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Case-fatality of acute ischemic stroke in stroke units of Latin American hospitals

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ABSTRACT

Background and Purpose: The Case-fatality of acute ischemic stroke in stroke units of Latin American hospitals is a multicenter registry from various stroke centers in Latin America, exploring demographic, clinical, imaging, and functional outcomes in acute ischemic stroke (AIS) patients, with the intention of determining case-fatality rates (in-hospital, 30 and 90 days follow up) and analyzing associated risk factors.

Methods: We conducted a retrospective cohort study using data from hospitalized AIS patients over 18 years of age, collected from 27 centers in 11 Latin American countries between January 1 and December 31, 2022. The effect size was estimated using the hazard ratio (HR) and 95 % confidence intervals (95 % CI) through Cox regression models to assess the association between time to 30-day fatality event and covariates.

Results: A total of 2,997 patients were included. The mean age was 68.7 years and 48.1 % were women. In-hospital case-fatality was 9.42 %, 277 patients (10.2 %) died within 30 days, and 90-day case-fatality was relatively close at 353 patients (13.3 %). Complications were reported in 31.3 % of cases, most frequently infections (18.5 %). Age over 75 years (HRa=2.28), hyperglycemia (HRa=1.28), baseline status (HRa=1.61), stroke severity according to NIHSS >26 (HRa=6.11) and the presence of neurological complications (HRa=3.2) were risk factors for 30-day follow up case-fatality in these patients.

Conclusion: AIS patients in Latin America stroke centers had an in-hospital case-fatality of 9.42 % and the 30-day case-fatality was 10.2 %. Older age, hyperglycemia, baseline status, stroke severity and neurological complications were the strongest predictors of early case-fatality. The findings underscore the need to optimize stroke management protocols in the region.

Instructions to authors

This manuscript complies with all instructions to authors.

Authorship requirements

The authorship requirements have been met and the final manuscript was approved by all authors.
This manuscript has not been published elsewhere and is not under consideration by another journal.

Reporting checklist

We use reporting checklist (Strobe Statement).

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Introduction

Stroke mortality accounts for a global age-standardized death rate (ASDR) of 87.4 per 100,000 people, with a female-to-male ratio of 0.72, making it the leading condition with the highest disability-adjusted life years (DALY) rates among all neurological conditions worldwide(1). When exploring acute ischemic stroke (AIS) fatality (44.2 per 100,000 people), significant regional differences emerge. Although stroke mortality has declined in high-countries due to improved prevention and care, low- and middle-income countries have seen a rise in ASDR from 1990 to 2021.[2]

Acute and early in-hospital (within 30 days) case-fatality for ischemic stroke (IS) varies significantly by region, ranging from 8.3 % to 19.1 %.[3,4] Strengthened stroke networks, broader access to reperfusion therapies, and standardized in-hospital care have improved outcomes globally, but disparities persist. Over the past decade, early in-hospital case fatality has shifted due to advances in stroke systems of care, medical technology and infrastructure, and standardized in-hospital stroke protocols.[4-6] However, these improvements are not uniformly distributed across regions.[2] For instance, the one-month fatality for IS is 14.2 % in Europe and 14.0 % in South America and the Caribbean, significantly higher than in Asia, which reports 10.8 % (RR 1.05; $p = 0.027$).[4]

When analyzing hospital registries representing Latin America, only five centers from Brazil, Chile and Argentina have published this data, leading to a subsequent under-representation of the region. This highlights the scarcity of high-quality, region-specific data compared to data-rich areas such as North America and Europe.[1,2] This limited availability of high-quality, region-specific data underscores the urgent need to strengthen research efforts in Latin America. Expanding stroke surveillance and generating robust evidence in this region are essential to inform effective policy-making, optimize resource allocation, and reduce persistent health disparities.

Several factors have been established as higher risks for early case-fatality,[7-10] but a more accurate analysis of their cumulative influence remains uncertain. Additionally, few of these studies have been conducted in Latin America; therefore, the understanding of the impact of these factors on our health systems has been poorly studied.

The Case-fatality of acute ischemic stroke in stroke units of Latin American hospitals is a multicenter registry from various stroke centers in Latin America, exploring demographic, clinical, imaging, and functional outcomes in AIS patients, with the intention of determining case-fatality rate (in-hospital, 30 and 90 days follow up) and analyzing associated risk factors.

Methods

Design and population

We conducted a retrospective, multicenter cohort study across hospitals in Latin America that manage AIS and are equipped to provide acute reperfusion therapies. Medical records of patients over 18 years of age hospitalized with the diagnosis of AIS from January 1 to December 31, 2022, requesting with International Classification of Diseases (ICD)-10: I63.0 – I63.9.

AIS was defined as an acute neurological deficit confirmed by the evidence of cell death due to ischemia in neuroimaging methods (i.e., brain CT scan or brain MRI), with a maximum time frame of 48 hours from the onset of clinical symptoms to the first medical evaluation in the emergency department.

Variables

The primary outcome variable of this study was death, with follow-up of vital status at 30- and 90-days post-event. The demographic variables included age, sex, and comorbidities (hypertension, diabetes mellitus, dyslipidemia, acute myocardial infarction [AMI], peripheral artery disease [PAD], cardiac arrhythmia, and cerebrovascular disease). Clinical variables considered included time from symptom onset to emergency department (ED) arrival, baseline functional status (estimated by the modified Rankin scale, [mRS] at admission),[11] vital signs upon admission (heart rate, body temperature, and systolic and diastolic blood pressure), the acute clinical presentation of the patient, and the severity of deficits estimated by the National Institutes of Health Stroke Scale (NIHSS) and divided into four groups: mild (0-4), moderate,[5-15] severe,[16-25] and very severe (>25).

The laboratory variables included in the study were those recorded at admission or the first test performed during hospitalization (up to a maximum period of 72 hours from the onset of clinical symptoms): the presence of hyperglycemia estimated by capillary glucose test equal to or greater than 180 mg/dL (based on American Diabetes Association's clinical thresholds for hyperglycemia in hospitalized patients), blood leukocyte count, the presence of anemia (defined according to local reference values of hemoglobin), serum lactate dehydrogenase (LDH), total serum protein count, serum albumin, serum C-reactive protein (CRP), and serum D-dimers. Imaging variables included the type of study, affected cerebral artery, and location (supratentorial or infratentorial or both). Treatment variables included intravenous or mechanical thrombectomy, onset-to-treatment time, surgical treatment (if applicable), and the type of secondary prevention initiated (single/double antiplatelet therapy or anticoagulation).

Hospital complications during follow-up were also recorded and defined as medical issues arising during the hospital stay according to the clinical definition and classification used in previous studies.[12,13] They were classified as neurological (seizures, recurrent stroke, symptomatic hemorrhagic transformation, and intracranial hypertension), infections (thoracic infection, urinary infection, or others), thromboembolic (pulmonary and deep vein thrombosis), and immobility-related complications (pressure ulcers and falls).[14] We used the classification of the "Trial of ORG 10172 in Acute Stroke Treatment" (TOAST) for the etiology of AIS.[15] Admission to intensive care units (ICU), functional outcome (estimated by the mRS at hospital discharge and 3 months after the event), and hospital length of stay were also recorded.

Data analysis

Each center provided the database in an anonymized spreadsheet, and all data were compiled into a single database for analysis using STATA® v17 software.

Categorical variables were summarized using frequencies and percentages, while quantitative variables were summarized using measures of central tendency and dispersion, either means and standard deviations or medians and interquartile ranges, depending on the data distribution. To assess the association between 30-day case-fatality and covariates, the Chi-square test was used for categorical variables, while the student's t-test or Mann-Whitney U test was used for quantitative variables after the results of the normality test using Shapiro-Wilk

Effect size was estimated using hazard ratio (HR) and 95 % confidence intervals (95 % CI) through Cox regression models to evaluate the association between time-to-event case-fatality at 30 days and covariates. Univariate analyses assessed crude hazard ratios (cHR) for each independent variable with 30-day case-fatality. Multivariate analysis was adjusted for sex, age, blood glucose test upon admission, hypertension, functional independence level according to baseline mRS, baseline NIHSS, neurological complications, and infectious complications. Arrhythmia and heart rate upon admission were excluded from the multivariate model due to high multicollinearity with hypertension. This was supported by a VIF>5 and correlation coefficients >0.70. Kaplan-Meier survival curves were generated for key predictors, including age ≥75 years, glucose ≥180 mg/dL, NIHSS severity groups, and neurological complications, to visually compare survival probabilities over time.

Model diagnostics included assessment of proportional hazards using Schoenfeld residuals, and influence diagnostics for outliers. Due to heteroscedasticity and clustering by country, robust standard errors were calculated using country-level clustering to adjust confidence intervals. A statistical significance level of <0.05 was used for all statistical tests.

Ethical considerations

Full confidentiality of patient data was maintained by limiting data access to researchers only. Data was anonymized before transferring to the coordinating center, and full confidentiality of patient data was maintained. The study followed the Declaration of Helsinki, the Belmont Report, and local regulations. Informed consent was waived due to the observational nature of the study.

The research protocol was approved before its execution by the ethics committee of the primary study site (César Vallejo University, Perú. Letter N° 006-CEI-EPM-UCV-2023) and by all institutional research committees of the hospitals participating in the study.

Results

Data was collected from 2,997 patients from 27 hospital centers in 11 countries (Fig. 1). High income countries: Chile, Uruguay, and Panama, and upper middle-income countries: Argentina, Brazil, Colombia, Costa Rica, Ecuador, Mexico, Paraguay, and Peru.

Women accounted for 48.1 % (1441 participants), with a mean patient age of 68.68 years (SD: 14.86). >72 % of the patients aged above 60 years.

At admission, mean systolic blood pressure (sBP) was 150.7 mmHg (SD: 29.5), while the mean diastolic blood pressure (dBP) was 85.1 mmHg (SD: 16.3). Elevated blood glucose ($\geq$180 mg/dL) was observed

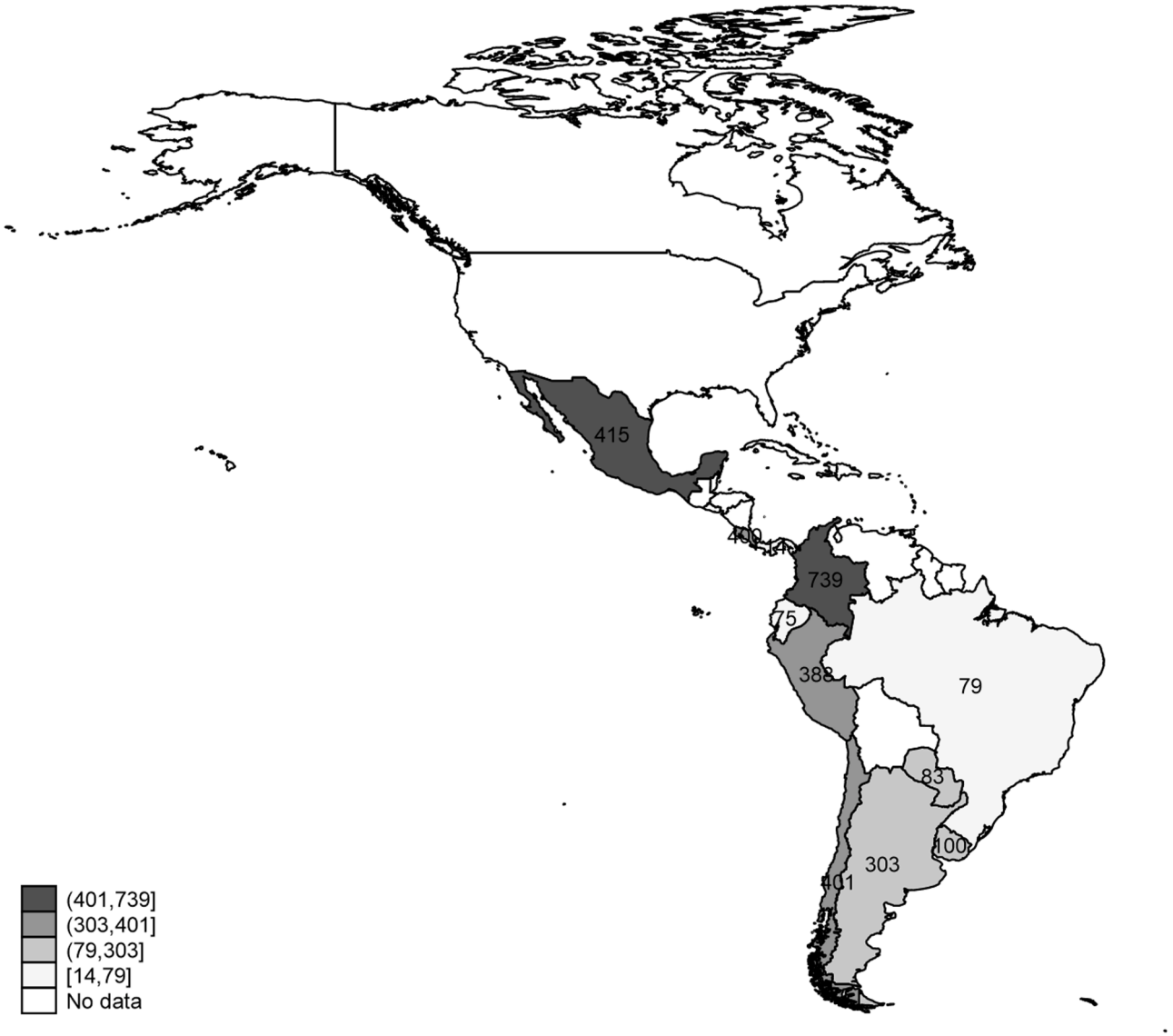

Fig. 1. Geographic distribution of acute ischemic stroke cases in 11 Latin American countries.
Shaded areas represent the total number of acute ischemic stroke (AIS) cases contributed by each country. The numbers within each country indicate the absolute number of cases analyzed. The intensity of the shading corresponds to quartiles of case volume distribution across countries:
Q4 (dark gray): 401–739 cases
Q3 (medium gray): 303–401 cases
Q2 (light gray): 79–303 cases
Q1 (very light gray): 14–79 cases
White: No data available.

in 61.4 % of patients. Comorbidities were highly prevalent (86.8 %), with hypertension being the most frequent (71.9 %).

A history of stroke was reported in 387 patients (13.8 %). The median hospital stay was 7 days (IQR 4-13), and the median time of stroke-door was 300 minutes (IQR 121-900).

The overall 30-day case-fatality rate was 10.2 % ($n = 277$). Notably, mortality varied substantially across countries, with Uruguay reporting the highest rate at 20.0 %, followed by Colombia (13.0 %) and Brazil (12.8 %), Peru (10.4 %), whereas Chile had the lowest rate at 4.1 %.

Complications occurred in 756 patients (31.3 %) with infectious complication being the most common (18.5 %) Neurological complications were present in 12.3 % of cases. (Table 1).

The mean age of those who died within 30 days was significantly higher than that of those who survived,73.11 years compared to 68.15 years ($p < 0.001$). There was a predominance of the female sex in those who died with respect to male sex (11.5 % vs. 9.1 % respectively, p-value=0.043). The mean systolic blood pressure was found to be slightly lower in those who died (147.39 mmHg) compared to those who survived (151.10 mmHg, $p = 0.022$). There was a significant association between elevated glucose levels ($\geq$ 180 mg/dL) and increased case-fatality rate (12.0 % vs. 6.4 %, $p < 0.001$).

Patients who were functionally dependent on baseline exhibited a significantly higher case-fatality rate (22.1 % vs. 9.4 %, $p < 0.001$). The severity of the stroke, as indicated by the NIHSS score, was found to be associated with increased risk of death. Specifically, patients with NIHSS scores ranging from 16 to 25 and above 26 exhibited higher case-fatality rates than those with lower scores (45.7 % and 43.2 %, respectively; $p < 0.001$).

The case-fatality rate was higher for patients who did not receive reperfusion therapy compared to those who received thrombolysis or thrombectomy (8.8 % vs. 24.2 %, $p < 0.001$). Patients who developed complications related to the nervous system, blood clots, infections, or immobility had significantly higher case-fatality rates. A higher proportion of non-survivors (39.0 %) than survivors (6.5 %) had neurological complications ($p < 0.001$). Please refer to Table 2 for further details.

In the crude model, men had a lower risk of 30-day case-fatality than women (HRc: 0.77; 95 % CI: 0.63-0.95; $p = 0.013$). However, after adjustment for confounders, this difference was not significant (HRa: 1.10; 95 % CI: 0.79-1.52; $p = 0.564$). Patients aged 75 years or older had a higher risk of death in both the crude (HRc: 1.91; 95 % CI: 1.48-2.48; $p < 0.001$) and adjusted analysis (HRa: 2.28; 95 % CI: 1.51-3.44; $p < 0.001$).

Regarding hemoglucotest levels on admission, those with values $\geq$ 180 mg/dL showed a higher risk of case-fatality in the crude analysis (HRc: 1.88; 95 % CI: 1.46-2.44; $p < 0.001$), which remained significant in the adjusted model (HRa: 1.28; 95 % CI: 1.01-1.63; $p = 0.042$). Hypertension was also an important risk factor in the crude analysis (HRc: 1.47; 95 % CI: 1.20-1.79; $p = 0.001$), although an inverse association was observed after adjustment, with hypertension being associated with a reduced risk of death (HRa: 0.77; 95 % CI: 0.60-0.99; $p = 0.042$).

High NIHSS scores were strongly associated with an increased risk of death in both the crude and adjusted models. Patients with an NIHSS score of 26 or higher had an HRc of 11.09 (95 % CI: 5.95-20.68; $p < 0.001$) and an HRa of 6.11 (95 % CI: 3.47-10.74; $p < 0.001$).

Regarding reperfusion therapies, mechanical thrombectomy was associated with an increased risk of case-fatality in the crude analysis (HRc: 2.04; 95 % CI: 1.39-2.99; $p < 0.001$), although this association was not significant after adjustment (HRa: 1.20; 95 % CI: 0.83-1.74; $p = 0.336$).

Finally, neurological complications were associated with a significantly increased risk of death in both the crude (HRc: 4.96; 95 % CI: 3.63-6.79; $p < 0.001$) and adjusted (HRa: 3.20; 95 % CI: 2.38-4.32; $p < 0.001$) models. In contrast, infectious complications, though associated with increased crude risk (HRc: 1.62), did not remain significant in the adjusted model (HRa: 0.92; $p = 0.674$), suggesting potential

Table 1
General characteristics of patients admitted for stroke in the 27 hospitals.

Characteristics	N (%)
Sex	
Female	1,441 (48.1 %)
Male	1,556 (51.9 %)
Age in years (SD)	68.68 (14.86)*
Age groups	822 (27.4 %)
0 to <60 years	
60 to <75 years	1,103 (36.8 %)
75 years and over	1,072 (35.8 %)
sBP mmHg (mean)	150.67 (29.50)*
< 185 mmHg	2,497 (87.1 %)
≥ 185 mmHg	370 (12.9 %)
dBP mmHg (mean)	85.120 (16.276)*
< 110 mmHg	2,649 (92.4 %)
≥ 110 mmHg	218 (7.6 %)
Heart rate on admission	
< 90 beats/min	1,870 (78.5 %)
≥ 90 beats/min	511 (21.5 %)
Hemoglucotest on admission	
< 180 mg/dl	948 (38.6 %)
≥ 180 mg/dl	1,509 (61.4 %)
Comorbidity	
No history	318 (13.2 %)
With history	2,099 (86.8 %)
Comorbidities (specified)	
High blood pressure ($n = 2996$)	2154 (71.9 %)
DM ($n = 2996$)	882 (29.4 %)
Dyslipidemia ($n = 2995$)	754 (25.2 %)
A.M.I ($n = 2418$)	240 (9.9 %)
P.A.I ($n = 2418$)	68 (2.8 %)
Arrhythmia ($n = 2996$)	379 (12.7 %)
History of stroke ($n = 2814$)	387 (13.8 %)
Time in hospital days (median)	7 (4 to 13)*
Time stroke-door in minutes (median)	300 (121 to 900)±
TOAST classification	
Large vessel artery	497 (17.5 %)
Lacunar	577 (20.3 %)
Cardioembolic	669 (23.5 %)
Infrequent causes	198 (7.0 %)
Indeterminate	903 (31.7 %)
Baseline Rankin	
Independent (mRS 0 to 2)	2,253 (90.2 %)
Dependent (mRS 3 to 5)	244 (9.8 %)
Baseline NIHSS	
0 to 4	964 (35.8 %)
5 to 15	1,137 (42.2 %)
16 to 25	519 (19.3 %)
26 to more	74 (2.7 %)
Affected cerebral artery	
MCA	1,491 (62.9 %)
ACA	93 (3.9 %)
ACP	162 (6.8 %)
Vertebral artery	96 (4.1 %)
Basilar artery	147 (6.2 %)
Two or more territories	225 (9.5 %)
Not determined	156 (6.6 %)
Reperfusion therapies	
None	2203 (78.3 %)
Thrombolysis	422 (15.0 %)
Mechanical thrombectomy	122 (4.3 %)
Thrombolysis + mechanical thrombectomy	66 (2.4 %)
Basal hemoglobin mg/dl (mean)	14.07 (2.22)*
Anemia	455 (18.5 %)
Neurological complication	
Yes	316 (12.3 %)
Thromboembolic complication	
Yes	178 (6.3 %)
Infectious complication	
Yes	495 (18.5 %)
Immobility complication	
Yes	86 (3.4 %)
Deceased within 30 days	
No deceased	2,425 (89.8 %)
Deceased	277 (10.2 %)
Died after 90 days	
No deceased	2310 (86.7 %)
Died	353 (13.3 %)

* Mean and standard deviation ± Median and interquartile range. SD: Standard Deviation; sBP: systolic blood pressure; dBP: diastolic blood pressure; A.M.I: Acute myocardial infarction. D.M: Diabetes Mellitus; P.A.I: Peripheral arterial insufficiency; mRS: modified Rankin Scale; MCA: Middle cerebral artery; ACA: Anterior cerebral artery; ACP: Posterior cerebral artery.

confounding by other clinical factors. Country-level clustering was used to adjust standard errors for regional heterogeneity. Full adjusted model details are available in Table 3.

Fig. 2 shows the 30-day survival curves.

Discussion

Key findings This study presents updated case-fatality estimates for AIS patients across Latin America and identifies key predictors of early mortality. The observed in-hospital and 30-day case-fatality rates (9.4 % and 10.2 %, respectively) are in line with global data from low- and middle-income countries and highlight areas for targeted intervention.

Age greater than 75 years (HRa=2.28), hyperglycemia (HRa=1.28), baseline status (HRa=1.61), stroke severity according to NIHSS > 26 (HRa=6.11) and the presence of neurological complications (HRa=3.2) were risk factors for 30-day follow up case-fatality in these patients.

Case fatality rates

Ischemic stroke, case fatality rates varied significantly based on the country's level of income. In high income countries, in-hospital case-fatality rates range from 3 % to 11 %, while in low- and middle-income countries (L-MICs), these rates increase to 7 %–15 %. In our cohort in-hospital case-fatality was 9.42 %. Consistent with these trends, reported in-hospital case-fatality rates were 3.1 % in Taiwan,[16] 5.5 % in United States,[17] 7.13 % in Spain,[18] 4.9 % in Germany[8] but 33.3 % in Tanzania,[18] 12.8 % in Ethiopia,[19] 24.0 % in Zambia,[20] and 21.6 % in Kenya[21]

In our study, the overall 30-day stroke case-fatality rate was 10.2 %. These findings are comparable to those reported by a review and meta-analysis study which concluded that worldwide 1-month mortality of ischemic stroke was 13.5 % with differences across regions (10.8 % in Asia, 14.2 % in Europe, 14.0 % in South America and Caribbean, 14.0 % in North America and 12.5 % in Australia and New Zealand),[1,4] recent literature showing that factors such as socioeconomic vulnerability, healthcare accessibility, and multimorbidity significantly influence stroke outcomes in Latin America.[22] The countries with the highest case-fatality rate in our study were Uruguay (20.0 %), followed by Colombia (13.0 %). Argentina presented a case-fatality rate of 12.4 % vs 27 % by Ameriso et al.,[23] Brazil 12.8 % vs 13.3 % reported Minelli et[24] and Chile 4.1 %; lower than the 11.7 % reported by Lavados et al.[25] These disparities may reflect heterogeneity in healthcare infrastructure, such as the availability of stroke units, reperfusion therapy access, and standardized care protocols. In particular, the markedly lower mortality in Chile could be attributed to stronger stroke networks and earlier access to care, whereas the high fatality observed in Uruguay may be influenced by delayed presentation, limited acute stroke resources, or a higher burden of comorbidities and older patient age.

The 90-days stroke case-fatality rate reported in our registry was 13.5 %, which is lower than reported in sub-Saharan Africa (25.5 %),[26] Zambia (22.0 %),[20] Australia (20.7 %)[27] and Kenya (33.7 %).[21] It is like the rates observed in Uganda (14 %)[28] and Korea (10.9 %)[29] but higher than those reported by other Australian study (6.4 %)[30]

A recent report on stroke mortality in Latin America from 1990 to 2019 revealed significant increases in mortality rates in several countries, including Venezuela (130.5 %), Suriname (92.8 %), Ecuador (75.4 %), Bolivia (66.4 %), Paraguay (56.4 %), Colombia (43.6 %), Chile (31.1 %), Brazil (24.0 %), and Peru (17.1 %). In contrast, decreases in stroke mortality were observed in Argentina (14.6 %) and Uruguay (9.6 %).[31]

Table 2
Characteristics according to condition at 30 days in patients admitted for stroke in the 27 hospitals.

Characteristics	Condition at 30 days: Not deceased	Died	p-value
Sex			
Female	1,158 (88.5 %)	150 (11.5 %)	**0.043**
Male	1,267 (90.9 %)	127 (9.1 %)	
Age in years (mean)	68.15 (14.64)	73.11 (14.92)	**<0.001***
Age groups			
0 to <60 years.	683 (92.3 %)	57 (7.7 %)	**<0.001**
60 to <75 years.	925 (91.8 %)	83 (8.2 %)	
75 years and older.	817 (85.6 %)	137 (14.4 %)	
sBP mmHg (mean)	151.10 (29.23)	147.39 (32.02)	**0.022***
< 185 mmHg	2,091 (89.4 %)	247 (10.6 %)	0.273
≥ 185 mmHg	317 (91.4 %)	30 (8.6 %)	
dBP mmHg (mean)	85.47 (15.98)	83.23 (19.05)	**0.037***
< 110 mmHg	2,231 (83.9 %)	250 (10.1 %)	0.154
≥ 110 mmHg	177 (86.8 %)	27 (13.2 %)	
Heart rate on admission			
< 90 beats/min	1,625 (90.6 %)	169 (9.4 %)	**<0.001**
≥ 90 beats/min	406 (84.4 %)	75 (15.6 %)	
Hemoglucotest on admission			
< 180 g/dl	844 (93.36 %)	60 (6.64 %)	**<0.001**
≥ 180 g/dl	1,265 (87.60 %)	179 (12.40 %)	
Comorbidity			
No history	282 (92.16 %)	24 (7.84 %)	0.096
With history	1,775 (89.03 %)	219 (10.97 %)	
High blood pressure			
No	689 (92.11 %)	59 (7.89 %)	**0.012**
Yes	1,735 (88.86 %)	218 (11.14 %)	
Diabetes Mellitus			
No	1,700 (89.90 %)	191 (10.10 %)	0.685
Yes	724 (89.39 %)	86 (10.61 %)	
Dyslipidemia			
No	1,837 (90.27 %)	198 (9.73 %)	0.113
Yes	586 (88.11 %)	79 (11.89 %)	
I.M.A			
No	1,863 (89.78 %)	212 (10.22 %)	0.068
Yes	194 (85.84 %)	32 (14.16 %)	
P.A.I			
No	2,005 (89.58 %)	233 (10.42 %)	0.073
Yes	52 (82.54 %)	11 (17.46 %)	
Arrhythmia			
No	2,132 (90.48 %)	224 (9.52 %)	**<0.001**
Yes	292 (84.63 %)	53 (15.37 %)	
History of stroke			
No	2,090 (89.99 %)	232 (10.01 %)	0.302
Yes	331 (88.25 %)	44 (11.75 %)	
Hospitalization time in days (median)	10.45 (13.38)	9.28 (8.31)	0.156*
Time stroke-door in minutes (median)	873.59 (2,144.73)	835.06 (2,008.29)	0.716±
TOAST			
Large vessel artery	362 (87.65 %)	51 (12.35 %)	0.263
lacunar	484 (90.80 %)	49 (9.20 %)	
cardioembolic	539 (87.80 %)	75 (12.20 %)	
c. infrecuentes	155 (90.64 %)	16 (9.36 %)	
undetermined	742 (90.37 %)	79 (9.63 %)	
Baseline Rankin			
Independent	1,947 (90.64 %)	201 (9.36 %)	**<0.001**
Dependent	183 (77.88 %)	52 (22.12 %)	
Baseline NIHSS			
0 to 4	912 (97.74 %)	21 (2.26 %)	**<0.001**
5 to 15	995 (91.96 %)	87 (8.04 %)	
16 to 25	374 (75.41 %)	122 (24.59 %)	
26 to more	38 (54.29 %)	32 (45.71 %)	

(*continued on next page*)

Table 2 (*continued*)

Characteristics	Condition at 30 days		p-value
	Not deceased	Died	
Affected cerebral artery			
MCA	1,271 (88.82 %)	160 (11.18 %)	0.289
ACA	80 (93.02 %)	6 (6.98 %)	
ACP	140 (90.32 %)	14 (9.68 %)	
A. Vertebral	87 (93.55 %)	6 (6.45 %)	
A. basilar	119 (88.15 %)	15 (11.85 %)	
2 or more territories	189 (85.92 %)	31 (14.08 %)	
not determined	125 (91.24 %)	11 (8.76 %)	
Reperfusion therapies			
None	1920 (91.2 %)	185 (8.8 %)	**<0.001**
Thrombolysis	361 (88.3 %)	48 (11.7 %)	
Mechanical thrombectomy	91 (75.8 %)	29 (24.2 %)	
Thrombolysis + mechanical thrombectomy	51 (78.5 %)	14 (21.5 %)	
Basal hemoglobin mg/dl (mean)	14.16 (2.27)	13.58 (2.38)	**<0.001***
Anemia (Hb<11 mg/dl)	164 (82.38 %)	35 (17.62 %)	**0.004**
No anemia (Hb≥11 mg/dl)	1,794 (90.15 %)	196 (9.85 %)	
Neurological complication			
No	1,856 (93.55 %)	128 (6.45 %)	**<0.001**
Yes	181 (60.95 %)	116 (39.05 %)	
Thromboembolic complication			
No	2,267 (89.93 %)	254 (10.07 %)	0.331
Yes	156 (87.61 %)	22 (12.39 %)	
Infectious complication			
No	1,768 (91.30 %)	169 (8.70 %)	**<0.001**
Yes	351 (76.47 %)	108 (23.53 %)	
Immobility complication			
No	1,977 (89.81 %)	224 (10.19 %)	**<0.001**
Yes	58 (74.36 %)	20 (25.64 %)	

P-values are obtained as chi-square, except for numerical variables. * P-value obtained by T-Student. ± *P*-value obtained by U Mann-Whitney. sBP: systolic blood pressure; dBP: diastolic blood pressure; A.M.I: Acute myocardial infarction. D.M: Diabetes Mellitus; P.A.I: Peripheral arterial insufficiency; mRS: modified Rankin Scale; MCA: Middle cerebral artery; ACA: Anterior cerebral artery; ACP: Posterior cerebral artery.

Demographic and baseline features

In our study, the baseline features associated with 30-day case-fatality, based on an adjusted multivariate logistic regression analysis, included a history of hypertension, functional dependency, older age (≥ 75 years), and higher heart rate (≥ 90 beats per minute). Similarly, an Ethiopian cohort reported that hypertension doubled the risk of mortality.[19] In contrast, an American cohort found that hypertension was associated with lower stroke case-fatality rate, potentially due to the use of medical therapies like antithrombotic medications and statins, which could have reduced stroke severity. This study also identified older age (≥ 60 years), atrial fibrillation, coronary artery disease, diabetes mellitus, and peripheral vascular disease as baseline factors linked to higher mortality.[17] The German Stroke Registers Study Group (ADSR) reported a statistically significant increase in mortality among the elderly (≥ 65 years) but found no association with hypertension. They also identified atrial fibrillation and stroke severity as factors associated with higher mortality.[8] An Iranian cohort showed increased mortality in older patients (≥ 60 years) but no association with hypertension.[32] A Lebanese study found that age (≥ 64 years) and hypertension were both associated with mortality, along with atrial fibrillation and coronary heart disease.[33] Supporting our findings, a report from Uganda found that prior disability (mRS 4-5) increased the risk of mortality fivefold in the unadjusted multivariate analysis, though this association was not significant in the adjusted model.[28] Additionally, a Taiwanese study

Table 3
Characteristics adjusted to death at 30 days in patients admitted for stroke in the 27 hospitals.

Características	HRc	CI 95 %	p-value	HRa	CI 95 %	p-value
Sex						
Female	Ref.			Ref.		
Male	0.77	0.63 – 0.95	**0.013**	1.10	0.79 – 1.52	0.564
Age in years (mean)						
0 to <60 years	Ref.			Ref.		
60 to <75 years	1.15	0.79 – 1.67	0.462	1.51	0.90 – 2.53	0.117
75 years and older	1.91	1.48 – 2.48	**<0.001**	2.28	1.51 – 3.44	**<0.001**
sBP mmHg (mean)						
< 185 mmHg	Ref.			NA		
≥ 185 mmHg	0.81	0.50 – 1.33	0.413			
dBP mmHg (mean)						
< 110 mmHg	Ref.			NA		
≥ 110 mmHg	1.10	0.80 – 1.53	0.533			
Heart rate on admission						
< 90 beats/min	Ref.			NA		
≥ 90 beats/min	1.54	1.02 – 2.35	**0.041**			
Hemoglucotest on admission						
< 180 g/dl	Ref.			Ref.		
≥ 180 g/dl	1.88	1.46 – 2.44	**<0.001**	1.28	1.01 – 1.63	**0.042**
Comorbidity						
No history	Ref.			NA		
With antecedent	1.23	0.90 – 1.69	0.191			
High blood pressure						
No	Ref.			Ref.		
Yes	1.47	1.20 – 1.79	**0.001**	0.77	0.60 – 0.99	**0.042**
D.M.						
No	Ref.			NA		
Yes	1.17	0.84 – 1.64	0.342			
Dyslipidemia						
No	Ref.			NA		
Yes	1.20	0.80 – 1.80	0.375			
I.M.A						
No	Ref.			NA		
Yes	1.32	0.95 – 1.85	0.102			
P.A.I						
No	Ref.			NA		
Yes	1.47	0.75 – 2.85	0.258			
Arrhythmia						
No	Ref.			NA		
Yes	1.31	1.04 – 1.66	**0.021**			
History of stroke						
No	Ref.			NA		
Yes	1.06	0.84 – 1.28	0.546			
TOAST						
large vessel artery	Ref.			NA		
lacunar	1.01	0.47 – 2.15	0.983			
Cardioembolic	0.93	0.62 – 1.40	0.742			
c. infrequent	0.71	0.38 – 1.32	0.275			
undetermined	0.99	0.67 – 1.46	0.956			
Baseline Rankin						
Independent	Ref.			Ref.		

(*continued on next page*)

Table 3 (*continued*)

Características	HRc	CI 95 %	p-value	HRa	CI 95 %	p-value
Dependent	2.11	1.54 – 2.90	**<0.001**	1.61	1.19 – 2.17	**0.002**
Baseline NIHSS						
0 to 4	Ref.			Ref.		
5 to 15	2.48	1.41 – 4.37	**0.002**	1.78	1.05 – 3.03	**0.034**
16 to 25	6.77	4.48 – 10.25	**<0.001**	5.44	3.42 – 8.65	**<0.001**
26 to more	11.09	5.95 – 20.68	**<0.001**	6.11	3.47 – 10.74	**<0.001**
Affected cerebral artery						
MCA	Ref.			NA		
ACA	0.58	0.26 - 1.29	0.181			
ACP	0.84	0.49 - 1.43	0.520			
A.Vertebral	0.64	0.29 - 1.43	0.277			
A. basilar	1.00	0.60 - 1.69	0.988			
2 or more territories	1.15	0.79 - 1.68	0.456			
not determined	0.84	0.45 - 1.54	0.568			
Reperfusion therapies						
None	Ref.			Ref.		
Thrombolysis	1.41	1.10 – 1.81	**0.007**	1.18	0.95 – 1.48	0.128
Mechanical thrombectomy	2.04	1.39 – 2.99	**<0.001**	1.20	0.83 – 1.74	0.336
Thrombolysis + mechanical thrombectomy	1.77	1.06 – 2.99	**0.030**	1.50	0.78 – 2.91	0.226
Anemia						
Not	Ref.			NA		
Yes	1.42	1.03 – 1.97	**0.033**			
Neurological complication						
No	Ref.			Ref.		
Yes	4.96	3.63 – 6.79	**<0.001**	3.20	2.38 – 4.32	**<0.001**
Thromboembolic complication						
No	Ref.			NA		
Yes	1.05	0.68 – 1.59	0.840			
Infectious complication						
No	Ref.			Ref.		
Yes	1.62	0.97 – 2.69	**0.065**	0.92	0.62 – 1.37	0.674
Immobility complication						
No	Ref.			NA		
Yes	1.52	0.78 – 2.96	0.220			

sBP: systolic blood pressure; dBP: diastolic blood pressure; A.M.I: Acute myocardial infarction. D.M: Diabetes Mellitus; P.A.I: Peripheral arterial insufficiency; mRS: modified Rankin Scale; MCA: Middle cerebral artery; ACA: Anterior cerebral artery; ACP: Posterior cerebral artery. HRc: Hazard ratio crude. HRa: Hazard ratio adjusted. All standard errors were adjusted by cluster according to country.

identified higher in-hospital heart rate as an independent predictor of all-cause mortality after stroke, with adjusted hazard ratios (HRs) of 1.23 (95 % CI 1.08-1.41) for a heart rate of 60-69 bpm, 1.74 (95 % CI 1.53-1.97) for 70-79 bpm, 2.16 (95 % CI 1.89-2.46) for 80-89 bpm, and 2.83 (95 % CI 2.46-3.25) for heart rates ≥ 90 bpm compared to the reference group (<60 bpm).[34] The PRoFESS study further supports these findings, showing that patients in the two highest heart rate quintiles (77-82 and >82 bpm) had an increased risk of all-cause mortality, with HR of 1.42 (95 % CI 1.19-1.69) and 1.74 (95 % CI 1.48-2.06), respectively, compared to the lowest quintile.[35]

Previously, it has been reported that 30-40 % of patients with acute stroke present with hyperglycemia upon admission.[36] In our series, we found that 61 % of patients had blood glucose levels greater than 180 mg/d, although 29 % had a history of diabetes, hyperglycemia has also been documented in patients without a history of diabetes, related to the increased release of stress hormones or undiagnosed diabetes.[37] The presence of hyperglycemia has been described as a factor associated with mortality,[38] which is consistent with our results.

Stroke severity and treatment

We observed in our study a significant relationship between case-fatality rate and individuals with higher NIHSS scores. This finding aligns with the existing literature, which has shown that 30-day case-fatality rate increases by 9 % for each unit increase in the NIHSS score.[39]>15 % of the patients received IV tPA, which is close to the IVT (intravenous therapy) goals of the high-income countries (HICs).[40] The MT (mechanical thrombectomy) rates, however, are behind the ideal due primarily to the lack of access to MT in Latin America,[41] despite the evidence of outcomes compared to the global findings.[42]

In the adjusted analysis, neither IVT nor MT was associated with case-fatality rate, and the statistical significance in the univariate analysis could be attributed to patients with more severe strokes and worse pre-stroke characteristics. These findings are consistent with literature, namely, the role of age, NIHSS, hyperglycemia, and higher initial systolic blood pressure for outcomes after both IVT and MT[43]

In-hospital complications

Up to 40 % of patients experienced some type of complication after stroke, with infectious complications being the most frequent, followed by neurological complications, that were more closely associated with case-fatality. A cross-sectional study in North American centers found non-neurological complications in 1 out of 4 patients[44]

The rate of infectious complications shows significant variation in reports from various studies. A meta-analysis by Westendorp et al. estimates a 30 % infection rate, with a 10 % rate for pneumonia and for urinary tract infections, like what we found in our population[45]

Regarding neurological complications, the results have been inconsistent. For example, seizures have been associated with in-hospital mortality, according to A. Nutakki et al.[20]; however, this association is lost when analyzing 90-day mortality, which was not statistically significant. A similar pattern is seen with cerebral edema,[46] which has been linked to increase in-hospital mortality. We also highlight the study by Pandian et al.,[12] who conducted a multicenter cohort study in India on complications in both ischemic and hemorrhagic acute stroke, including 449 patients in the final analysis of clinical outcomes. They reported infectious complications as the most common, and among neurological complications, they observed a stroke recurrence rate of 1.3 %, seizures at 3.8 %, and other events at 0.7 %. Additionally, the presence of neurological complications was not associated with poor prognosis in these patients.

Neurological complications such as malignant cerebral edema, hemorrhagic transformation, or seizures may directly reflect the severity of the initial ischemic insult or delays in receiving specialized care, including access to neurocritical units or advanced imaging. Their strong association with early mortality highlights the importance of early identification and standardized management of these complications in stroke protocols. These findings suggest a need for better training, early warning systems, and capacity-building in stroke units across the region to mitigate their impact on short-term outcomes.[20,46]

The rate of neurological complications in these previous studies has been lower compared to what was reported in our study, which was 12.3

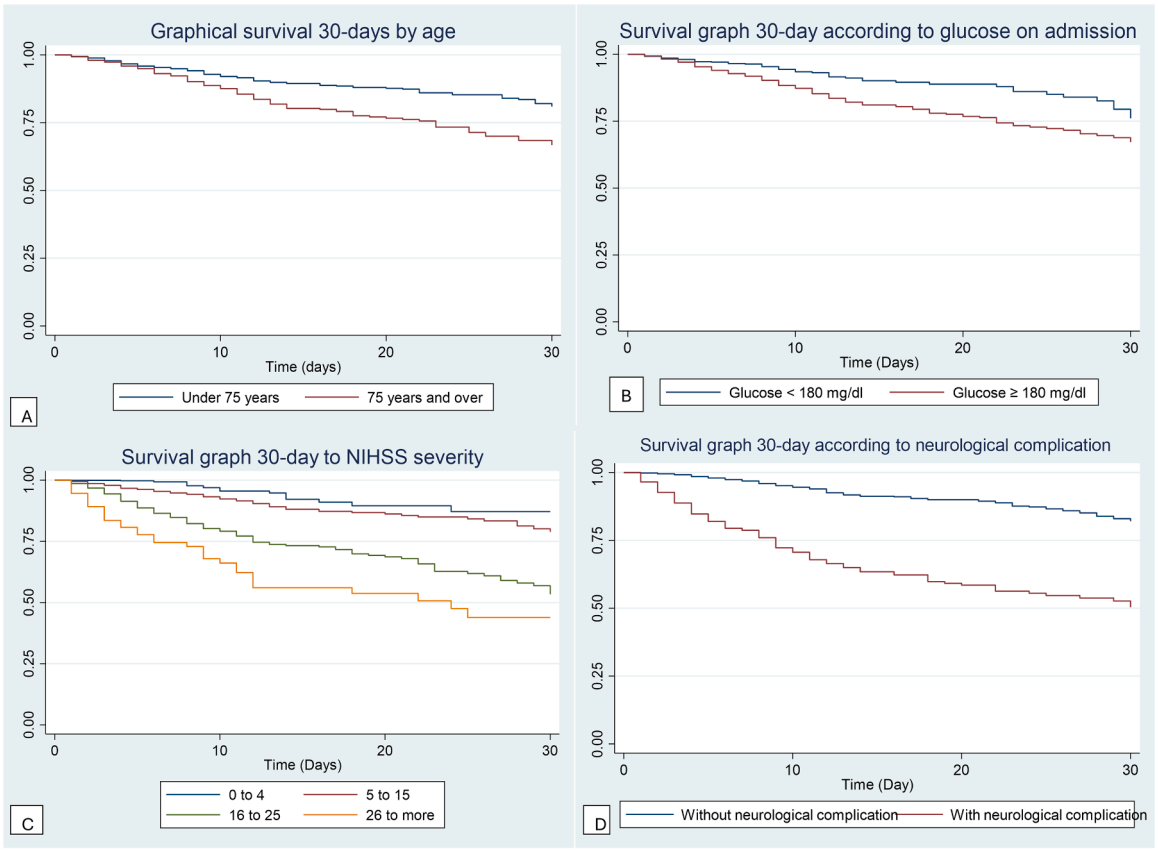

Fig. 2. Survival curves 30-days by clinical conditions in patients with stroke.

%, and this difference may explain the variations in statistical findings in our cohort.

Strengths and limitations

This study contributes to the understanding of stroke mortality in Latin America, a region often underrepresented in global stroke research. By analyzing 2,997 patients for 12 months, it was possible to analyze factors associated with mortality in AIS patients.

Although numbers as low as 14 patients for one year (in Panama) do not allow for generalization of the results to a country level, the multicenter design across 11 countries aims to ensure regional representation, capturing diverse clinical practices, healthcare systems, and population characteristics. This study collected detailed clinical and laboratory data, including NIHSS scores, baseline functional status, and imaging findings. Therefore, it was possible to analyze the impact of variables such as age, stroke severity, and laboratory findings on case-fatality outcomes. Also, the granularity of data allowed the run of adjusted multivariate models, mainly to understand the correlation between neurological complications and case-fatality. The study also evidenced the disparities in access to reperfusion therapies in the region, such as mechanical thrombectomy. This finding adds to the evidence used to advocate policy changes in Latin America.

Despite its strengths, the study has several limitations. First, the retrospective observational design restricts causal inference and relies on the quality of existing medical records, which could bring variability in the reported findings. Selection bias or missing data, especially 90-day outcomes, may have resulted from the choice of this design. No data was available regarding socioeconomic factors, healthcare accessibility, and pre-hospital care, among other missing characteristics, which are known to influence stroke outcomes. The study would benefit from integrating these variables to contextualize case-fatality disparities observed across countries, which might reflect underreporting rather than actual outcomes.

Our study was limited in terms of sociodemographic variables (only age and sex were collected), which could have provided critical context to interpret variations in case-fatality rates across countries. As demonstrated in preceding studies, the educational attainment of the population, income, health insurance coverage, and access to healthcare have been identified as significant determinants of stroke outcomes. The absence of this data may have distorted our findings, potentially leading to an underestimation of the role of structural inequalities. Furthermore, the participating centers in this study are predominantly urban, tertiary-level hospitals with the capacity to deliver reperfusion therapy and are not representative of the full healthcare system within each country. Therefore, our results should not be extrapolated to national populations; rather, they are referential to the clinical performance and outcomes observed in the selected institutions. Future research should aim to incorporate socioeconomic profiling and include a broader spectrum of healthcare settings to improve the generalizability and relevance of findings at the population level.

Finally, the study's focus on referral hospitals with reperfusion capabilities may not generalize to smaller, resource-limited centers where a substantial proportion of Latin America's stroke population is treated. This selection could skew the results toward better-equipped facilities, underestimating the true regional burden of stroke mortality.

This study significantly contributes to the knowledge of stroke mortality in Latin America. However, future studies should incorporate a prospective design, expand to include non-specialized centers and explore broader determinants of health, to draw a more accurate and comprehensive picture of stroke outcomes in the region.

Conclusion

Acute in-hospital case-fatality was 9.42 %, 30-day case-fatality was 10.2 %, while 90-day case-fatality was 13.3 %. Older age, hyperglycemia, baseline status, stroke severity and neurological complications were the highest risk factors for 30-day case-fatality after stroke. The findings of this study highlight the importance of analyzing local protocols to diminish the cumulative risk of the factors associated with the highest case-fatality.

CRediT authorship contribution statement

Miguel A. Vences: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Investigation, Data curation, Conceptualization. **Miguel A. Barboza:** Writing – review & editing, Writing – original draft, Resources, Methodology, Formal analysis, Conceptualization. **Leonardo Augusto Carbonera:** Writing – review & editing, Writing – original draft, Validation, Investigation, Formal analysis, Data curation. **Virgilio E. Failoc-Rojas:** Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Formal analysis, Data curation. **Julieta Rosales:** Writing – review & editing, Writing – original draft, Resources, Methodology, Data curation. **Pablo Amaya:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Data curation. **Pablo Lavados:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Data curation.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

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