ORIGINAL ARTICLE

Complications as important predictors of disability in ischemic stroke

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ABSTRACT

BACKGROUND

Stroke is the main cause of disability and death in many countries. The high incidence of disability in stroke survivors requires special attention to determine various predictive factors of disability. This study aimed to identify the various predictive factors of disability in ischemic stroke.

METHODS

This study was a cross sectional study on 4510 ischemic stroke patients. Each patient's data had been recorded in the electronic stroke registry of Bethesda Hospital. Ischemic stroke diagnosis was confirmed by brain CT scan, which was interpreted by a neurologist and a radiologist. Disability was assessed using the modified Rankin scale. Predictors of disability were assessed. Multiple logistic regression analysis was used to analyse the data.

RESULTS

The subjects were predominantly males, >60 years of age, and suffered stroke for the first time. The incidence of disability was 31.5% (1420/4510). Multiple logistic regression analysis showed that the presence of complications (OR: 6.43; 95% CI: 4.74-8.73; p<0.001), decreased level of consciousness (OR: 4.82; 95% CI: 3.95-5.90; p <0.001), onset ≥3 hours (OR: 1.93; 95% CI: 1.52-2.45; p<0.001), recurrent stroke (OR: 1.63; 95% CI: 1.39-1.90; p<0.001), and age >60 years (OR: 1.55; 95% CI: 1.35-1.79; p<0.001) were independent predictive factors of disability.

CONCLUSION

We demonstrated that a substantial proportion of patients with ischemic stroke become disabled. And the presence of complications was the most predictive factor of disability in ischemic stroke.

Keywords: Stroke, ischemic, cohort study, predictive factors, disability

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INTRODUCTION

The four main non-communicable diseases according to the World Health Organization (WHO) are cardiovascular disease (coronary heart disease and stroke), cancer, chronic respiratory disease, and diabetes.[1] In many countries, stroke is the main cause of disability and death.[2-4] Disability is defined as a lack of ability to perform activities or tasks in the range considered normal for a human being.[5]

Stroke causes negative impacts for most of the stroke survivors.[6] About 25% to 74% of 50 million stroke survivors in the world experience physical, cognitive, and emotional decline. They also require partial or full assistance to perform activities of daily living (ADL).[7] Ninety percent of stroke patients showed residual symptoms. One-third of them were not able to continue their ADL as usual.[8] Cross-sectional research by Hong et al.[9] showed that 35% of stroke survivors are dependent on caregivers to perform ADL.

Post-stroke disability exerts a negative impact on the socioeconomic status,[10] because stroke survivors with disability become a burden for their family.[11] The high incidence of disability in stroke survivors requires special attention to find out various predictive factors of disability. There have been only a few studies on stroke disability in Indonesia and the research on predictive factors of disability in Indonesia is not yet satisfactory. Previous studies in Indonesia were concerned with the degree of disability among patients with degenerative disease (including stroke),[12] the psychological burden caused by post-stroke disability,[13] and citicoline injections to improve disability in stroke patients,[14] but not on the factors contributing to post-stroke disability. The present study is a new study on stroke disability in Indonesia, involving a large number of subjects. By knowing the predictive factors, we may make a program to reduce the incidence of disability among stroke survivors. This study aimed to identify the various predictive factors of disability in ischemic stroke.

METHODS

Research design

In this cross-sectional design we analyzed the data from 4510 patients who were ischemic stroke during an approximately 7.5-year period (from June 2009 to December 2016) at Bethesda Hospital, Yogyakarta, Indonesia. Each subject had been followed up from the first day until they were discharged from the hospital. Their data were recorded in the electronic stroke registry of Bethesda Hospital.

Study subjects

The subjects were ischemic stroke patients who met the inclusion criteria i.e: (i) ischemic stroke, (ii) hospitalized at Bethesda Hospital, Yogyakarta, Indonesia, (iii) hospitalized between June 2009 to December 2016, and (iv) their data had been recorded in the electronic stroke registry of Bethesda Hospital. The exclusion criteria were: (i) incomplete data and (ii) death during hospitalization.

Measurements

Ischemic stroke diagnosis was confirmed by brain CT scan, interpreted by a neurologist and a radiologist. Ischemic stroke diagnosis was established using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification as a reference, i.e: (i) large-artery atherosclerosis, (ii) cardioembolism, (iii) small-vessel occlusion, (iv) stroke of other determined etiology, and (v) stroke of undetermined etiology. [15] Ischemic stroke subjects were assigned to two groups: subjects with disability and subjects without disability (as controls). Assessed variables comprised gender, age, stroke history, disability status, stroke symptoms, comorbidity, complications during hospitalization, and onset. Based on age, the subjects were grouped into: ≤60 years old and >60 years old. Based on stroke history, the subjects were divided into those with first-time stroke and those with recurrent stroke.

Disability status was defined as limitations in performing activities and tasks on an acceptable level of social norm [5] and on this basis the subjects were differentiated into those without disability and those with disability. Disability status was measured on a modified Rankin score (mRS) scale.[16] Subjects without disability included subjects who were independent without any sequelae and no significant disability (mRS score 0 and 1). Subjects with disability included subjects with moderate disability, moderately severe disability, and severe disability with a home care program (mRS score 2 to 5). The subjects who had died (mRS score 6) were excluded from this study. Decreased level of consciousness was the only stroke symptom observed, and the subjects were differentiated into subjects with decreased level of consciousness and without decreased level of consciousness. Decreased level of consciousness was defined as any state of arousal other than compos mentis (i.e. somnolence, stupor, coma, and delirium), appearing suddenly, and confirmed by neurological and physical examination.

Based on comorbidity the subjects were differentiated into subjects with comorbidity and without comorbidity. Comorbidities assessed in this study included type 2 diabetes mellitus (DM2), hypertension, dyslipidemia, ischemic heart disease (IHD), and atrial fibrillation. Hypertension was diagnosed based on the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure- 8 (JNC 8) criteria. Hypertension was defined as systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$90 mmHg or consuming antihypertensive drugs. DM2 diagnosis was made based on American Diabetes Association criteria. DM2 was defined as fasting plasma glucose $\geq$126 mg/dL, or 2-hour plasma glucose $\geq$200 mg/dL during oral glucose tolerance test, or random plasma glucose $\geq$200 mg/dL with classic symptoms of hyperglycemia, or A1C $\geq$6.5%, or consuming antidiabetic drugs.

The diagnosis of dyslipidemia was made based on American Association of Clinical Endocrinologists criteria. Dyslipidemia was defined as an any increase in level of blood lipids: low density lipoprotein cholesterol level $\geq$140 mg/dL, high density lipoprotein cholesterol <40 mg/dL, triglyceride level >200 mg/dL, and/or total cholesterol level >200 mg/dL. IHD diagnosis was made based on American Heart Association criteria. IHD included stable angina pectoris; which was confirmed by cardiac stress test; unstable angina pectoris, ST-elevation myocardial infarction (STEMI), and non STEMI, confirmed by electrocardiography (ECG). Atrial fibrillation (AF) was defined as an irregularly irregular heart beat confirmed by ECG test.

Based on complications during hospitalization the subjects were also differentiated into subjects with complications and without complications. Complications assessed in this study included urinary tract infection (UTI), pneumonia, gastrointestinal bleeding, and decubitus ulcer. UTI was defined as an infection in any part of the urinary tract during hospitalization, confirmed by physical examination and urinalysis. Pneumonia was defined as pulmonary infection confirmed by physical examination, blood test, and chest radiograph. Gastrointestinal bleeding was defined as bleeding in any part of the gastrointestinal tract with hematemesis and/or melena as the symptom(s). Decubitus ulcer was defined as any change in the color of the skin and the presence of a wound in the skin and underlying soft tissues covering bony areas compromized by pressure. On the basis of stroke onset the subjects were grouped into those with an onset of <3 hours and those with an onset of $\geq$3 hours. Stroke onset was defined as the beginning of stroke symptom(s).

Statistical analysis

Univariate analysis was performed to identify subject characteristics. Bivariate analysis was conducted by analyzing disability status with

Table 1. Distribution of characteristics and clinical features of the subjects (n=4510)

Characteristics	n (%)
Gender	
Male	2680 (59.4)
Female	1830 (40.6)
Age (years)	
≤60	2015 (44.7)
>60	2495 (55.3)
Stoke history	
First stroke	3379 (74.9)
Recurrent stroke	1131(25.1)
Decreased level of consciousness	
Yes	604 (13.4)
No	3906 (86.6)
Comorbidity	
Yes	3430 (76.1)
No	1080 (23,9)
Complication	
Yes	306 (6.8)
No	4204 (93.2)
Onset (hours)	
<3	538 (11.9)
≥3	3972 (88.1)
Disabilty	
Yes	1420 (31.5)
No	3090 (68.5)

age, gender, stroke history, decreased level of consciousness, presence of comorbidity, presence of complications, and stroke onset. Multiple logistic regression analysis was performed to determine the independent predictive factor(s) of disability. Statistical significance was set at p<0.05.

Ethical clearance

This study was verified by Duta Wacana Christian University Ethical Research Committee. The ethical clearance number was 418/c.16/FK/2017.

RESULTS

From June 2009 to December 2016, there were 6526 subjects who had suffered from ischemic stroke, among whom 331 had died and 1685 had incomplete data and were excluded from this study. Table 1 shows the basic characteristics of the remaining 4510 subjects.

The subjects were predominantly males, >60 years old, and suffered stroke for the first time. The incidence of disability was 31.5% (1420/4510). Most of the subjects had no decreased level of consciousness, had a comorbidity, and did not experience any complication during hospitalization. A total of 68.5% subjects were independent without any sequelae after discharge from the hospital. Most of the subjects came to the hospital ≥3 hours after stroke onset.

Bivariate analysis indicated that the presence of complications was the strongest predictive factor of disability (OR: 2.83; 95%CI: 2.63-3.05; p<0.001) (Table 2), followed by decreased level of consciousness and recurrent stroke. Male gender (OR: 0.88; 95%CI: 0.81-0.96; p=0.008) and the presence of comorbidity (OR: 0.80, 95%CI: 0.73-0.88, p<0.001) were predictive factors of disability.

Bivariate analysis was followed by multiple logistic regression analysis (Table 3), which showed that the presence of complications (OR: 6.43; 95%CI: 4.74-8.73; p<0.001), decreased level of consciousness (OR: 4.82, 95%CI: 3.95-5.90; p<0.001), onset ≥3 hours (OR: 1.93, 95%CI: 1.52-2.45; p<0.001), recurrent stroke (OR: 1.63; 95%CI: 1.39-1.90; p<0.001), and age >60 years (OR: 1.55; 95% CI: 1.35-1.79; p<0.001) were

Table 2. Risk factors of various clinical parameters of disability

Characteristics	With disabilty	Without disability	OR	95% CI	p value
Gender: Male	803	1877	0.88	0.81-0.96	0.008
Age: >60 years	935	1560	1.55	1.41-1.70	<0.001
Stroke history: Recurrent stroke	486	645	1.55	1.42-1.69	<0,001
Decreased level of consciousness: Yes	420	184	2.71	2.52-2.92	<0.001
Comorbidity: Yes	1021	2409	0.80	0.73-0.88	<0.001
Complication: Yes	243	63	2.83	2.63-3.05	<0.001
Onset ≥3 hours	1302	2670	1.49	1.26-1.76	<0.001

Table 3. Factors associated with risk of disability by multiple logistic regression analysis

Characteristics	aOR	95% CI	p value
Age: >60 years	1.55	1.35-1.79	<0.001
Stroke history: Recurrent Stroke	1.63	1.39-1.90	<0.001
Decreased level of consciousness: Yes	4.82	3.95-5.90	<0.001
Comorbidity: Yes	0.74	0.63-0.86	<0.001
Complication: Yes	6.43	4.74-8.73	<0.001
Onset: ≥3 hours	1.93	1.52-2.45	<0.001

aOR : Adjusted Odds ratio

independent predictive factors of disability. In this study, the presence of comorbidity was not significant for increased disability risk. Gender was not a predictive factor of disability.

DISCUSSION

Stroke is one of the common causes of morbidity worldwide, as has been proved by many previous studies. The present study showed that the incidence of disability was 31.5%, for which several studies had also indicated similar results. Research by Sridharan et al. [17] showed that 42.4% of stroke subjects suffered from mild disability, 43% were moderately disabled, and 14.6% were bedridden. In Malaysia, about 87% of post-stroke patients needed assistance for ambulation of varying degree and 40% still required assistance after 3 months.[18] In the present study, the reduced incidence of disability among stroke survivors was the result of stroke management in the multidiciplinary unit of the hospital where this study was conducted. Recent studies have shown that stroke-related disability may be substantially reduced by emergency treatment of acute stroke in dedicated stroke units.[19] A guideline for systematic stroke management is highly recommended to prevent complications, thus reducing the incidence of post-stroke disability.[9] Good stroke prevention and treatment may reduce the mortality and morbidity rates due to stroke.[20]

Our study showed that the subjects were predominantly males, >60 years old, and suffered stroke for the first time, which was similar to previous studies. The incidence of stroke increases sharply with age.[21] A study by Ghani et al.[22] showed that the prevalence of stroke increases sharply at the age >45 years. The Vascular Health and Risk Management study [23] showed that the incidence of stroke is 1.25 times higher in males. Most of the subjects in the present study experienced stroke for the first time (74.9%). In 2015, there were about 795,000 people in the United States who continued to experience a new or recurrent stroke and approximately 610,000 of these were first events.[24]

In our study, most of the subjects did not experience a decreased level of consciousness, contrary to the study by Lisabeth et al.,[25] who stated that decreased level of consciousness was the most frequent non-traditional stroke symptom (p<0.03). However, the result of our study corresponds to some earlier studies, suggesting that decreased level of consciousness was the rarest, whereas the most frequent symptom was limb weakness.[20,26]

Most of the subjects in our study had comorbidity (76.1%), which is similar to many previous studies. Since stroke is a multifactorial disease, stroke patients frequently have various comorbidities such as hypertension, diabetes mellitus, heart disease, and others.[27-29]

About 31.5% of our subjects experienced disability after stroke. Of the various factors that trigger disability analyzed in this study, the presence of complications was the strongest predictive factor of disability, followed by decreased level of consciousness and recurrent stroke. Male gender and the presence of comorbidity did not increase the disability risk. Our study showed that the presence of complications increased the risk of disability 6.43 times, while decreased level of consciousness increased the risk of disability 4.828 times. These

results are similar to those of earlier studies. Tong et al.[30] state that post-stroke complications worsen outcome. Complications aggravate the degree of disability and increase the risk of recurrent stroke. Complications are related to poor outcomes in the 3 months post-stroke.[28] Disability-Adjusted Life Year (DALY) is a parameter to measure the morbidity and mortality rate due to a disease. The more complications experienced by stroke patients, the more they are likely to become disabled.[9]

A study by Nadeau et al.[31] conducted in Canada showed that decreased level of consciousness was an independent predictive factor of poor outcome. Early disturbance of consciousness in stroke increases the risk of post-stroke disability 3.372 times in 3 months.[32] Decreased level of consciousness and low Glasgow Coma Scale (GCS) score are associated with a poor outcome in ischemic stroke patients.[33]

Other independent predictive factors of our study were onset ≥3 hours, recurrent stroke, and age >60 years. This result was also similar to previous studies. Ischemic stroke sufferers who receive treatment within 3 hours of onset will gain 4.4 disability-free years of life.[34] Thrombolytic therapy given within 3 hours after the onset increases good outcome 1.75 times.[35] Stroke history is the main predictive factor of disability.[6] A total of 50% of patients with recurrent stroke suffer permanent disability.[36] The Perth Community Stroke Study of 1989-1990 also identified stroke recurrence as a prognostic factor of disability, using logistic regression analysis after adjusting for sex.[37]

Good outcome of stroke sufferers is highest in the age range of 18 to 35 years and declines by 3.1 to 4.2% per decade until the age of 75 years.[35] Stroke sufferers aged 65 to 84 years are at risk of disability in the next 5 years. Stroke sufferers aged 75 to 84 years have a 5.7 times higher risk of disability.[37]

The present study indicates that male gender is not a predictive factor of disability. The prevalence of stroke is higher in males, but the incidences of disability and dependence in performing ADL are higher in females,[39,40] who are 4.3 times more dependent than males after a stroke attack.[41]

The finding that the presence of comorbidity is a predictive factor of disability, is consistent with the results of previous research. The degree of disability will be severe if accompanied by various comorbidities such as diabetes mellitus,[42] heart disease (atrial fibrillation and ischemic heart disease), and hypertension.[43]

A limitation of our study is that mRS is likely not the best measure of minor disability and future studies should consider other measures of disability. We also did not find out what made these patients disabled and this would be of interest in designing future studies. Another limitation is that the electronic stroke registry in Bethesda Hospital is a secondary data source, so there is the possibility of errors in the data input process by the operator. The strength of this research is the large sample size and the fact that the types of variable listed in the electronic stroke registry were relatively complete.

CONCLUSION

This study demonstrated that the presence of complications was the most important predictive factor of disability in ischemic stroke. Knowledge of the predictive factors of disability increases the alertness and awareness of medical personnel to conduct real efforts to reduce the number of post-stroke disabilities.

CONFLICT OF INTEREST

Competing interests: no relevant disclosure.

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the Bethesda Hospital as the center where this study was conducted.

CONTRIBUTORS

RTP contributed to collect the subjects' data, managed ethical clearance, and completed the manuscript. RDLRS contributed to data analysis, literature search, and writing the draft. All authors have read and approved the final manuscript. ✚

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