Risk Factors for Acute Heart Failure and Impact on In-Hospital Mortality after Stroke

Shogo Shima, MD,* Masaki Shinoda, MD, PhD,† Osamu Takahashi, MD, PhD,‡ Akihiko Unaki, MD, PhD,§ Tetsuya Kimura, MD, PhD,§ Yoshikazu Okada, MD, PhD,* and Yasunari Niimi, MD, PhD ‖

Background: In the acute phase of stroke, some patients develop cardiac events. It could be fatal in their clinical courses. We aimed to investigate acute heart failure after stroke onset and stratify the patients by establishing a predictive model. *Methods*: This single-center, observational study included stroke patients diagnosed at the Department of Neurology and Neurosurgery from January 2013 to December 2014. Baseline characteristics and clinical findings on admission were analyzed for acute heart failure after stroke. We assessed risk factors using multivariable logistic regression, and set a risk score to evaluate the association with poor outcomes. *Results*: Of 532 stroke patients, 27 (5%) developed acute heart failure within the 7 days after admission. We identified 4 risk factors for acute heart failure after stroke: atrial fibrillation (odds ratio [OR], 5.9; 95% confidence interval [CI], 2.5-14.0; $P < .001$), history of cardiac disease (OR, 3.6; 95% CI, 1.3-9.1; $P = .01$), Glasgow Coma Scale score ≤ 8 (OR, 4.5; 95% CI, 1.7-12.0; $P = .003$), and serum albumin < 35 g/L (OR, 3.4; 95% CI, 1.4-8.4; $P = .008$). Furthermore in-hospital mortality rate was higher (37% [n = 10/27] versus 9.9% [n = 50/505], $P = .001$) in patients with poststroke heart failure. Higher predictive scores were associated with increased mortality. *Conclusions*: Acute heart failure can develop in the early phase of stroke and lead to poor outcomes. It is foreseeable and preventable by stratifying and monitoring high-risk patients.

Key Words: Stroke—heart failure—risk factors—outcome

Introduction

Some stroke patients develop cardiovascular events such as heart failure (HF), myocardial infarction, and arrhythmias.[1-4] Patients with stroke have a risk of heart disorders because of those mutual underlying conditions, eg, systemic arteriosclerosis, diabetes mellitus, and hypertension. In addition, neurohormonal changes and increased sympathetic nervous activity caused by the acute stress response after stroke are thought to affect the onset of cardiac events.[5-7] Takotsubo cardiomyopathy is the 1 example.[8] The sequence of events in stroke can be life-threatening. About 2%-6% of patients die from cardiac causes in the early stage of ischemic stroke.[1,9] Therefore, it is desirable to identify the triggers of stroke-related cardiac events to predict the occurrence in high-risk patients, and to prevent their development with pretreatment and intervention.

From the *Department of Neurosurgery, St. Luke's International Hospital, Tokyo, Japan; †Department of Neurosurgery, Kyosai Tachikawa Hospital, Tokyo, Japan; ‡Division of General Internal Medicine, Department of Medicine, St. Luke's International Hospital, Tokyo, Japan; §Department of Neurology, St. Luke's International Hospital, Tokyo, Japan; and ‖Department of Neuroendovascular Therapy, St. Luke's International Hospital, Tokyo, Japan.

Received October 1, 2018; revision received February 12, 2019; accepted February 23, 2019.

Competing interests and funding: The authors declare no conflicts of interest.

Author contributions: S.S. extracted and analyzed the data, interpreted the results, and wrote the manuscript. M.S. guided the study design. O.T. contributed the data analysis and the interpretation of the results. A.U. and T.K. contributed the data collection and reviewed the paper. Y.O. and Y.N. reviewed and made some revisions of the paper.

Address correspondence to Shogo Shima, MD, Tokyo, Japan. E-mail address: shisho@luke.ac.jp.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.02.030

Although some studies have shown the risk of cardiac adverse events after stroke, the timing of the onset of the events are not set and consistent. Literatures reporting HF caused in the acute stage of stroke are limited. The aim of this study is to focus on the development of acute heart failure (AHF) in the early phase of stroke, especially within 7 days after stroke onset and investigate its risk factors and the association with outcomes by using the findings on admission. We also attempted to stratify the risk of poststroke HF by establishing a predictive model and a simple scoring system.

Methods

Study Design and Patient Population

This study is a single-center, retrospective study that enrolled patients diagnosed with ischemic stroke, intracerebral hemorrhage at the Department of Neurology and Neurosurgery in our hospital from January 2013 to December 2014. The eligible patients were over 20 years of age. Computed tomography and/or magnetic resonance image findings were interpreted by 2 radiologists, then clinical diagnoses were made by trained neurologists or neurosurgeons. Transient ischemic attack, traumatic intracranial bleeding, and hemorrhage caused by tumor were excluded. Patients who had been transferred to other hospitals before assessment and sustained cardiopulmonary arrest or received do-not-treat/do-not-resuscitate orders on arrival were also excluded.

We divided these subjects into 2 cohorts based on the presence or absence of AHF and retrospectively reviewed their clinical characteristics. The St. Luke's International Hospital Research Ethics Committee (Tokyo, Japan) approved the study protocol.

Definition of Poststroke Acute Heart Failure

Patients with AHF have the typical symptoms, eg breathlessness at rest or during exertion, peripheral edema, distention of the jugular veins, and pulmonary rales. They are confirmed by the objective evidence of cardiac dysfunction such as hypoxemia, tachycardia, oliguria, cardiomegaly, and pulmonary edema in chest X-ray.[10,11] Diagnosis of HF was made by such symptoms and physical examination findings based on the Framingham Diagnostic criteria (the diagnosis requires the concurrent presence of either 2 major, or 1 major and 2 minor criteria as provided in the supplementary file).[12] Patients who met the criteria and received an intervention such as use of some diuretics, cardiac monitoring, or admission to the cardiac care unit were considered to be in a state of HF. We solely targeted HF within 7 days after stroke onset.

Demographic and Clinical Characteristics

Demographic information collected from medical records included age, sex, body mass index (BMI), and past medical history including hypertension, hyperlipidemia, diabetes mellitus, atrial fibrillation, and cardiac disease (coronary artery disease, cardiomyopathy, chronic HF, and valvular heart disease). The severity of the patients with cardiac disease was graded by New York Heart Association functional classification (severity assessment scale of HF classifying patients in 1 of 4 categories as provided in the supplementary file. Class I indicates no symptoms, Class II indicates mild symptom, Class III indicates marked symptom, and Class IV indicates severe symptoms.).[10] Among 50 patients with cardiac disease, 43 patients were classified as Class I, 4 patients were classified as II, 2 patients were classified as III, and 1 patient was classified as IV.

Baseline clinical data retrieved from admission records included types of stroke (ischemic or hemorrhagic stroke), etiology of ischemic stroke, presence or absence of the treatment with tissue plasminogen activator (t-PA) and/or endovascular thrombectomy, locations of intracerebral hemorrhage, blood pressure, heart rate, and Glasgow Coma Scale (GCS; scoring system to describe the level of consciousness from 3 to 15, with 3-8 points suggesting severe brain injury, 9-12 suggesting moderate brain injury, and 13-15 suggesting mild brain injury) score on arrival.[13,14] We dichotomized the GCS score at 8 to evaluate the influence of a severe consciousness disturbance. Initial laboratory parameters included serum albumin, white blood cell count, C-reactive protein (CRP), aspartate transaminase, alanine transaminase, blood urea nitrogen, estimated glomerular filtration rate, activated partial thromboplastin time, and prothrombin time-international normalized ratio (PT-INR). In adults, the normal reference range of human serum albumin is commonly reported to be 3.5-5 g/L.[15,16] Therefore, serum albumin was dichotomized at 35 g/L to define and evaluate hypoalbuminemia.

Outcome Measures

Outcome was assessed using length of hospital stay and all-cause mortality during hospital stay. Short-term mortality was examined because we focused on acute effects induced by stroke.

Statistical Analysis

Statistical analysis was performed with SPSS (version 22.0; IBM, Armonk, New York). Variables were expressed as mean ± standard deviation, median (interquartile range: 25th-75th percentile), or number of patients (%), as appropriate. Pearson's χ^2 test or Fisher's exact test were used for differences in proportions of categorical variables. We evaluated the normality of data with the Shapiro-Wilk test, and homogeneity of variance with the Leven test, then used Student's t test for independent continuous variables and the Mann-Whitney U test for non-normally distributed variables. To investigate a simple predictive model for the onset of AHF after stroke, we selected not a proportional hazards model but a logistic regression model for multivariable analysis. Parameters with $P < .05$ in the univariate analysis were incorporated into the multivariable analysis using a stepwise forward method. The odds ratio (OR) and 95% confidence interval were calculated for each variable. We evaluated the goodness-of-fit of the predictive model by assessing calibration with the Hosmer-Lemeshow test and discrimination with the area under the receiver operating characteristic curve. Differences were considered statistically significant at $P < .05$ and P values were two-sided.

Results

Prevalence of Acute Heart Failure and Patient Characteristics

Of 551 patients with stroke, 532 were identified for inclusion in this study. Five patients were excluded based on the cardiopulmonary arrest or do-not-resuscitate orders on arrival, and 14 were excluded because of hospital transfer. AHF was diagnosed in 27 (5%) patients (Fig 1), primarily in the first 3 days after admission (Fig 2). Table 1 shows baseline demographic data and previous history. Among all patients, 321 (60.3%) were men, and the mean age was 70 years ± 14 years. Baseline characteristics were similar between the 2 groups except that patients with AHF had a higher prevalence of atrial fibrillation and history of cardiac disease (56% [n = 15/27] versus 14.5% [n = 73/505]; $P < .001$ and 33.3% [n = 9/27] versus 8.1% [n = 27/505]; $P < .001$, respectively). The severity of the symptoms in the patients with cardiac disease did not affect the onset of poststroke HF, comparing the incidence rate of HF between patients in New York Heart Association Class I and Class II or more (16.3% [n = 7/43] versus 28.6% [n = 2/7]; $P = .595$).

Clinical parameters in patients with and without AHF are also shown in Table 1. Although there was a significant difference in ischemic stroke due to cardiac embolism ($P < .001$), it would be influenced by the correlation with atrial fibrillation. The number of patients with severe consciousness disturbance (GCS ≤ 8) was significantly larger in the AHF group than in the non-AHF group (30% [n = 8/27] versus 13.7% [n = 69/505]; $P = .042$). On arrival, the heart rate was faster in patients with AHF (median 96, interquartile range 73-108 versus 79, 69-93; $P = .015$). Baseline laboratory data on admission documented an association between AHF and serum albumin <35 g/L ($P = .001$), CRP ($P < .001$), and PT-INR ($P = .016$).

Risk Factors for Acute Heart Failure

Based on the results of univariate analysis, we chose 7 variables, including atrial fibrillation, history of cardiac disease, GCS score ≤ 8, heart rate, serum albumin < 35 g/L, CRP, and PT-INR, as candidates for models of multivariable analysis. The variable of Cardiac embolism was eliminated, because it could interact with the variable of atrial fibrillation in terms of the multicollinearity. Logistic regression analysis with stepwise forward method demonstrated that atrial fibrillation (OR, 5.9; 95% CI, 2.5-14.0; $P < .001$), history of cardiac disease (OR, 3.6; 95% CI, 1.3-9.6; $P = .01$), GCS score ≤ 8 (OR, 4.5; 95% CI, 1.7-12.0; $P = .003$), and serum albumin < 35 g/L (OR, 3.4; 95% CI, 1.4-8.4; $P = .008$) were independent predictive risk factors for AHF after stroke (Table 2). This predictive model

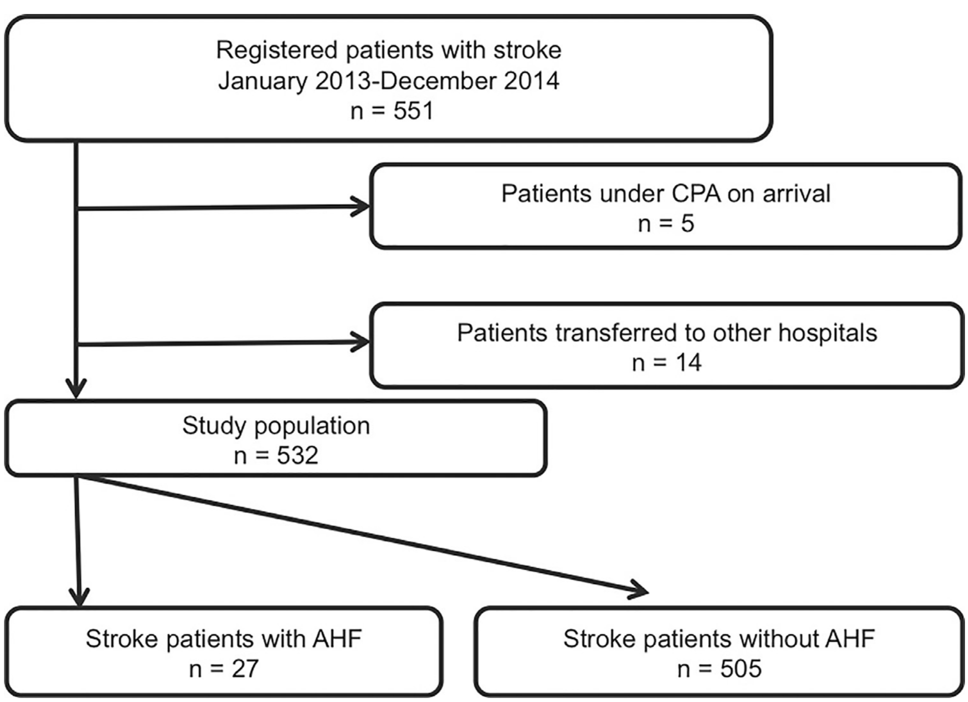

Figure 1. *Flow chart of patient allocation. Abbreviations: AHF: acute heart failure; CPA: cardiopulmonary arrest.*

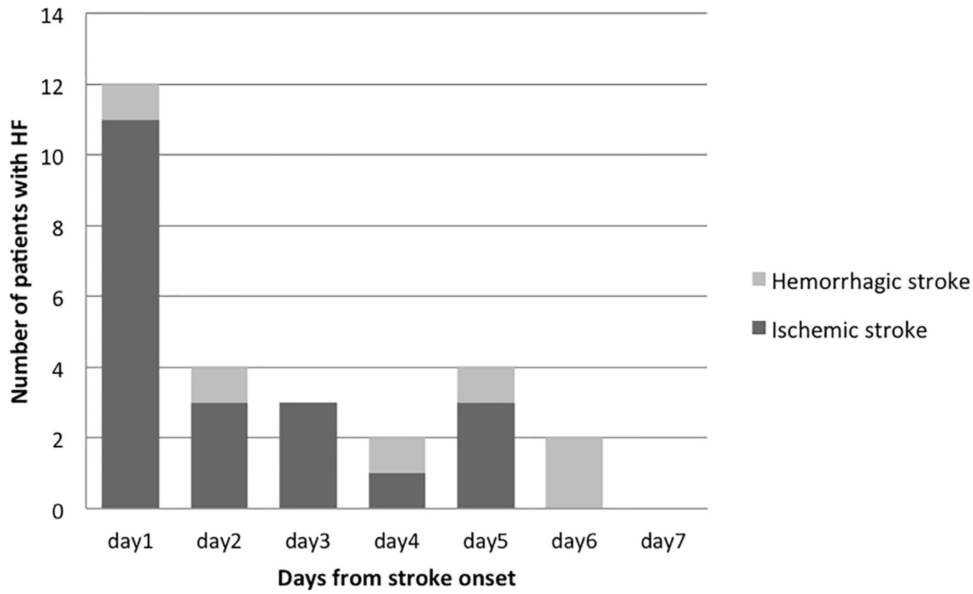

Figure 2. *Development of acute heart failure according to days after stroke onset.*

adequately fit the original data with the Hosmer-Lemeshow test ($P = .80$). We then assigned each item a value of 1 or 2 based on standardized coefficients (Atrial fibrillation = 2, the others = 1) and gave each patient a score ranging from 0 to 5 according to the combination of risk factors. As seen in Table 3, the proportion with AHF increases from 1.3% (n = 4/314) up to 57.1% (n = 4/7) with an increase in the risk score. The receiver operating characteristic curve derived from the risk score is shown in Figure 3. The area under the curve for prediction of AHF after stroke derived from the risk score was .806 (95% CI, .713-.899), indicating good accuracy. A cutoff of 1 predicts poststroke AHF with a sensitivity of 85.2 % and specificity of 38.6%.

Outcomes

The length of hospital stay for patients with AHF was significantly longer than for patients without AHF (median 25 days, interquartile range 12-37 versus 16, 8-29; $P = .029$). The evaluation of all-cause in-hospital mortality revealed that 37% (n = 10/27) of patients with AHF versus 9.9% (n = 50/505) of patients without AHF had died, resulting in an approximately five-fold increase in the OR (OR, 5.4; 95% CI, 2.3-12.3; $P < .001$). The in-hospital mortality rate ranged from 1.3% up to 42.9% in response to an increase in the risk score derived from the predictors and there was a remarkable increase in mortality rate from 1.3% to 33.9% with an increase in risk score from 0 to 1 (Table 3).

Discussion

Some studies examining the HF after stroke have not set the timing of the onset of HF, so it could occur because of the other mechanisms except the impact of stroke. This is the first study analyzing predictive factors for HF in the early stage of stroke, especially within 7 days after onset. As the previous studies have shown, we reaffirmed atrial fibrillation and history of cardiac disease as the risk factors of poststroke HF.[3,9] In addition, we newly identified another 2 predictive factors: severe consciousness disturbance on arrival, and hypoalbuminemia. With this predictive model, we can simply forecast poststroke HF from the patient state on admission without some detailed and time-consuming cardiac examinations.

It is obvious that past medical history of cardiac disease and preexisting atrial fibrillation predispose to AHF, based on established evidence.[10,17,18] These 2 clinical states induce cardiac fragility and contribute to lower tolerance for specific stress reactions such as a catecholamine surge and increase in neuroendocrine hormones that are seen in stroke patients. Such physiological changes can cause myocardial injury within a few days after stroke onset.[19] Brain natriuretic peptide (BNP) is a vasoactive peptide hormone with natriuretic, diuretic, and vasodilator activity, and is a biomarker of HF. It is secreted from both cerebral and cardiac sources in the acute phase of stroke.[7,20] Elevated concentrations of BNP in response to severe stroke can directly stimulate autonomic cardiovascular control and cause hemodynamic derangement.[21] Moreover, the association between poor improvement in the GCS score and elevation of BNP in stroke patients has also been reported.[22] We assume that the relationship between low GCS score on admission and poststroke HF in our study is explained by the high concentration of BNP, as a reflection of severe brain injury. Our research also indicates that hypoalbuminemia contributes to the onset of HF. Serum albumin maintains the circulatory system through multiple mechanisms including a colloid oncotic effect, antioxidant and anti-inflammatory properties, and binding capacity for endogenous proteins.[15,23] Hence, hypoalbuminemia could cause myocardial edema

Table 1. *Baseline demographic and clinical characteristics of stroke patients*

Variables	Total (n =532)	AHF (n = 27)	non-AHF (n = 505)	*P* value
Demographic variables				
Age*, y	70 ± 14	74 ± 14	69 ± 14	.077
Male sex†	321 (60.3)	14 (51.9)	307 (60.8)	.420
BMI‡, kg/m^2	23.0 (20.2-25.5)	23.4 (18.4-27.5)	23.0 (20.2-25.5)	.491
Past medical history				
Hypertension†	275 (51.7)	11 (40.8)	264 (52.3)	.323
Hyperlipidemia†	133 (25.0)	4 (14.8)	129 (25.5)	.259
Diabetes mellitus†	121 (22.7)	8 (30)	113 (22.3)	.479
Atrial fibrillation†	88 (16.5)	15 (56)	73 (14.5)	<.001
History of cardiac disease†	50 (9.4)	9 (33.3)	41 (8.1)	<.001
Type and etiology of stroke				
Ischemic stroke†	338 (63.5)	21 (77.8)	317 (62.8)	.151
Large-artery atherosclerosis	127 (23.9)	3 (11.1)	124 (24.6)	.162
Cardiac embolism	96 (18.0)	17 (63.0)	79 (15.6)	<.001
Lacunar infarctions	88 (16.6)	1 (3.7)	87 (17.2)	.066
Unknown or other etiology	27 (5.1)	0 (0)	27 (5.3)	.387
t-PA and/or mehanical thrombectomy	12 (2.2)	1 (3.7)	11 (2.2)	.468
Hemorrhagic stroke†	194 (36.5)	6 (22.2)	188 (37.2)	.151
Subcortical area	36 (6.8)	0 (0)	36 (7.1)	.244
Putamen	75 (14.1)	2 (7.4)	73 (14.5)	.405
Thalamus	47 (8.8)	1 (3.7)	46 (9.1)	.498
Caudate	5 (.9)	0 (0)	5 (.01)	1.0
Cerebral ventricule	1 (.2)	0 (0)	1 (.01)	1.0
Brain stem	20 (3.8)	3 (11.1)	17 (3.3)	.075
Cerebellum	10 (1.9)	0 (0)	10 (.02)	1.0
Admission status				
GCS score ≤ 8†	77 (14.5)	8 (30)	69 (13.7)	.042
Systolic BP‡, mmHg	163 (143-187)	150 (132-189)	163 (143-187)	.406
Diastolic BP‡, mmHg	90 (76-106)	90 (68-101)	90 (76-107)	.317
Heart rate‡, bpm	79 (69-94)	96 (73-108)	79 (69-93)	.015
Laboratory data on admission				
Serum albumin < 35 g/L†	72 (13.6)	10 (37.0)	62 (12.2)	.001
White blood cell‡, 10^3/μL	7.1 (5.5-9.4)	7.6 (5.6-9.5)	7.1 (5.5-9.4)	.373
C-reactive protein‡, mg/L	1.0 (.4-4.1)	4.9 (1.1-27)	.9 (.4-3.4)	<.001
AST‡, U/L	23 (19-30)	24.0 (18-36)	23 (19-30)	.746
ALT‡, U/L	18 (14-27)	16 (13-24)	18 (14-27)	.572
BUN‡, mmol/L	5.66 (4.51-7.35)	7.21 (4.71-8.60)	5.64 (4.48-7.21)	.106
eGFR‡, mL/min/1.73 m^2	73.0 (57.1-91.3)	63.2 (51.0-91.3)	73.8 (58.4-91.3)	.203
APTT‡, s	27.0 (24.9-29.4)	27.2 (24.6-32.7)	26.9 (24.9-29.2)	.332
PT-INR‡	.91 (.86-.97)	.97 (.88-1.08)	.91 (.86-.96)	.016
In-hospital measures				
Length of stay‡, d	17 (8-29)	25 (12-37)	16 (8-29)	.029
All-cause death†	60 (11.3)	10 (37)	50 (9.9)	.001

Abbreviations: AHF, acute heart failure; ALT, alanine transaminase; aPTT, activated partial thromboplastin time; AST, aspartate transaminase; BMI, body mass index; BP, blood pressure; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; GCS, Glasgow Coma Scale; PT-INR, prothrombin time-international normalized ratio; t-PA, tissue plasminogen activator.

*Mean ± SD.

†n (%).

‡Median (interquartile range; 25th-75th percentile).

and aggravate oxidative stress after stroke, resulting in cardiac dysfunction.

The incidence rate of HF was lower than that of cardiac adverse events in previous studies (5% versus 17%-19%).[3,9] This is presumably because we restricted the date of occurrence of AHF to within the first 7 days. On the other hand, as in previous studies suggesting that serious cardiac events occur on days 2 and 3 after stroke,[9,24] most cases of AHF were observed in the first 3 days after admission in our study. It is plausible to infer that this period coincides with the peak of catecholamine release and neuroendocrine activation.

Table 2. *Predictive factors for poststroke heart failure*

Variables	Multivariable analysis		
	β coefficient	OR (95% CI)	*P* value
Atrial fibrillation	1.8	5.9 (2.5-14.0)	<.001
History of cardiac disease	1.3	3.6 (1.3-9.6)	.01
GCS score ≤ 8	1.5	4.5 (1.7-12.0)	.003
Serum albumin < 35 g/L	1.2	3.4 (1.4-8.4)	.008

Abbreviations: GCS, Glasgow Coma Scale; OR, odds ratio; CI, confidence interval.

Table 3. *Poststroke heart failure and in-hospital death according to risk score*

Risk score	Patients (n = 505)	Poststroke HF (n = 27)	In-hospital death (n = 60)
0	314	4 (1.3%)	4 (1.3%)
1	112	6 (5.3%)	38 (33.9%)
2	63	4 (6.3%)	10 (15.9%)
3	36	9 (25%)	5 (13.8%)
4 or 5	7	4 (57%)	3 (42.9%)

Abbreviation: HF, heart failure.

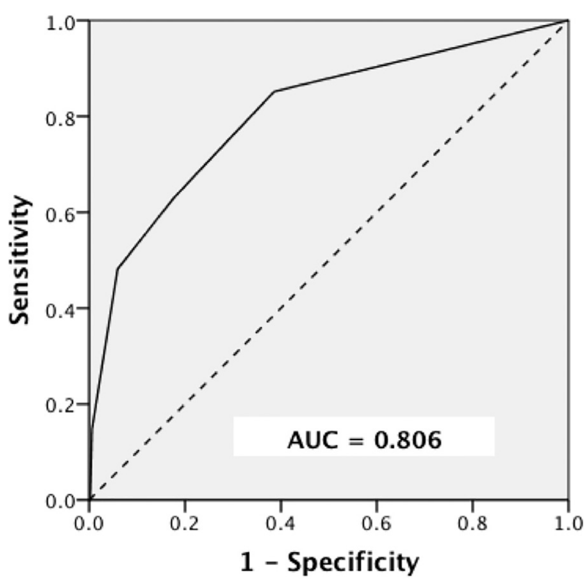

Figure 3. *Receiver operating curve for prediction of poststroke heart failure based on risk scores. Area under the curve is .806 (95% confidence interval, .713-.899).*

We also identified the association of HF with poor outcome in stroke patients. In-hospital mortality in patients with poststroke HF was high. To prevent poor outcomes, screening of high-risk patients is required. The risk score of the predictive model indicates high sensitivity at lower cut-off points, making it useful for screening. If patients have 1 risk factor, we can stratify those at risk for poststroke HF with 85.2% sensitivity.

There are some limitations in our study. This study is a retrospective design with inherent limitations leading to potential ascertainment bias. Although we adopted the criteria of the Framingham study for the definition of AHF, clinical ascertainment were left to the discretion of each clinician. Hence, we could have introduced a quantitative evaluator of cardiac function such as ejection fraction using echocardiography, but we could not adopt it because of the data deficiency. Furthermore, we did not consider iatrogenic influences. Operative interventions may exert some effect on stress reactions. Osmotic agents such as mannitol and hypertonic saline are commonly used in stroke to treat brain edema and increased intracranial pressure, however, the hypertonic load predisposes to development of congestive HF.[25] Finally, the risk score is thought to be useful for screening of poststroke HF, but should be validated in a further prospective cohort study before clinical application.

Conclusions

In summary, severe stroke patients with cardiac comorbidities and hypoalbuminemia occasionally proceed to AHF within a few days after stroke onset. Poststroke HF possibly lengthens hospital stay and increases in-hospital mortality. In consideration of these consequences, we should stratify high-risk patients and use preemptive interventions in the early stage of stroke to avoid poor outcomes.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.02.030.

References

1. Touze E, Varenne O, Chatellier G, et al. Risk of myocardial infarction and vascular death after transient ischemic attack and ischemic stroke: a systematic review and meta-analysis. Stroke 2005;36:2748-2755.

2. Myers MG, Norris JW, Hachinski VC, et al. Cardiac sequelae of acute stroke. Stroke 1982;13:838-842.
3. Ois A, Gomis M, Cuadrado-Godia E, et al. Heart failure in acute ischemic stroke. J Neurol 2008;255:385-389.
4. Christensen H, Fogh Christensen A, Boysen G. Abnormalities on ECG and telemetry predict stroke outcome at 3 months. J Neurol Sci 2005;234:99-103.
5. Benedict CR, Loach AB. Clinical significance of plasma adrenaline and noradrenaline concentrations in patients with subarachnoid haemorrhage. J Neurol Neurosurg Psychiatry 1978;41:113-117.
6. Koenig MA, Puttgen HA, Prabhakaran V, et al. B-type natriuretic peptide as a marker for heart failure in patients with acute stroke. Intensiv Care Med 2007; 33:1587-1593.
7. Tung PP, Olmsted E, Kopelnik A, et al. Plasma B-type natriuretic peptide levels are associated with early cardiac dysfunction after subarachnoid hemorrhage. Stroke 2005;36:1567-1569.
8. Templin C, Ghadri JR, Diekmann J, et al. Clinical features and outcomes of takotsubo (stress) cardiomyopathy. N Engl J Med 2015;373:929-938.
9. Prosser J, MacGregor L, Lees KR, et al. Predictors of early cardiac morbidity and mortality after ischemic stroke. Stroke 2007;38:2295-2302.
10. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;37:2129-2200.
11. Alberts VP, Bos MJ, Koudstaal P, et al. Heart failure and the risk of stroke: the Rotterdam study. Eur J Epidemiol 2010;25:807-812.
12. McKee PA, Castelli WP, McNamara PM, et al. The natural history of congestive heart failure: the Framingham study. N Engl J Med 1971;285:1441-1446.
13. Sternbach GL. The Glasgow coma scale. J Emerg Med 2000;19:67-71.
14. Rimel RW, Giordani B, Barth JT, et al. Disability caused by minor head injury. Neurosurg 1981;9:221-228.
15. Arques S, Ambrosi P. Human serum albumin in the clinical syndrome of heart failure. J Card Fail 2011;17:451-458.
16. Franch-Arcas G. The meaning of hypoalbuminaemia in clinical practice. Clin Nutr 2001;20:265-269.
17. Kawashiro N, Kasanuki H, Ogawa H, et al. Heart Institute of Japan—Department of Cardiology I. Clinical characteristics and outcome of hospitalized patients with congestive heart failure: results of the HIJC-HF registry. Circ J 2008;72:2015-2020.
18. Kimura K, Minematsu K, Yamaguchi T. Japan Multicenter Stroke Investigators C. Atrial fibrillation as a predictive factor for severe stroke and early death in 15,831 patients with acute ischaemic stroke. J Neurol Neurosurg Psychiatry 2005;76:679-683.
19. Ay H, Koroshetz WJ, Benner T, et al. Neuroanatomic correlates of stroke-related myocardial injury. Neurology 2006;66:1325-1329.
20. Tomida M, Muraki M, Uemura K, et al. Plasma concentrations of brain natriuretic peptide in patients with subarachnoid hemorrhage. Stroke 1998;29:1584-1587.
21. Makikallio AM, Makikallio TH, Korpelainen JT, et al. Natriuretic peptides and mortality after stroke. Stroke 2005;36:1016-1020.
22. McGirt MJ, Blessing R, Nimjee SM, et al. Correlation of serum brain natriuretic peptide with hyponatremia and delayed ischemic neurological deficits after subarachnoid hemorrhage. Neurosurgery 2004;54:1369-1373. discussion 73-4.
23. Arques S, Roux E, Stolidi P, et al. Usefulness of serum albumin and serum total cholesterol in the prediction of hospital death in older patients with severe, acute heart failure. Arch Cardiovasc Dis 2011;104:502-508.
24. Putaala J, Lehto M, Meretoja A, et al. In-hospital cardiac complications after intracerebral hemorrhage. Int J Stroke 2014;9:741-746.
25. Qureshi AI, Suarez JI. Use of hypertonic saline solutions in treatment of cerebral edema and intracranial hypertension. Critical Care Med 2000;28:3301-3313.