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In-hospital mortality of atrial fibrillation-associated acute ischemic stroke in the intensive care unit

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ORIGINAL ARTICLE

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Background: Although atrial fibrillation (AF)-associated acute ischemic stroke (AIS) is on the rise, is devastating, and life-threatening, there is limited data on the clinical course and in-hospital mortality of patients treated in the intensive care unit (ICU). This study aimed to describe the clinical course and factors associated with in-hospital mortality in AF-associated AIS patients admitted to the ICU.

Methods: This study was a retrospective analysis of a prospective nationwide multicenter cohort including non-valvular AF-AIS patients receiving ICU care admitted to 14 stroke centers in South Korea from 2017 to 2020. In-hospital outcomes, including in-hospital mortality and neurological deterioration (ND) have been described.

Results: Amongst 2,487 AF-associated AIS patients, 259 (10.4%) were treated in the ICU. In-hospital mortality and ND occurred in 8.5% and 17.0% of the patients, respectively. Higher rates of initial National Institute for Health Stroke Scale scores, symptomatic steno-occlusive lesions, and CHA_2DS_2-VASc (Congestive Heart Failure, Hypertension, Age ≥75 [Doubled], Diabetes Mellitus, Prior Stroke or Transient Ischemic Attack [Doubled], Vascular Disease, Age 65–74, Female) scores were found in those with in-hospital mortality. The CHA_2DS_2-VASc score after admission increased the risk of in-hospital mortality (odds ratio [OR], 1.48; 95% confidence interval [CI], 1.00–2.18) were associated with in-hospital mortality. Antithrombotic use within 48 hours was related to decreased in-hospital mortality (OR, 0.26; 95% CI, 0.10–0.67).

Conclusion: ICU care in AF-associated AIS is common, and the establishment of optimal treatment strategies in the ICU may be needed.

Keywords: Stroke; Atrial fibrillation; Cerebral infarction; Critical care; Intensive care units

INTRODUCTION

Atrial fibrillation (AF) is a major risk factor for ischemic stroke, contributing to an incremental risk of more than five times [1]. Furthermore, AF was associated with more severe symptoms and a greater than 30-day mortality risk among acute ischemic stroke (AIS) patients as per the Framingham sub-study [2]. As AF prevalence increases with age from 0.1% in those aged < 55 years to 9.0% in those aged 80 years or older [3], the number of AF-related embolic events is estimated to triple by 2050 with an increasing average life span [4]. Therefore, discussions on treatment strategies for this devastating, life-threatening, and increasing AF-associated AIS is essential to improve patient care [5].

Proper management in the intensive care unit (ICU) is known to improve outcomes in neurological diseases [6]. For AIS, ICU care is focused on post-reperfusion management, cerebral edema/increased intracranial pressure (IICP) treatment, determination of surgical options, prevention of stroke progression and recurrence, and airway/respiratory support [7,8]. If AF-AIS patients have greater infarct size, infarct growth, and hemorrhagic transformation rates [9], dedicated ICU care for the indicated AF-AIS patients is essential, and the role of ICU care should especially be highlighted in them. However, data regarding AF-AIS patients treated in the ICU are scarce.

Understanding individual profiles and clinical courses may be required to establish optimal treatment strategies to enhance outcomes in AF-AIS patients in the ICU. In this study, we aimed to describe baseline characteristics and stroke information in AF-associated AIS patients treated in the ICU, compared to those who did not; further, the clinical parameters associated with in-hospital mortality using clinical data from a prospective nationwide multicenter AF cohort study were investigated.

METHODS

Study subjects

Among AIS patients admitted to 14 stroke centers in Korea, the East Asian Ischemic Stroke Patients with Atrial Fibrillation Study (EAST-AF) Part II was used to provide risk stratification tools for assessing the risk of stroke recurrence by collecting clinical and neuroimaging characteristics potentially associated with clinical outcomes. The EAST-AF Part II prospectively enrolled patients with nonvalvular AF. These patients included those with priorly known AF and AF diagnosed after stroke upon routine electrocardiography, automatic electrocardiography monitoring or 24-hour Holter monitoring during their hospital stay. Clinical information and outcome data were derived from the Clinical Research Collaboration for Stroke in Korea (CRCS-K) registry [10].

A total of 15,353 patients admitted to the EAST-AF-Part II participating centers between October 26, 2017, and March 31, 2020, were screened. Amongst 2,690 non-valvular AF patients who provided informed consent, we included 2,489 patients who completed clinical and neuroimaging data from the prospective registry in this study (Fig. 1). After excluding two patients with essential clinical information, 2,487 patients were included in the analysis. In total, 259 ICU patients were enrolled in the current study. ICU admission was determined by neurological (malignant middle cerebral artery infarction, stroke causing decreased consciousness, in need of treatment for increased intracranial cerebral pressure or monitoring, etc.), cardiopulmonary (cardiac arrest, heart failure, pneumonia, pulmonary embolism, acute respiratory distress syndrome requiring intubation and ventilator support), and other clinical conditions. Physicians determined the need for ICU care [6,11].

Data collection and outcome assessment

Clinical data were obtained from the CRCS-K database, including records of intensive care during hospital stay. Information on sex, age, vascular risk factors including hypertension, diabetes, dyslipidemia, smoking status, history of stroke and coronary heart disease, and heart failure was further collected. Data on prior antithrombotic and premorbid functional statuses were also collected. Stroke information such as systolic and diastolic blood pressure, initial glucose level, initial National Institute for Health Stroke Scale (NIHSS) score, symptomatic steno-occlusive lesion (> 50% stenosis or occlusion) [12], emergent revascularization therapy (intravenous thrombolysis and endovascular treatment [EVT]),

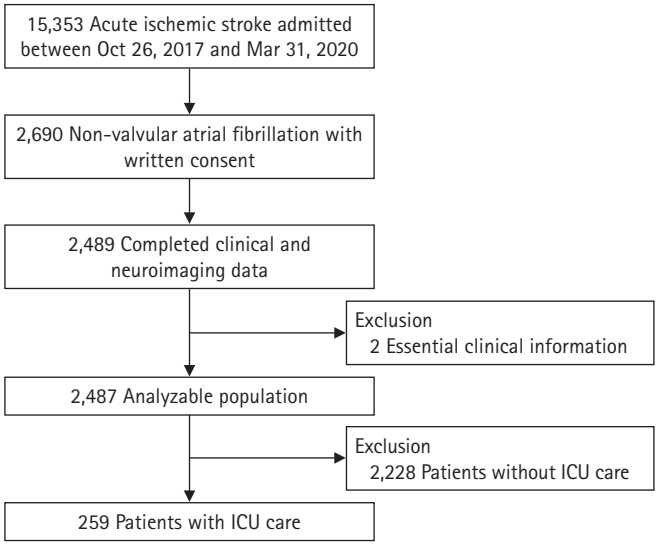

Fig. 1. Study population. ICU, intensive care unit.

and acute antithrombotic treatment including antiplatelet and anticoagulant therapy within 48 hours of admission were evaluated. Door-to-needle time was defined in 89 patients who underwent intravenous thrombolysis and an onset-to-arrival of < 24 hours. Door-to-puncture time was defined in 99 patients who underwent EVT and an onset-to-arrival of < 24 hours, and onset-to-reperfusion time was defined in 79 patients who underwent EVT, ≥ 2a thrombolysis in cerebral infarction, and an onset-to-arrival of < 24 hours.

The primary outcome was in-hospital mortality rate. Among the three discharge states, in-hospital mortality, transfer to other departments, and discharge, the occurrence of in-hospital mortality was analyzed. In-hospital mortality included patients with hopeless discharge. The occurrence of neurological deterioration (ND) was also assessed. ND was defined as any new neurological symptoms or signs worsening among patients with a total NIHSS score ≥ 2 or an increase in the NIHSS subscore of ≥ 1 for consciousness or motor function level, occurring during the hospital stay within 3 weeks of onset [13]. Stroke recurrence, stroke progression, symptomatic hemorrhagic transformation, and other causes including myocardial infarction, pulmonary embolism, deep vein thrombosis, or unknown etiologies constituted ND. Stroke recurrence was determined as having new discrete lesions on brain imaging. Stroke progression was defined as neurologic deterioration lasting more than 24 hours due to progressive ischemia, swelling, or perilesional edema of the infarcted area, distinguished from stroke recurrence with brain imaging, which is caused by new discrete lesions [14]. Amongst stroke progression, brain swelling/IICP was defined as ND caused by swelling of infarcted tissue or perilesional edema that was confirmed by a physician with brain imaging. Symptomatic hemorrhagic transformation was diagnosed as per European Cooperative Acute Stroke Study (ECASS) criteria, defined as any hemorrhage site found on brain imaging that caused a decrease in the NIHSS score of ≥ 4 [15,16]. The modified Rankin scale scores at discharge and number of admission days were also obtained. The change in NIHSS score from the initial NIHSS score to the discharge NIHSS score was calculated.

Statistical analysis

Baseline characteristics and stroke information of patients in the ICU were described as mean ± standard deviation or median (interquartile range [IQR]), as appropriate. The discharge status and proportion of ND were described. Patients who received ICU care were further distinguished based on the occurrence of in-hospital mortality. We compared the baseline characteristics and stroke information between patients with and without in-hospital mortality. Clinical parameters that differed between the two groups were determined using the chi-square test or Fisher's exact test for categorical variables and Student *t*-test or Mann Whitney *U*-test for continuous variables, as appropriate. Among variables of $P < 0.05$ in difference between the two groups, the relationship between in-hospital mortality and clinical parameters in difference was analyzed by binary logistic regression model. We established multivariable models as follows: (1) unadjusted model and (2) adjusted model with the initial NIHSS score. With substantial validated predictability, the initial NIHSS score was chosen as a variable for adjustment [17]. Due to the limited number of outcomes, the variables were adjusted with the initial NIHSS score. If the CHA_2DS_2-VASc (Congestive Heart Failure, Hypertension, Age ≥ 75 [Doubled], Diabetes Mellitus, Prior Stroke or Transient Ischemic Attack [Doubled], Vascular Disease, Age 65–74, Female) score was related to the outcome, variables that were components of the CHA_2DS_2-VASc score were not included in the multivariable model, considering potential multicollinearity. Multicollinearity between the initial NIHSS score and the variables was evaluated using the variance inflation factor, and no significant relationship was found. Odds ratios (ORs) and 95% confidence intervals (CIs) were also calculated. Data were analyzed using R 4.1.3, and a *P*-value of < 0.05 was considered statistically significant.

RESULTS

Demographics and stroke information were described for patients receiving ICU care (Table 1). The median age was 78 (IQR, 69–83) and the median CHA_2DS_2-VASc score was 5.5 ± 1.3. Antithrombotics prior to the index stroke were used in 43.2% of patients. The median NIHSS score was 14 (IQR, 8–19) and 53.7% of the patients underwent emergent revascularization therapy. Among the AF-associated AIS patients treated in the ICU, in-hospital mortality occurred in 22 patients (8.5%) (Table 2). Two-thirds of the patients were discharged. ND occurred in 17.0% of patients. Stroke progression occurred in 10.4% of the patients and was the most frequent subtype of ND, which included 5.8% of the patients whose ND was caused by brain swelling or increased intracranial cerebral pressure. Symptomatic hemorrhagic transformation was observed in 2.3% of patients. After admission, the median decrease in the NIHSS score was 3.

Comparing patients without in-hospital mortality among AF-associated stroke in the ICU, patients with in-hospital mortality were older, had higher CHA_2DS_2-VASc score, initial NIHSS score, proportion of symptomatic steno-occlusive lesions, and lower acute antithrombotic treatment within 48 hours (Table 3).

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Table 1. Baseline characteristics of atrial fibrillation-associated acute ischemic stroke patients with intensive care management

Variable	Value (n=259)
Sex	
Female	128 (49.4)
Male	131 (50.6)
Age (yr)	78 (69–83)
Onset to arrival	87.0 (43.5–290.5)
Vascular risk factor	
Hypertension	182 (70.3)
Diabetes	88 (34.0)
Dyslipidemia	72 (27.8)
Current smoking	36 (13.9)
History of stroke	56 (21.6)
History of coronary heart disease	42 (16.2)
Heart failure	35 (13.5)
CHA_2DS_2-VASc score	5.5±1.3
Prior antithrombotics	112 (43.2)
Premorbid mRS	0 (0–1)
Stroke information	
Systolic BP (mmHg)	151.3±27.9
Diastolic BP (mmHg)	87.7± 19.0
Initial glucose (mg/dL)	152.3±79.5
Initial NIHSS score	14 (8–19)
Symptomatic steno-occlusive lesion	168 (64.9)
Emergent revascularization therapy	139 (53.7)
Door to needle time (min)[a]	40.0 (27.0–53.0)
Door to punture time (min)[b]	107.0 (76.0–142.5)
Onset-to-reperfusion time (min)[c]	229.0 (187.5–295.0)
Antithrombotics within 48 hours	210 (81.1)

Values are presented as number (%), median (interquartile range), or mean±standard deviation.
mRS, modified Rankin scale; BP, blood pressure; NIHSS, National Institutes of Health Stroke Scale.
[a]Defined in 89 patients who underwent intravenous thrombolysis and an onset-to-arrival of <24 hours; [b]Defined in 99 patients who underwent endovascular treatment and an onset-to-arrival of <24 hours; [c]Defined in 79 patients who underwent endovascular treatment, with thrombolysis in cerebral infarction of ≥2a, and an onset-to-arrival of <24 hours.

Table 2. In-hospital outcomes of atrial fibrillation-associated acute ischemic stroke patients treated in the intensive care unit

Outcome	Study population (n=259)
Discharge state	
In-hospital mortality[a]	22 (8.5)
Transfer to other departments	59 (22.8)
Discharge	178 (68.7)
Early neurological deterioration	44 (17.0)
Stroke recurrence	6 (2.3)
Ischemic recurrence	5 (1.9)
Hemorrhagic recurrence	1 (0.4)
Stroke progression	27 (10.4)
Brain swelling/IICP	15 (5.8)
Symptomatic hemorrhagic transformation	6 (2.3)
Others	5 (1.9)
mRS at discharge	4 (2–5)
Admission day	15.4±19.0
Discharge NIHSS score	6 (2–16)
NIHSS score change	3 (0–9)

Values are presented as number (%), median (interquartile range), or mean±standard deviation.
IICP, increased intracranial pressure; mRS, modified Rankin scale; NIHSS, National Institute of Health Stroke Scale.
[a]In-hospital mortality includes hopeless discharge.

In the logistic regression model, the initial NIHSS score increased the odds of in-hospital mortality in the unadjusted model (OR, 1.11; 95% CI, 1.05–1.19) (Table 4). When adjusted for the initial NIHSS score, CHA_2DS_2-VASc score (OR, 1.48; 95% CI, 1.00–2.18]) increased the risk of in-hospital mortality, while symptomatic steno-occlusive disease (OR, 2.72; 95% CI, 0.76–9.68) did not. Antithrombotic use 48 hours after admission was associated with a low mortality risk (OR, 0.26; 95% CI, 0.10–0.67).

DISCUSSION

In this retrospective analysis of a multicenter prospective cohort of AF-associated AIS patients, approximately one-tenth of the patients were managed in the ICU. The CHA_2DS_2-VASc score was associated with increased in-hospital mortality, whereas antithrombotic treatment within 48 h was related to low in-hospital mortality. ND and stroke progression, including brain swelling, were frequently observed in these patients. A decrease in the NIHSS score from admission to discharge was observed.

Several studies on AIS patients receiving ICU care have reported variable hospital mortality and functional outcomes [11,18]. Compared with previous literatures (25%–40%), the in-hospital mortality rate was quite low (8.5%). This finding might be attributable to the variable indications of ICU admission according to hospital policy or physicians' decisions. An observational study of neurological and neurosurgical ICU in Korea reported similar in-hospital mortality (7.3% for ICU and 4.7% for neurosurgical ICU), comparable to the current study [6]. This study also suggests the potential benefit of ICU care with the improvement of NIHSS score of 3 points at discharge, and the rates of patients with an indication of neurological treatment. As neurological aspects of ICU care in AIS patients concentrate on post-reperfusion therapy and ND [7,8,19,20], this study reported that emergent revascularization therapy reported in 53.7% of ICU-treated patients could be a potential target population for the neurological

Table 3. Comparison of baseline characteristics and outcomes in atrial fibrillation-associated acute ischemic stroke patients treated in the intensive care unit according to in-hospital mortality

Variable	In-hospital mortality (+) (n=22)	In-hospital mortality (–) (n=237)	*P*-value
Sex			0.163[a]
Female	14 (63.6)	114 (48.1)	
Male	8 (36.4)	123 (51.9)	
Age (yr)	81 (76–86)	78 (68–83)	0.029[f]
Onset to arrival	101.0 (41.0–391.0)	87.0 (44.0–277.0)	0.810
Vascular risk factor			
Hypertension	13 (59.1)	169 (71.3)	0.230[a]
Diabetes	11 (50.0)	77 (32.5)	0.097[a]
Dyslipidemia	4 (18.2)	68 (28.7)	0.455[b]
Current smoking	3 (13.6)	33 (13.9)	1.000[b]
History of stroke	4 (18.2)	52 (21.9)	0.793[b]
History of coronary heart disease	6 (27.3)	36 (15.2)	0.141[a]
Heart failure	1 (4.5)	34 (14.3)	0.328[b]
CHA_2DS_2-VASc score	6.1±1.3	5.4±1.3	0.022
Prior antithrombotics	9 (47.4)	103 (42.9)	0.706[b]
Premorbid mRS	0 (0–2)	0 (0–1)	0.125
Stroke information			
Systolic BP (mmHg)	155.5±29.8	150.9±27.8	0.462
Diastolic BP (mmHg)	95.8±29.2	86.9±17.7	0.175
Initial glucose (mg/dL)	170.5±62.0	150.6±80.8	0.264
Initial NIHSS score	19 (14–24)	14 (7–18)	0.002[f]
Symptomatic steno-occlusive lesion	19 (86.4)	149 (62.9)	0.027[a,f]
Emergent revascularization therapy	10 (45.5)	129 (54.4)	0.419[a]
Door to needle time (min)[c]	37.0 (35.0–45.5)	40.5 (26.0–53.0)	0.790
Door to punture time (min)[d]	108.0 (92.0–160.0)	107.0 (75.0–142.0)	0.484
Onset to reperfusion time (min)[e]	367.0 (269.5–423.0)	226.0 (184.0–285.0)	0.164
Antithrombotics within 48 hours	11 (50.0)	199 (84.0)	<0.001[a,f]

Values are presented as number (%), median (interquartile range), or mean±standard deviation.
mRS, modified Rankin scale; BP, blood pressure; NIHSS, National Institutes of Health Stroke Scale.
[a]Chi-square test; [b]Fisher's exact test; [c]Defined in 89 patients who underwent intravenous thrombolysis and an onset-to-arrival of <24 hours; [d]Defined in 99 patients who underwent endovascular treatment and an onset-to-arrival of <24 hours; [e]Defined in 79 patients who underwent endovascular treatment, with thrombolysis in cerebral infarction of ≥2a, and an onset-to-arrival of <24 hours; [f]Indicates $P<0.05$.

Table 4. Odds ratio of variables for associating in-hospital mortality in atrial fibrillation-associated acute ischemic stroke patients treated in the intensive care unit

Variable	Model	OR of variables		OR of initial NIHSS score	
		OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
CHA_2DS_2-VASc score (per 1 point increment)	Unadjusted	1.52 (1.06–2.19)	0.024		
	Adjusted with NIHSS	1.48 (1.00–2.18)	0.049	1.11 (1.04–1.18)	0.002
Symptomatic steno-occlusive lesion	Unadjusted	3.74 (1.08–13.00)	0.038		
	Adjusted with NIHSS	2.72 (0.76–9.68)	0.123	1.11 (1.04–1.18)	0.003
Antithrombotics within 48 hours	Unadjusted	0.19 (0.08–0.47)	<0.001		
	Adjusted with NIHSS	0.26 (0.10–0.67)	0.005	1.10 (1.03–1.17)	0.007
Initial NIHSS score (per 1 point increment)	Unadjusted	1.11 (1.05–1.19)	<0.001		

OR, odds ratio; NIHSS, National Institute of Health Stroke Scale; CI, confidence interval.

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management in the ICU.

Several clinical parameters have been associated with in-hospital mortality in patients with ICU-treated AF-associated AIS. The CHA_2DS_2-VASc score is a well-established risk stratification tool for stroke and thromboembolism in AF [21]. CHA_2DS_2-VASc score has been reported as an independent value to predict long-term mortality in AF patients [22]. The current study suggests that the CHA_2DS_2-VASc score could be utilized for predicting the in-hospital mortality of ICU-treated AF-associated AIS patients, and a meticulous inspection of adverse events in patients with high scores might be needed to enhance in-hospital outcomes. Symptomatic steno-occlusive lesions showed a tendency to increase mortality risk without statistical significance in the current study. In the previous literature, symptomatic steno-occlusive lesions were associated with unfavorable functional outcomes in AIS patients [22]. In the era of EVT for AIS patients [23], treatment strategies for the failed recanalization cases might be developed in neurocritical care, which constituted 86% of the expired patients in the current study. Furthermore, although EVT was performed in the indicated patients, a treatment plan for obtained recanalization with a large infarct core is also needed, as AF is one of the risk factor for futile recanalization following EVT [24].

The lower risk of mortality in patients receiving acute antithrombotic treatment might be attributable to the preventive effect as well as selection bias. Acute antithrombotic therapy has been proven to reduce the risk of stroke recurrence and has been applied to AIS patients in current practice [25,26]. However, a discrepancy in stroke severity (median initial NIHSS score of 19 vs. 14 in patients who died and survived, respectively) infers a difference in neurologic and medical conditions between the two groups. Therefore, a cautious interpretation is needed for acute antithrombotic treatment in patients with ICU-treated AF-associated AIS. In the acute phase of AF-associated ischemic stroke, physicians often face a great dilemma in initiating anticoagulation and optimal timing of commencement due to the risk of hemorrhagic transformation [27]. As a larger infarction is a strong predictor of hemorrhagic transformation in AF-associated stroke [28], guidelines on starting anticoagulation therapy recognize a distinction in their recommendations according to stroke severity [29,30]. Ongoing trials on anticoagulation timing are expected to provide high-level of evidence with safety and efficacy profiles [31,32]. A thoughtful risk-benefit balance in initiating anticoagulation therapy based on individual clinical situations is required for severe AF-associated AIS patients.

This study has several strengths. To our knowledge, this is the largest prospective AF cohort study in Asia, consisting of 14 nationwide stroke centers. This cohort represents the current clinical status and real-life practice of AF stroke management in Korea. As we collected data from a nationwide multicenter prospective cohort, we also attempted to reduce bias in the enrollment of participants. This cohort had a high outcome capture rate (3-month capture rate, 99%), on which this study could provide relatively accurate outcome information.

However, this study has several limitations. First, as decisions of ICU admission vary according to the centers' policy in the indication, medical resources, and physicians' opinions, the variable effect of the center or physician might be present. Detailed information on the indication for ICU admission and the time from onset to ICU admission were not available. Second, some patients with irreversible neurological damage with very severe stroke or underlying incurable progressive diseases, including malignancy, could have rejected ICU care, but resulted in in-hospital mortality and might not have been included in this study. Third, specific echocardiographic findings, such as left atrium diameter or cardiac markers, including brain natriuretic peptide or cardiac enzymes, were not included in the analysis. Further studies involving specific cardiac markers are warranted in the future.

In conclusion, ICU care is common in patients with AF-associated ischemic stroke. Initial stroke severity and CHA_2DS_2-VASc score increased the risk of in-hospital mortality whereas antithrombotic treatment was associated with decreased risk. To improve patient outcomes in AF-associated AIS, establishing optimal treatment strategies with upcoming high-level evidence may be required.

ARTICLE INFORMATION

Ethics statement

The study was reviewed and approved by the Institutional Review Boards of the participating centers (No. B-1705/396-306). Written informed consent was obtained from all patients.

Conflict of interest

No potential conflict of interest relevant to this article.

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Additional contributions

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REFERENCES

1. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke 1991;22:983-8.
2. Lin HJ, Wolf PA, Kelly-Hayes M, Beiser AS, Kase CS, Benjamin EJ, et al. Stroke severity in atrial fibrillation: the Framingham Study. Stroke 1996;27:1760-4.
3. Go AS, Hylek EM, Phillips KA, Chang Y, Henault LE, Selby JV, et al. Prevalence of diagnosed atrial fibrillation in adults: national implications for rhythm management and stroke prevention: the AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study. JAMA 2001;285:2370-5.
4. Yiin GS, Howard DP, Paul NL, Li L, Luengo-Fernandez R, Bull LM, et al. Age-specific incidence, outcome, cost, and projected future burden of atrial fibrillation-related embolic vascular events: a population-based study. Circulation 2014;130:1236-44.
5. De Marchis GM, Sposato LA, Kühne M, Dittrich TD, Bonati LH, Fischer U, et al. New avenues for optimal treatment of atrial fibrillation and stroke prevention. Stroke 2021;52:1490-9.
6. Jeong JH, Bang J, Jeong W, Yum K, Chang J, Hong JH, et al. A dedicated neurological intensive care unit offers improved outcomes for patients with brain and spine injuries. J Intensive Care Med 2019;34:104-8.
7. Behrouz R. Critical care management of the acute ischemic stroke patient. Pract Neurol 2010;19-25.
8. Jeon SB, Koh Y, Choi HA, Lee K. Critical care for patients with massive ischemic stroke. J Stroke 2014;16:146-60.
9. Tu HT, Campbell BC, Christensen S, Desmond PM, De Silva DA, Parsons MW, et al. Worse stroke outcome in atrial fibrillation is explained by more severe hypoperfusion, infarct growth, and hemorrhagic transformation. Int J Stroke 2015;10:534-40.
10. Kim BJ, Park JM, Kang K, Lee SJ, Ko Y, Kim JG, et al. Case characteristics, hyperacute treatment, and outcome information from the clinical research center for stroke-fifth division registry in South Korea. J Stroke 2015;17:38-53.
11. Alonso A, Ebert AD, Kern R, Rapp S, Hennerici MG, Fatar M. Outcome predictors of acute stroke patients in need of intensive care treatment. Cerebrovasc Dis 2015;40:10-7.
12. Kang J, Park TH, Lee KB, Park JM, Ko Y, Lee SJ, et al. Symp-

https://doi.org/10.18700/jnc.220063

tomatic steno-occlusion in patients with acute cerebral infarction: prevalence, distribution, and functional outcome. J Stroke 2014;16:36-43.
13. Jeong HG, Kim BJ, Yang MH, Han MK, Bae HJ. Neuroimaging markers for early neurologic deterioration in single small subcortical infarction. Stroke 2015;46:687-91.
14. Park TH, Lee JK, Park MS, Park SS, Hong KS, Ryu WS, et al. Neurologic deterioration in patients with acute ischemic stroke or transient ischemic attack. Neurology 2020;95:e2178-91.
15. Choi JC, Lee JS, Park TH, Cho YJ, Park JM, Kang K, et al. Pre-stroke antiplatelet effect on symptomatic intracranial hemorrhage and functional outcome in intravenous thrombolysis. J Stroke 2016;18:344-51.
16. Hacke W, Kaste M, Fieschi C, von Kummer R, Davalos A, Meier D, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian Acute Stroke Study Investigators. Lancet 1998;352:1245-51.
17. Smith EE, Shobha N, Dai D, Olson DM, Reeves MJ, Saver JL, et al. Risk score for in-hospital ischemic stroke mortality derived and validated within the Get With the Guidelines-Stroke Program. Circulation 2010;122:1496-504.
18. Pilato F, Silva S, Valente I, Distefano M, Broccolini A, Brunetti V, et al. Predicting factors of functional outcome in patients with acute ischemic stroke admitted to neuro-intensive care unit: a prospective cohort study. Brain Sci 2020;10:911.
19. Lee SH, Park KJ, Park DH, Kang SH, Jung YG, Park JY. Early in-hospital management of acute ischemic stroke. J Neurointensive Care 2019;2:8-13.
20. Sharma D, Smith M. The intensive care management of acute ischaemic stroke. Curr Opin Crit Care 2022;28:157-65.
21. Lip GY, Nieuwlaat R, Pisters R, Lane DA, Crijns HJ. Refining clinical risk stratification for predicting stroke and thromboembolism in atrial fibrillation using a novel risk factor-based approach: the euro heart survey on atrial fibrillation. Chest 2010;137:263-72.
22. Gažo vá A, Leddy JJ, Rexová M, Hlivák P, Hatala R, Kyselovič J. Predictive value of CHA2DS2-VASc scores regarding the risk of stroke and all-cause mortality in patients with atrial fibrillation (CONSORT compliant). Medicine (Baltimore) 2019;98:e16560.
23. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association. Stroke 2021;52:e364-467.
24. Shahid AH, Abbasi M, Larco JL, Madhani SI, Liu Y, Brinjikji W, et al. Risk factors of futile recanalization following endovascular treatment in patients with large-vessel occlusion: systematic review and meta-analysis. Stroke Vasc Interv Neurol 2022;2:e000257.
25. International Stroke Trial Collaborative Group. The International Stroke Trial (IST): a randomised trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. Lancet 1997;349:1569-81.
26. Wang Y, Wang Y, Zhao X, Liu L, Wang D, Wang C, et al. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med 2013;369:11-9.
27. Seiffge DJ, Werring DJ, Paciaroni M, Dawson J, Warach S, Milling TJ, et al. Timing of anticoagulation after recent ischaemic stroke in patients with atrial fibrillation. Lancet Neurol 2019;18:117-26.
28. Lee JH, Park KY, Shin JH, Cha JK, Kim HY, Kwon JH, et al. Symptomatic hemorrhagic transformation and its predictors in acute ischemic stroke with atrial fibrillation. Eur Neurol 2010;64:193-200.
29. Clarke DJ, Burton LJ, Tyson SF, Rodgers H, Drummond A, Palmer R, et al. Why do stroke survivors not receive recommended amounts of active therapy? Findings from the ReAcT study, a mixed-methods case-study evaluation in eight stroke units. Clin Rehabil 2018;32:1119-32.
30. Heidbuchel H, Verhamme P, Alings M, Antz M, Hacke W, Oldgren J, et al. EHRA practical guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation: executive summary. Eur Heart J 2013;34:2094-106.
31. Åsberg S, Hijazi Z, Norrving B, Terént A, Öhagen P, Oldgren J. Timing of oral anticoagulant therapy in acute ischemic stroke with atrial fibrillation: study protocol for a registry-based randomised controlled trial. Trials 2017;18:581.
32. Best JG, Arram L, Ahmed N, Balogun M, Bennett K, Bordea E, et al. Optimal timing of anticoagulation after acute ischemic stroke with atrial fibrillation (OPTIMAS): protocol for a randomized controlled trial. Int J Stroke 2022;17:583-9.