

Incidence Rate and Risk Factors for In-Hospital Ischemic Stroke among 83,990 Hospitalized Patients

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Background: Details of in-hospital stroke are unknown. This study aimed to clarify the incidence rate and risk factors for in-hospital stroke among all inpatients.

Methods: This retrospective single-center study included consecutive patients admitted to our hospital. Patients aged <18 years, discharged within 24 h, and admitted to the neurology and neurosurgery departments were excluded. The incidence rate for in-hospital stroke was calculated, and patients were divided into stroke and control groups based on ischemic stroke occurrence, and the risk factors were assessed using multivariate analysis.

Results: Of the 83,990 enrolled patients, 101 (0.12%) developed stroke. The stroke group had a higher proportion of patients with older age (76 vs 69 years; $P < .01$), hypertension (49% vs 26%; $P < .01$), diabetes mellitus (34% vs 22%; $P = .01$), atrial fibrillation (25% vs 8%; $P < .01$), cardiovascular disease (20% vs 11%; $P = .01$), and emergency admission (68% vs 32%; $P < .01$) compared to the control group. The risk factors for in-hospital stroke were old age (odds ratio [OR], 1.03; $P < .01$), hypertension (OR, 1.57; $P = .04$), diabetes mellitus (OR, 1.61; $P = .03$), atrial fibrillation (OR, 2.43; $P < .01$), emergency admission (OR, 3.38; $P < .01$), and low serum albumin (OR, 0.66; $P = .03$).

Conclusion: The incidence rate of in-hospital stroke was 0.12% and the independent risk factors were old age, history of hypertension, diabetes mellitus, atrial fibrillation, emergency admission, and low serum albumin. (J Nippon Med Sch 2025; 92: 181–187)

Key words: atrial fibrillation, inpatient, risk factor, stroke

Introduction

In-hospital stroke (IHS) accounts for 2.2–16.6% of all acute stroke cases^{1–4}. Patients with IHS are reported to have late detection^{5,6}, lower recombinant tissue-type plasminogen activator (rt-PA) use⁷, poor outcomes⁸, and longer hospital stays^{9,10}. Furthermore, the mortality rate for IHS cases is two to three times that of out-of-hospital stroke cases^{9,11}. Many factors contribute to the incidence of IHS including prior invasive procedures and cardiac disease, oncological and hematological diseases, history of stroke, dehydration, or fever, and withdrawal of an-

tithrombotic drugs due to interventional procedures^{5,12}. However, the previous studies of incidence rates and risk factors investigated all stroke patients, not all hospitalized patients. Therefore, the incidence rate and risk factors for IHS among hospitalized patients—without comparing out-of-hospital onset stroke—must be determined to facilitate early IHS detection and treatment. Thus, this study aimed to investigate the incidence rate and risk factors associated with IHS among all hospitalized patients.

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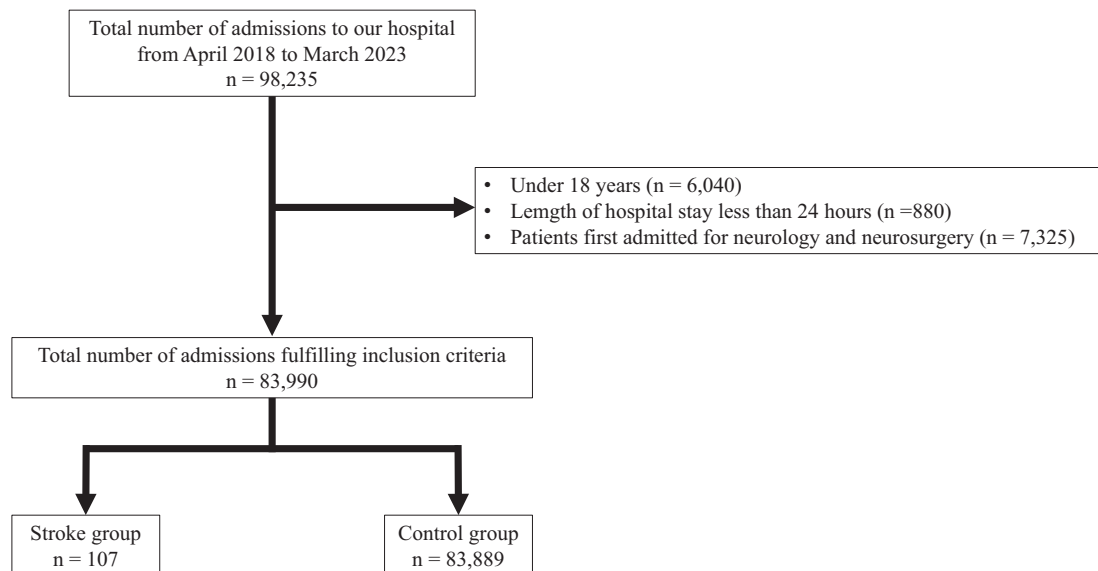


Fig. 1 Flow chart of patient inclusion and exclusion

A total of 98,235 patients admitted to our hospital between April 2018 and March 2023 were enrolled in this study. Patients under 18 years of age ($n = 6,040$), discharged within 24 h ($n = 880$), or first admitted to the neurology and neurosurgery departments ($n = 7,325$) were excluded. Finally, 83,990 patients were included in this study. The patients were then divided into the stroke group, which included patients with in-hospital stroke, and the control group, which included patients without in-hospital stroke.

Materials and Methods

Study Design, Patients, and Ethical Approval

This retrospective single-center cohort study used the inpatient database of Nippon Medical School Hospital, Tokyo, Japan. The study was approved by the institutional review board of Nippon Medical School (approval no. O-2023-682) and was conducted in accordance with the principles of the revised Declaration of Helsinki. The opt-out method was used to recruit participants, and the requirement for written consent was waived. Patients consecutively admitted to our academic medical center between April 2018 and March 2023 were assessed. Patients younger than 18 years or discharged within 24 h were excluded. Those admitted to the neurology and neurosurgery departments were also excluded from the study to remove in-hospital onset recurrent stroke patients (Fig. 1).

In-Hospital Stroke

IHS was defined as an acute ischemic stroke that occurred during hospitalization. All patients underwent brain magnetic resonance imaging or computed tomography, and stroke neurologists diagnosed IHS. Using the International Classification of Diseases, 10th Revision, we searched the entire hospital inpatient database to identify patients with IHS who were registered as having an ischemic stroke after admission. These patients were re-confirmed using the prospective hospital-based acute

stroke registry.

Data Collection

The following clinical information was obtained from the inpatient database: age, sex, body mass index, length of stay, number of days from admission to IHS, emergency or elective admission, primary diagnosis, active cancer, surgical procedures, medications (including antiplatelets, anticoagulants, or statins), medical history (including hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation, or cardiovascular disease), and laboratory findings (including glucose, hemoglobin, creatinine, C-reactive protein, and albumin levels). The primary diagnosis and medical history data were extracted using the International Classification of Diseases, 10th Revision codes (**Supplementary Table 1**: https://doi.org/10.1272/jnms.JNMS.2025_92-209). Blood examination data were obtained for patients immediately evaluated before IHS. Active cancer was defined as cancer diagnosed within 6 months of a recent admission, any treatment for cancer within the previous 6 months, or recurrent or metastatic cancer. Anticoagulant therapy was defined as the use of warfarin, dabigatran, rivaroxaban, apixaban, or edoxaban. Antiplatelet therapy was defined as the use of aspirin, clopidogrel, cilostazol, or prasugrel.

Statistical Analysis

The incidence rate of IHS was calculated. The number of days from admission to IHS occurrence and the pri-

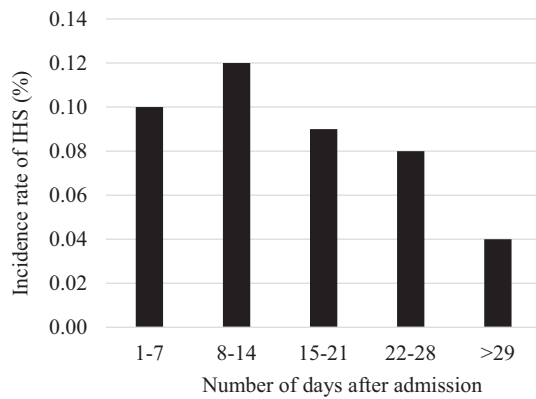


Fig. 2 The incidence rate of IHS according to the number of days from admission to stroke onset. The incidence rates were 0.10 in the first week, 0.12 in the second week, 0.09 in the third week, 0.08 in the fourth week, and 0.04 after the fourth week, respectively.

mary diagnosis of patients with IHS were evaluated. All inpatients were then divided into a stroke group comprising patients who developed IHS and a control group comprising patients who did not develop IHS. The characteristics of the two groups were investigated, and multivariate logistic regression analysis was performed to measure odds ratios (ORs) and 95% confidence intervals (CIs) for risk factors independently associated with IHS. Univariate analysis included age, sex, and other variables ($P < .05$). Finally, a predictive scoring system for IHS, with a total score of 10 points, was developed by assigning points based on the ORs for independent risk factors identified in multivariate analysis. The ratio of the incidence rate of achieving 1-2, 3-6, and 7-10 points in the score was then calculated when the incidence rate for 0 points was set to 1.

Categorical variables are expressed as numerical values and percentages and were compared using the chi-square test. Continuous variables are expressed as medians and interquartile ranges (IQRs) and were analyzed using the Mann-Whitney U test. A two-sided P -value of $< .05$ was considered statistically significant. All statistical analyses were performed using R software v. 4.2.2 Patched (R Foundation for Statistical Computing, Vienna, Austria).

Role of the Funding Source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

During the study period, 98,225 patients were admitted to the hospital. Of these, 6,040 patients were younger

than 18 years, 880 patients were hospitalized for <24 h, and 7,325 patients were admitted to the neurology or neurosurgery departments. Therefore, 83,990 patients were included in the study. IHS occurred in 101 of the patients; thus, the incidence rate of IHS among all hospitalized patients was 0.12%.

Fig. 2 shows the interval (days) from admission to IHS occurrence. The incidence rate was 0.10 in the first week, 0.12 in the second week, 0.09 in the third week, 0.08 in the fourth week, and 0.04 after the fourth week. The distribution of diagnoses at admission in patients with IHS is shown in **Supplementary Figure 1** (https://doi.org/10.1272/jnms.JNMS.2025_92-209). Cardiovascular disease was the most diagnosed disease (35%, $n = 36$), followed by oncological (22%, $n = 22$), gastrointestinal (9%, $n = 9$), and orthopedic or traumatic (6%, $n = 6$) diseases.

Patients in the stroke group were significantly older than those in the control group (mean age, 76 [69-83] years vs 69 [54-77] years; $P < .01$; **Table 1**). The proportion of males in the stroke group was 51%, which did not differ significantly from that in the control group (55%). The stroke group had a significantly higher prevalence of hypertension—the most common comorbidity—diabetes mellitus, atrial fibrillation, and cardiovascular disease. The proportion of emergency admissions was higher in the stroke group than in the control group. Anticoagulants were used more frequently in the stroke group than in the control group, whereas both antiplatelet and statin use were similar in the two groups. No significant differences in the proportions of patients with active cancer or hyperlipidemia were observed between the two groups. Endovascular treatment was performed in 40 patients in the stroke group (40%), and five patients (5%) received a tissue-type plasminogen activator. No baseline covariate or outcome data were missing, except for 7,201 (9%) cases with missing blood data. Patients in the stroke group had lower hemoglobin and albumin levels and higher creatinine, C-reactive protein, and glucose levels. Multivariate logistic regression analysis revealed that older age, history of hypertension, diabetes mellitus, and atrial fibrillation, emergency admission, and low serum albumin were independent risk factors associated with IHS (**Table 2**). Patients in the stroke group had significantly longer hospital stays (36 vs 8 days; $P < .01$) and higher mortality rates (15% vs 3%; $P < .01$) than those in the control group.

The risk score was as follows: age ≥ 75 years = 1 point, hypertension = 1 point, diabetes mellitus = 1 point, atrial fibrillation = 2 points, emergency admission = 3 points,

Table 1 Patient characteristics of the stroke and control groups

Characteristic	Stroke group	Control group	P-value
	n = 101	n = 83,889	
Age, years, median [IQR]	76 [69–83]	69 [54–77]	<.01
Male, n (%)	51 (51)	46,379 (55)	.37
BMI, kg/m ² , median [IQR]	22 [19–24]	22 [20–25]	.33
Medical history			
Hypertension, n (%)	49 (49)	21,370 (26)	<.01
Diabetes mellitus, n (%)	34 (34)	18,666 (22)	.01
Hyperlipidemia, n (%)	21 (21)	11,816 (14)	.06
Atrial fibrillation, n (%)	25 (25)	6,640 (8)	<.01
Cardiovascular disease, n (%)	20 (20)	9,406 (11)	.01
Active cancer, n (%)	37 (37)	34,679 (41)	.36
Emergency admission, n (%)	69 (68)	26,785 (32)	<.01
Surgical procedures, n (%)	28 (28)	28,193 (34)	.25
Oral medication			
Anticoagulants, n (%)	33 (33)	12,531 (15)	<.01
Antiplatelets, n (%)	18 (18)	12,965 (16)	.49
Statins, n (%)	29 (29)	21,014 (25)	.42
Blood test, median			
Hemoglobin, g/dL, [IQR]	12.1 [10.4–13.6]	12.6 [11–14]	.02
Creatinine, mg/dL, [IQR]	0.9 [0.8–1.2]	0.8 [0.6–1.1]	<.01
Albumin, g/dL, [IQR]	3.5 [3.1–3.9]	3.8 [3.4–4.2]	<.01
CRP, mg/dL, [IQR]	0.8 [0.2–4.2]	0.3 [0.1–1.8]	<.01
Glucose, mg/dL, [IQR]	136 [107–165]	110 [96–136]	<.01

BMI, body mass index; CRP, C-reactive protein; IQR, interquartile range

Table 2 Multivariate logistic regression models for the probability of developing in-hospital stroke

Variable	OR	95% CI	P-value
Age	1.03	1.01–1.05	<.01
Male sex	0.72	0.48–1.09	.12
Hypertension	1.57	1.03–2.4	.04
Diabetes mellitus	1.61	1.05–2.46	.03
Atrial fibrillation	2.43	1.30–4.53	<.01
Cardiovascular disease	1.07	0.63–1.81	.80
Emergency admission	3.38	2.14–5.34	<.01
Anticoagulants	1.05	0.59–1.86	.88
Hemoglobin, 1 g/dL [†]	1.04	0.94–1.15	.42
Creatinine, 1 mg/dL [†]	0.92	0.78–1.09	.33
Albumin, 1 g/dL [†]	0.66	0.46–0.96	.03
CRP, 1 mg/dL [†]	0.39	0.95–1.02	.35

CI, confidence interval; CRP, C-reactive protein; OR, odds ratio.

[†] Blood data records were missing for 7,201 cases (9%).

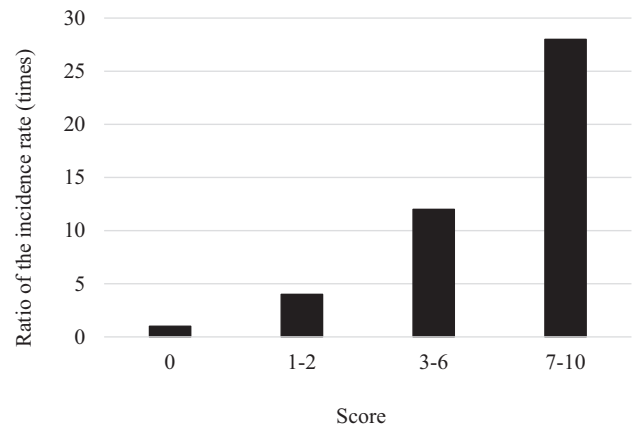


Fig. 3 Ratio of in-hospital stroke incidence rates

A score named the HEA³D score (hypertension = 1, emergency admission = 3, age ≥ 75 years = 1, atrial fibrillation = 2, albumin concentration <3 g/dL = 2, diabetes mellitus = 1) was created with points weighted using the odds ratio based on independent risk factors derived from multivariate analysis, with a total score of 10 points. The incidence rate ratios for scores of 1–2, 3–6, and 7–10 points in the HEA³D score were then calculated, with the incidence rate for 0 points set to 1. The ratio of the incidence rate of in-hospital stroke was 3.6, 11.6, and 28.4 for the scores of 1–2, 3–6, and 7–10 points, respectively.

and albumin concentration <3 g/dL = 2 points. The score was termed HEA³D (hypertension, emergency admission, age, atrial fibrillation, albumin, diabetes mellitus). The proportions of IHS patients with HEA³D scores of 0, 1-2, 3-6, and 7-10 were 0.02%, 0.06%, 0.21%, and 0.51%, respectively (Fig. 3).

Discussion

The present study had three significant findings. First, the incidence rate for IHS was 0.12%. Second, incidence was higher during initial hospitalization. Third, the independent risk factors for IHS were older age, history of hypertension, diabetes mellitus, and atrial fibrillation, emergency admission, and low serum albumin.

To the best of our knowledge, this is the first study to identify detailed risk factors for IHS among all hospitalized patients. Only one other study reported the incidence rate of IHS in hospitalized patients: 22 patients with a first stroke were identified among 71,874 hospitalized patients, an incidence rate of 0.03%¹³, which was lower than in our study. The duration of the previous study was 1 year, and patients only received a diagnosis when a ward physician referred them. Therefore, variability in the study terms, target patients, and diagnostic methods for stroke may account for the differences in the incidence rates for IHS.

In previous reports, 23-29% of patients with IHS were diagnosed with cardiovascular disease on admission^{5,13,14}. Similarly, in this study, cardiovascular disease was the most common cause of admission in the stroke group (35%). Cardiac sources of embolism are the most frequent risk factors for IHS and may explain the high incidence of IHS in cardiovascular departments¹⁴. Oncological disease was the second most common cause of admission; however, active cancer was not a risk factor for IHS. Other studies have not reported differences in the incidence of cerebral infarction between patients with and without cancer^{15,16}, similar to the present study.

In the present study, older age was a risk factor for IHS which is consistent with previous reports¹⁷. Approximately 90% of strokes in the general population occur in patients older than 60 years¹⁸. Similarly, in the Japan Stroke Data Bank, the median age at stroke onset is 70 (59-79) years¹⁹. Among hospitalized patients, older patients are more likely to develop stroke. In this study, the proportions of patients with hypertension, diabetes mellitus, and atrial fibrillation were significantly higher in the stroke group than in the control group. Previous studies reported no significant differences between IHS and out-

of-hospital stroke for patients with hypertension and diabetes; however, patients with atrial fibrillation had a significantly higher incidence of IHS than out-of-hospital stroke^{1,5,8,11,17,20}. In this study, the proportion of emergency admissions in the stroke group was 68%, which was significantly higher than that in the control group and similar to previous reports¹³. Emergency hospitalization for fracture or gastrointestinal bleeding requires temporary antithrombotic drug withdrawal, thereby increasing the risk of stroke, which may explain the high rate of IHS among emergently hospitalized patients in this study. Additionally, low serum albumin, which indicates malnutrition and inflammation, was associated with IHS in this study, which is consistent with previous results²¹⁻²⁴. Inflammatory activation of macrophages and other immune system cells produces more cytokines, causing protein synthesis in the liver to switch from albumin to other acute-phase proteins²⁵.

Finally, as compared with a HEA³D score of 0, scores of ≥ 3 and ≥ 7 points were associated with 12-fold and 28-fold increases in the incidence rate, respectively. We believe that assessing IHS risk at admission will lead to early detection, which increases treatment options, including rt-PA and endovascular therapy^{26,27}. Therefore, informing medical personnel that patients with a score ≥ 3 have a high risk of developing IHS could hasten detection and treatment.

This study had some limitations. First, the results may not be generalizable to all populations or settings because this was a single-center, retrospective study. Second, the absence of blood test data may have affected the results. Third, we excluded patients hospitalized in the neurology and neurosurgery departments because it was difficult to identify whether inpatients developed recurrent IHS. This might have affected the incidence rate. Fourth, although the incidence rate for IHS is low, it results in severe symptoms and is associated with a poor prognosis. Medical professionals should therefore be made aware of the risk factors, so that early detection and treatment can be initiated. We believe that developing a scoring system to stratify risk could be useful. However, the present HEA³D score was validated using the same data, so a validation study is needed. Fifth, the hospital is a university hospital with approximately 800 beds, including a 60-bed advanced emergency center and a 20-bed surgical intensive care unit. The cardiac surgery department at the hospital performs approximately 300-400 of cardiac operations each year. The risk factors for IHS might differ in relation to hospital size. Sixth, events

after admission, such as catheter examination and sudden changes in vital signs, could increase the risk of IHS but were not assessed in this study. Finally, the incidence rate for IHS depends on illness severity, so further multicenter studies are required.

In conclusion, the incidence rate of IHS was 0.12% among 83,990 hospitalized patients. The independent risk factors for IHS were old age, hypertension, diabetes mellitus, atrial fibrillation, emergency admission, and low serum albumin. Moreover, the HEA³D score is a valuable assessment method for alerting medical personnel to the early detection of IHS. However, further prospective multicenter trials are required to investigate the IHS risk comprehensively.

Data Availability: Data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Seira Sakurai: Investigation, Writing - Original Draft, Writing - Review & Editing, Visualization. Kentaro Suzuki: Project administration, Conceptualization, Supervision. Takuya Nishino: Resources, Software, Formal analysis. Daisuke Hayashi: Resources. Tomonari Saito: Investigation. Yuki Sakamoto: Investigation. Junya Aoki: Investigation. Yasuhiro Nishiyama: Investigation. Kazumi Kimura: Conceptualization, Methodology, Supervision, Project administration.

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Conflict of Interest: Dr. Kimura received personal fees from Daiichi Sankyo Co. and personal fees from Bayer Healthcare Co Ltd. All other authors declare no conflicts of interest.

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