creating dichotomous variables for ischemic stroke (Infarct, ICD-10 code: I63.X), subarachnoid hemorrhage (SAH, ICD-10 code: I60.X), and intracerebral hemorrhage (ICH, ICD-10 code: I61.X). In addition, admission MRIs of cases with a non-specified stroke (ICD-10 codes: I64.X and I62.X) were reviewed and coded as infarct, SAH or ICH according to the radiological report (n = 20).

Residential location was grouped into 4 categories according to the region of residence at admission and the proportion of the population belonging to the lowest income level in the capital (Metropolitan) region using the current tool for socioeconomic characterization in Chile (2010-2015: Chilean National Socio-Economic Characterization Survey (CASEN); 2016-2021: Social Household Registry, Ministry of Social Development). Throughout the study period, boroughs with the lowest proportion of inhabitants in the low-income level were located in the east (highest-income boroughs: Lo Barnechea, Vitacura, Providencia, Las Condes, La Reina, and Ñuñoa) and central (high-income borough: Santiago) areas of the capital region. The remaining boroughs of the capital region were grouped into the middle- and low-income boroughs category.

Gender was categorized as male or female (non-binary was not recorded in the database). The period of admission was grouped into 4-year categories. Length of hospital stay was examined as a discrete variable (days). Health insurance (public/private) was used as a social determinant of health.

Clinical variables were extracted from the IR-DRG list of secondary diagnoses and codified as present or absent after a comprehensive review of ICD-10 codes. All variables with a prevalence higher than 2% in the total sample were selected for descriptive and bivariate analyses. Clinical variables examined include hypertension, diabetes, dyslipidemia (including all records of hypercholesterolemia, hypertriglyceridemia, hyperglyceridemia, dyslipidemia, and lipoprotein disorders), obesity, arrythmia (including all records of tachyarrhythmia, bradyarrhythmia, and users of a pacemaker or defibrillator), tobacco (smoking), alcohol, and drug consumption (including abuse, intoxication, dependence, abstinence, and other mental disorders related to substance use), congenital heart disease (CHD), coronary artery disease (CAD), obstructive sleep-disordered breathing syndrome, chronic kidney disease (CKD), mood and anxiety disorders (MADs, excluding adaptative disorders), hematological disorder (including records of all types of anemia, polycythemia, thrombocytopenia, thrombocytosis, cytopenia, thrombophilia, long-term use of anticoagulants, and other unspecified defects), chronic headache, and intracranial vascular malformation (including all records of aneurysms, arteriovenous malformations, and congenital alterations of intracranial blood vessels).

The studied event was an adverse vital or neurological outcome at discharge, including all records of in-hospital case fatality and acquired neurological deficit (ND), categorized as present or absent. In-hospital case fatality was extracted from the circumstances of the discharge

database field. In addition, survival was checked for all patients transferred to another hospital, and deaths within 30 days of admission were considered an event. ND included all records of cerebrovascular disease sequelae (ICD-10 code: I61.X) and diagnoses related to hemiparesis and paralytic syndromes, aphasia, dysarthria and anarthria, visual field defects, dysphagia, ataxia and dyscoordination, cognitive impairment, and other deficits due to stroke. Other diagnoses such as spinal cord disease, unspecified (1 case, 0.10%) and cerebellar ataxia in diseases classified elsewhere (2 cases, 0.19%) were not included as acquired neurological deficits due to the lack of specificity of the registry. No records of other stroke-related deficits were found.

Records of long-term neurological or visual deficit or chronic swallowing disorders, including cerebral palsy, congenital non-vascular malformations of the central nervous system, neurodegenerative and neuromuscular diseases, blindness, and achalasia, were excluded from the ND category.

Revascularization therapy has been shown to modify disease progression.[16,17] Therefore, it was included as an adjustment variable in all multivariate models. Information on intravenous thrombolytic therapy (IVT) for acute ischemic stroke was obtained from the IR-DRG procedure list and coded as present or absent (n = 23; 2.21%). No other recanalization treatment was recorded.

Data analyses

Variables were reported as absolute and relative frequencies (categorical) and median and interquartile ranges (numerical). Confidence intervals (95% CI) of crude and adjusted odds ratios (OR) were calculated using Woolf approximation by simple logistic regression. Multiple logistic regression models were conceptualized, exploring the role of explanatory variables on the odds of the event. Model 1 included all confounders identified after a comprehensive evaluation of structural relations between variables using a directed acyclic graph (DAG) to determine causal pathways and the nature of the association between the covariates and the event.[18] Models 2 and 4 were performed with a stepwise backward variable selection method to avoid statistical overfitting. Effect-modifying role of covariates on the relation between explanatory variables and the event in the models was evaluated by first-order interaction terms (Models 3 and 4). Multiple imputation using chained equations was used for missing data (residential location: 2.11% and health insurance: 2.97%. Total: 4.99%) using multivariate regression estimates. Significance was set at 0.05. All statistical analyses were performed in STATA/BE 17.0 software for macOS.

Results

Among 4,335 hospital discharges recorded in the institutional IR-DRG system from January 2010 to December 2021 with the diagnosis of cerebrovascular disease, 1,043 are records of patients aged 18 to 64 with a first-ever stroke (Fig. 1).

Table 1 resumes the sociodemographic and clinical features of the studied sample stratified by the stroke type. Most participants had an ischemic stroke (82.45%), 5.66% had a SAH and 11.89% had an ICH.

Adverse outcomes

Two hundred sixty-three patients (25.22%) had the studied event, of whom 246 (23.59%) with at least one

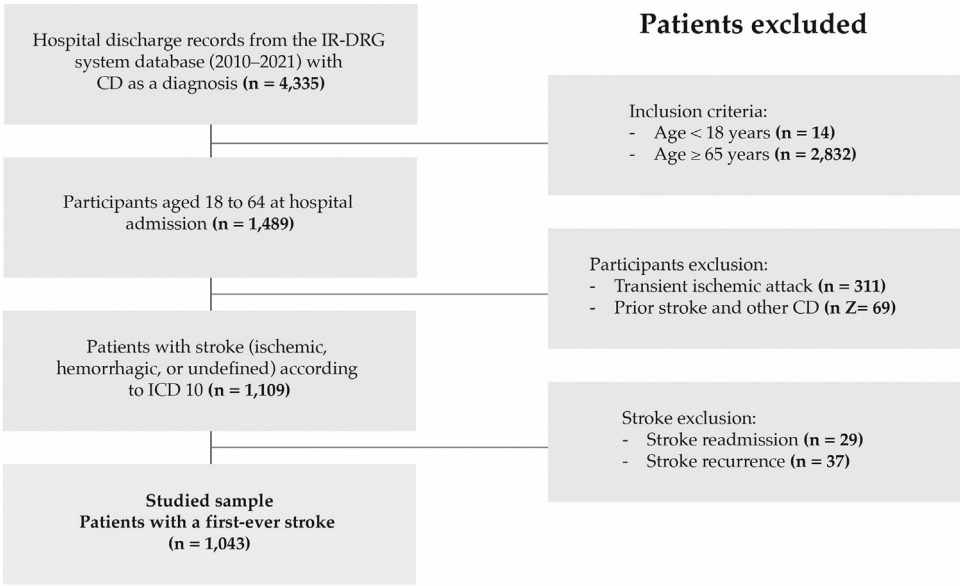

Fig. 1. *Flow chart of the study. CD: Cerebrovascular Disease. ICD 10: International Classification of Diseases 10.*

Table 1. *Baseline characteristics of the studied sample, by stroke type.*

	Overall (n=1,043)	SAH (n=59)	ICH (n=124)	Ischemic (n=860)
Gender				
Male	630 (60.40)	24 (40.68)	72 (58.06)	534 (62.09)
Female	413 (39.60)	35 (59.32)	52 (41.94)	326 (37.91)
Age (years)				
18−39	243 (23.30)	20 (33.90)	29 (23.39)	194 (22.56)
40−54	287 (27.52)	15 (25.42)	38 (30.65)	234 (27.21)
55−59	219 (21.00)	12 (20.34)	25 (20.16)	182 (21.16)
60−64	294 (28.19)	12 (20.34)	32 (25.81)	250 (29.07)
Median (IQR)	54 (45−60)	53 (41−59)	54 (45.5−60)	55 (46−60)
Hospital stay (days), median (IQR)	5 (3−8)	6 (4−12)	7 (3.5−11.5)	5 (3−8)
Period (years)				
2010−2013	352 (33.75)	26 (44.07)	40 (32.26)	286 (33.26)
2014−2017	357 (34.23)	21 (35.59)	33 (26.61)	303 (35.23)
2018−2021	334 (32.02)	12 (20.34)	51 (41.13)	271 (31.51)
During the COVID-19 pandemic	137 (13.14)	2 (3.39)	25 (20.16)	110 (12.79)
Residential location				
Capital region boroughs				
Highest-income	167 (16.36)	7 (11.86)	20 (16.26)	140 (16.69)
High-income	105 (10.28)	6 (10.17)	13 (10.57)	86 (10.25)
Middle- and low-income	574 (56.22)	31 (52.54)	72 (58.54)	471 (56.14)
Non-capital region	175 (17.14)	15 (25.42)	18 (14.63)	142 (16.92)
Health insurance				
Public	448 (44.27)	37 (63.79)	61 (50.41)	466 (55.94)
Private	564 (55.73)	21 (36.21)	60 (49.59)	367 (44.06)
Clinical features				
No comorbidities	150 (14.38)	16 (27.12)	20 (16.13)	114 (13.26)
Hypertension	519 (49.76)	25 (42.37)	76 (61.29)	418 (48.60)
Diabetes	191 (18.31)	2 (3.39)	19 (15.32)	170 (19.77)
Dyslipidemia	315 (30.20)	8 (13.56)	18 (14.52)	289 (33.60)
Smoking	285 (27.33)	13 (22.03)	32 (25.81)	240 (27.91)
Obesity	82 (7.86)	6 (10.17)	17 (13.71)	59 (6.86)
Heart disease	232 (22.24)	2 (3.39)	14 (11.29)	216 (25.12)
Arrhythmia	96 (9.20)	0 (0.00)	9 (7.26)	87 (10.12)
Atrial fibrillation	60 (5.75)	0 (0.00)	4 (3.23)	56 (6.51)
CHD	80 (7.67)	0 (0.00)	0 (0.00)	80 (9.30)
CAD	82 (7.86)	2 (3.39)	7 (5.65)	73 (8.49)
SDB	54 (5.18)	0 (0.00)	12 (9.68)	42 (4.88)
CKD	39 (3.74)	0 (0.00)	7 (5.65)	32 (3.72)
Stages 3−5	21 (2.01)	0 (0.00)	7 (5.65)	14 (1.63)
MADs	84 (8.05)	3 (5.08)	7 (5.65)	74 (8.60)
Drugs consumption	99 (9.49)	8 (13.56)	12 (9.68)	79 (9.19)
Psychoactive or unspecified	71 (6.81)	4 (6.78)	9 (7.26)	58 (6.74)
Cocaine of cannabinoids	24 (2.30)	4 (6.78)	3 (2.42)	17 (1.98)
Sedatives or hypnotics	5 (0.48)	0 (0.00)	1 (0.81)	4 (0.47)
Alcohol consumption	54 (5.18)	2 (3.39)	7 (5.65)	45 (5.23)
Hematological disorder	65 (6.23)	3 (5.08)	8 (6.45)	54 (6.28)
Long-term anticoagulants use	20 (1.92)	1 (1.69)	2 (1.61)	17 (1.98)
Chronic headache	81 (7.77)	8 (13.56)	10 (8.06)	63 (7.33)
Intracranial vascular malformation	24 (2.30)	1 (1.69)	7 (5.65)	16 (1.86)

SAH: Subarachnoid Hemorrhage. ICH: Intracerebral Hemorrhage. CHD: Congenital Heart Disease. CAD: Coronary Artery Disease. SDB: Obstructive Sleep-Disordered Breathing Syndrome. CKD: Chronic Kidney Disease. MADs: Mood and Anxiety Disorders. During COVID-19 pandemic includes records from March 11, 2020 (WHO declaration). Dyslipidemia includes all records of hypercholesterolemia, hypertriglyceridemia, hyperglyceridemia, dyslipidemia, and lipoprotein disorders. Arrhythmia includes all records of tachyarrhythmia, bradyarrhythmia, and users of a pacemaker or defibrillator. Variables of tobacco (smoking), alcohol, and drug consumption include abuse, intoxication, dependence, abstinence, and other mental disorders related to substance use. MADs excludes adaptive disorders. Hematological disorder includes records of all types of anemia, polycythemia, thrombocytopenia, thrombocytosis, cytopenia, thrombophilia, long-term use of anticoagulants, and other unspecified defects not associated with a diagnosis of neoplasm. Intracranial vascular malformation includes all records of aneurysms, arteriovenous malformations, and congenital alterations of intracranial blood vessels.

Table 2. *Crude and Adjusted odds ratios (OR) and their 95% confidence interval (CI) for factors associated to adverse vital and neurological short-term outcomes.*

	Crude OR (95% CI)	Adjusted OR1 (95% CI)	Adjusted OR2 (95% CI)
Stroke type			
SAH	Reference	-	-
ICH	3.80 (1.59−9.10)	-	-
Ischemic	2.46 (1.10−5.50)	-	-
Gender			
Male	0.90 (0.68−1.20)	Reference	-
Female	1.10 (0.83−1.47)	1.28 (0.94−1.74)	-
Age (years)			
18−39	Reference	Reference	-
40−54	1.68 (1.12−2.52)	1.73 (1.12−2.67)	-
55−59	1.40 (0.90−2.16)	1.35 (0.84−2.18)	-
60−64	1.39 (0.92−2.10)	1.31 (0.82−2.08)	-
Period (years)			
2010−2013	Reference	Reference	-
2014−2017	1.08 (0.78−1.50)	1.03 (0.73−1.45)	-
2018−2021	0.67 (0.47−0.95)	0.55 (0.37−0.80)	-
Residential location			
Capital region boroughs			
Highest-income	Reference	Reference	-
High-income	1.82 (1.01−3.26)	1.90 (1.03−3.48)	-
Middle- and low-income	1.95 (1.26−3.03)	2.07 (1.31−3.27)	-
Non-capital region	1.28 (0.74−2.19)	1.34 (0.77−2.35)	-
Public health insurance	1.68 (1.26−2.24)	1.63 (1.21−2.21)	-
Clinical features			
No comorbidities	0.81 (0.54−1.23)	-	0.93 (0.59−1.46)
Hypertension	1.16 (0.87−1.53)	-	0.95 (0.70−1.29)
Diabetes	1.46 (1.03−2.07)	-	1.29 (0.89−1.87)
Dyslipidemia	0.83 (0.61−1.14)	-	0.73 (0.52−1.02)
Smoking	0.98 (0.71−1.34)	-	0.92 (0.67−1.28)
Obesity	1.70 (1.06−2.74)	-	1.67 (1.02−2.74)
Heart disease	1.31 (0.95−1.81)	-	1.40 (1.00−1.93)
Arrhythmia	1.39 (0.88−2.19)	-	1.34 (0.84−2.15)
Atrial fibrillation	1.40 (0.80−2.46)	-	1.24 (0.70−2.22)
Congenital heart disease	0.92 (0.54−1.57)	-	1.06 (0.61−1.86)
Coronary artery disease	1.60 (0.99−2.59)	-	1.06 (0.61−1.86)
SDB	1.66 (0.93−2.95)	-	1.65 (0.91−3.00)
Chronic kidney disease	2.38 (1.24−4.56)	-	2.43 (1.23−4.78)
Stages 3−5	2.27 (0.94−5.44)	-	2.22 (0.88−5.62)
MADs	1.63 (1.02−2.62)	-	2.00 (1.21−3.30)
Drugs consumption	1.19 (0.75−1.89)	-	1.19 (0.73−1.93)
Alcohol consumption	1.15 (0.62−2.12)	-	1.09 (0.58−2.06)
Hematologic disorder	1.24 (0.71−2.16)	-	1.54 (0.86−2.77)
Vascular malformation	0.59 (0.20−1.73)	-	0.59 (0.19−1.78)

SAH: Subarachnoid Hemorrhage. ICH: Intracerebral Hemorrhage. CHD: Congenital Heart Disease. CAD: Coronary Artery Disease. SDB: Obstructive Sleep-Disordered Breathing Syndrome. MADs: Mood and Anxiety Disorders. Adjusted OR1 describes the association between each social variable and the event adjusted by stroke type and clinical variables. Adjusted OR2 describes the association between each clinical variable and the event adjusted by stroke type and social factors. Confidence intervals of crude and adjusted odds ratios were calculated using Woolf approximation.

ND. The in-hospital case fatality risk for the studied period was 1.63% (n = 17).

In decreasing order, the ND recorded were hemiparesis or hemiplegia (9.40%), aphasia or dysarthria (8.15%), dysphagia (7.48%), unspecified cerebrovascular disease sequelae (3.26%), and visual field deficit (2.01%). Most had an isolated deficit (18.98%), while 3.93% and 0.67% had 2 and 3 concomitant deficits.

Factors associated with adverse outcomes

Table 2 summarizes the findings from the crude and adjusted ORs for bivariate analyses. Each explored

Table 3. *Multivariate analysis: associated factors for in-hospital death and neurological deficit.*

	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)	Model 4 OR (95% CI)
Stroke type				
SAH	Reference	Reference	Reference	Reference
ICH	3.76 (1.52−9.29)	3.83 (1.56−9.36)	3.76 (1.52−9.32)	3.87 (1.58−9.51)
Ischemic	2.35 (1.02−5.40)	2.31 (1.02−5.25)	2.35 (1.02−5.44)	2.30 (1.01−5.25)
Gender				
Male	Reference	Reference	-	-
Female	1.22 (0.88−1.68)	1.16 (0.85−1.57)	-	-
Age (years)				
18−39	Reference	Reference	Reference	Reference
40−54	1.86 (1.19−2.91)	1.67 (1.09−2.55)	1.79 (1.14−2.81)	1.67 (1.08−2.60)
55−59	1.30 (0.79−2.13)	1.19 (0.75−1.89)	1.25 (0.76−2.05)	1.20 (0.74−1.94)
60−64	1.34 (0.83−2.16)	1.23 (0.80−1.90)	1.31 (0.81−2.11)	1.27 (0.80−2.01)
Period (years)				
2010−2013	Reference	Reference	Reference	Reference
2014−2017	0.98 (0.69−1.39)	1.03 (0.73−1.46)	0.99 (0.70−1.40)	1.04 (0.74−1.47)
2018−2021	0.52 (0.35−0.77)	0.58 (0.40−0.85)	0.51 (0.35−0.76)	0.58 (0.40−0.84)
Residential location				
Capital region boroughs				
Highest-income	Reference	Reference	Reference	Reference
High-income	1.60 (0.85−2.99)	1.57 (0.84−2.91)	1.56 (0.83−2.91)	1.56 (0.84−2.90)
Middle- and low-income	1.76 (1.10−2.80)	1.76 (1.11−2.78)	1.72 (1.08−2.75)	1.74 (1.10−2.76)
Non-capital region	1.26 (0.71−2.23)	1.26 (0.72−2.22)	1.23 (0.69−2.17)	1.24 (0.71−2.18)
Public health insurance	1.61 (1.18−2.20)	1.63 (1.20−2.22)	1.61 (1.18−2.20)	1.65 (1.22−2.25)
Clinical features				
No comorbidities	1.05 (0.60−1.22)	-	1.11 (0.63−1.95)	-
Hypertension	0.85 (0.60−1.83)	-	-	-
Hypertension: yes				
Male	-	-	Reference	Reference
Female			1.75 (1.13−2.73)	1.60 (1.04−2.45)
Hypertension: no				
Male	-	-	1.55 (1.01−2.37)	1.48 (0.01−0.12)
Female	-	-	1.30 (0.79−2.13)	1.22 (0.79−1.91)
Diabetes	1.28 (0.87−1.90)	-	1.29 (0.87−1.91)	-
Dyslipidemia	0.68 (0.48−0.98)	-	0.69 (0.48−0.98)	-
Smoking	0.91 (0.64−1.29)	-	0.88 (0.62−1.25)	-
Obesity	1.79 (1.06−3.02)	1.71 (1.04−2.83)	1.81 (1.07−3.08)	1.77 (1.07−2.95)
Arrhythmia	1.28 (0.78−2.10)	-	1.25 (0.76−2.07)	-
CHD	1.07 (0.58−1.95)	-	1.11 (0.60−2.02)	-
CAD	1.80 (1.06−3.05)	1.79 (1.07−2.98)	1.90 (1.12−3.24)	1.92 (1.14−3.22)
SDB	1.57 (0.83−2.98)	-	1.64 (0.86−3.12)	-
CKD	2.27 (1.12−4.59)	2.24 (1.13−4.46)	2.34 (1.15−4.75)	2.38 (1.18−4.77)
MADs	1.94 (1.15−3.28)	1.98 (1.18−3.30)	2.03 (1.19−3.44)	2.02 (1.20−3.38)
Drugs consumption	1.18 (0.70−1.97)	-	1.17 (0.70−1.97)	-
Alcohol consumption	1.18 (0.61−2.30)	-	1.19 (0.61−2.33)	-
Hematologic disorder	1.24 (0.66−2.33)	-	1.29 (0.69−2.41)	-
Vascular malformation	0.64 (0.20−2.00)	-	0.61 (0.19−1.94)	-

SAH: Subarachnoid Hemorrhage. ICH: Intracerebral Hemorrhage. CHD: Congenital Heart Disease. CAD: Coronary Artery Disease. SDB: Obstructive Sleep-Disordered Breathing Syndrome. MADs: Mood and Anxiety Disorders. All models were adjusted for revascularization therapy for acute ischemic stroke. Model 1 includes all studied variables (Imputations = 10. Number of observations = 1043. $F = 2.67$; $p < 0.001$). Model 2 includes variables selected by a backward stepwise process starting with all variables studied in model 1 (Imputations = 10. Number of observations = 1043. $F = 4.00$; $p < 0.001$). Model 3: include all studied variables and a first-order interaction term for gender and hypertension (Imputations = 10. Number of observations = 1043. $F = 2.70$; $p < 0.001$. Interaction term (sex#hbp): $p = 0.019$). Model 4 includes variables selected by a backward stepwise process starting with all variables studied in model 3 (Imputations = 10. Number of observations = 1043. $F = 3.79$; $p < 0.001$. Interaction term (sex#hbp): $p = 0.032$). Confidence intervals of crude and adjusted odds ratios were calculated using Woolf approximation.

bivariate association for social factors was adjusted by stroke type and clinical features (adjusted OR1) to evaluate the independent influence of social determinants on the event probability. In the same way, bivariate associations for clinical features were adjusted by stroke type and social factors (adjusted OR2). This approach allowed observing the adjusted effect of significant associated factors, including age, period of stroke occurrence, residential location, obesity, coronary artery disease (CAD), chronic kidney disease (CKD), and mood and anxiety disorders (MADs) on the event probability.

All multivariate models showed that patients who suffered an ICH or ischemic stroke had higher odds of the event than patients with SAH. Also, participants aged 40−54 had 67 to 86% greater chances of the event than those younger than 40 years (Table 3).

Using the Bayesian information criterion (BIC), model 2 best fits the sample data. According to this model, the chance of adverse outcomes was 76% higher in residents of middle- and low-income boroughs than highest-income boroughs (95% CI, 1.11−2.78). Moreover, the chance of the event was 63% higher in patients covered by public health insurance compared to those with a private one (95% CI, 1.20−2.22).

All models revealed that patients diagnosed with obesity, CAD, CKD, or MADs had higher odds of the event than individuals without these health conditions (Table 3). Also, models 3 and 4 showed that women with arterial hypertension had 1.60 to 1.75 higher odds of the event than men with this disease.

Although each additional day of hospitalization increased the odds of the event by 7% (95% CI, 1.05−1.10), the hospital stay was considered a collider of components of the main causal pathway in the development of adverse outcomes; thus, this variable was not included in the adjustment.

Discussion

In this observational study evaluating 1,043 individuals aged 18 to 64 with a first-ever stroke from a predominantly Hispanic population, results reveal social and clinical factors associated with in-hospital case fatality and adverse neurological short-term deficits. After adjusting for confounders, age, residential location in areas with a high percentage of middle- and low-income boroughs, public health insurance coverage, obesity, MADs, CAD, and CKD are associated with the event, suggesting a possible role as risk factors for an unfavorable vital and functional outcome following a stroke.

Using causal modeling, this study aimed to identify modifiable clinical and social risk factors for short-term outcomes after stroke. From this perspective, initial stroke severity, lesion size, and other stroke-related characteristics, known predictors of functional and vital outcomes, are components of the pathophysiologic pathway involved in developing neurological morbidity and mortality instead of confounders. Therefore, although analysis of these stroke-related characteristics is appropriate to identify individual predictive factors, their inclusion in population-level causal research needs to be carefully interpreted.

Like previous studies for long-term mortality and DALYs after stroke, our findings show that age is the main non-modifiable factor associated with adverse short-term outcomes, displaying a higher risk in participants older than 40 years [1].

In our sample, gender modifies the effect of the arterial hypertension on the probabilities of the event. Hypertensive women have higher adjusted odds of the event than men with this diagnosis; however, no gender differences are found in patients without this disease. According to the literature, young women have a higher incidence of embolic ischemic stroke and poststroke mortality risk than men, likely due to gender-related factors, such as oral contraceptives, pregnancy, and puerperium, and a higher prevalence of autoimmune illness [3,19]. Although including individuals mostly aged 50 to 64 and the absence of pregnant and puerperal women in the database could explain no gender differences in the odds of the event among participants without arterial hypertension, worse outcomes in women with this disease could also reflect differences in blood pressure control before admission, access to care, and stroke-related features by gender [20,21].

In contrast to the increased stroke annual mortality rate in young adults reported by the CDC between 2010 and 2016 [2], our findings show that the odds of the studied event declined significantly throughout the studied period. Likewise, data from the Department of Health Statistics and Information of Chile reveals that the cerebrovascular disease annual mortality rate among the 15-to-64-year-old population decreased by 29.7% from 2010 to 2021 [22].

Participants covered by private health insurance or residents in higher-income boroughs have lower odds of the event than those covered by public health insurance or residents in areas of the capital city with an elevated proportion of middle- and lower-income boroughs, suggesting the existence of socioeconomic determinants related to short-term outcomes following a stroke. In this way, evidence from high-income countries suggests that occupational factors, such as physical labor and more than 40 working hours per week, and belonging to low socioeconomic levels are associated with a higher incidence of stroke, a higher prevalence of poststroke neurological morbidity, lower access to opportune reperfusion treatment, and a higher prevalence of CVRF compared to the high socioeconomic level group [6,7,23].

It is noteworthy that MADs are associated with higher odds of the studied event. A meta-analysis of cohort studies, including approximately 320,000 participants with

2−29 years of follow-up, reveals that individuals with depression have a 1.45 times greater risk of stroke than those without this disorder [24]; however, this secondary study did not evaluate stroke outcomes. Among the possible explanations for the higher incidence of stroke in patients with mental illness are genetic, drug-related factors, and an increased prevalence of CVRF [25]. Nonetheless, acute physical and mental stress and its associated vascular pathophysiological changes could be an alternative pathway for the occurrence of cerebrovascular disease, the severity of the stroke, and the increased likelihood of adverse vital and functional outcomes.

Obesity increases the adjusted odds of the event in all studied models. This result contrasts with prior studies raising obesity as a protective factor for vital and functional outcomes after stroke [26]. A recent cross-sectional observational study, including 1,033 records from 60 US health centers, analyzing the effect of nutritional status on the relation between ischemic stroke and 3-month case fatalities or functional impairment, shows a significative non-linear tendency, suggesting that overweight and obese patients could have lower adjusted odds of adverse outcomes than normal, underweight, and severely obese individuals[27]. The greater nutritional reserve during the initial phase of recovery and the higher relative frequency of thrombotic compared to embolic ischemic stroke in obese individuals are possible explanations for this association [27,28].

Our results reveal that participants with CKD have higher odds of the event occurring in all multivariate models studied. In this regard, an observational study performed a decade ago, using the Fukuoka Stroke Registry—including 3,778 individuals with a first-ever stroke and 1,320 diagnosed with CKD—revealed that the adjusted odds of death or functional impairment within hospitalization and neurological morbidity at discharge are significantly increased in patients with CKD without a dose-dependent relation between glomerular filtration rate and outcomes [29]. Furthermore, although a relatively small number of individuals with CKD are analyzed in this study, there are differences in the effects of the disease by patient age, with higher odds of the event in the younger group, raising awareness of the need for further research on CVRF in adolescents and young adults with CKD.

Finally, the studied sample represents 24.65% of cerebrovascular disease records in patients older than 17 years during the studied period. This proportion is lower than reported by the National Health Survey (2016−2017) [30], likely because this last study captures only stroke survivors, and the rate of post-stroke deaths is considerably more elevated in participants older than 64 years than in younger ones.

Limitations

The present study had limitations that should be considered when interpreting the findings. The simultaneous measurement of explanatory variables and the event limits the inference of causality. In interpreting the results, it is also important to note that neurological dysfunction at hospital discharge does not necessarily lead to permanent functional impairment. Therefore, the factors associated with adverse short-term outcomes found in this investigation should be considered in future longitudinal studies to clarify an eventual causal role, as well as their link to long-term outcomes.

Analysis of patients from high-complexity hospitals could overestimate the prevalence of the event due to a possible selection of a higher proportion of cases with greater initial stroke severity and comorbidities. In this way, excluding patients with a history of stroke and chronic neurological conditions reduces the risk of including participants with long-term deficits preceding the stroke in the outcome estimation.

Although health insurance and resident location differences in the event distribution reinforce the existence of a significant influence of social determinants on stroke clinical outcome, the lack of data reflecting socioeconomic—especially educational attainment and individual income—and occupational factors limits our estimation of the total effect of social inequality on the risk of the studied event.

The reliability of the IR-DRG system data depends on the systematization and quality of the clinical records. Therefore, discrepancies in coding practices, individual differences in knowledge of the system, and diagnostic expertise could affect the dependability of the collected information. Although the IR-DRG system facilitates the homogenization of discharge diagnoses, it is limited when analyzing clinical predictors of discharge outcomes due to the lack of specific neurological diagnoses and description of the degree of overall functional impairment.

Finally, the lack of high-quality and standardized national registries of clinical and epidemiological data during the post-discharge phase of stroke patients limits the tracking of long-term functional outcomes. Systematic data collection is a common challenge in developing countries, limiting access to reliable data needed for public policy planning.

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Declaration of Competing Interest

The authors have declared that no competing interests exist.

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