Baseline Stroke Severity as a Predictor of 30-Day Post-Ischemic Stroke Disability Outcome

Tingkat Keparahan Awal Stroke Sebagai Faktor Prediktor Luaran Disabilitas 30 Hari pada Pasien Stroke Iskemik

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ABSTRACT

More than 50% of patients who survived stroke have a chronic disability. The National Institute of Health Stroke Scale (NIHSS) is a scoring system to determine the neurologic deficit of a stroke patient. This study analyzed stroke severity based on baseline NIHSS score as a determinant for 30-day post-ischemic stroke disability. This study method uses a retrospective cohort design based on medical records and stroke registry of ischemic stroke patients in Bethesda Hospital Yogyakarta. During admission, the predictive factors for the disability of the study subjects were evaluated. The baseline NIHSS assessment score was measured at 1x24 hours after admission. Disability was measured using a simplified modified Rankin Scale questionnaire (smRSq) Indonesian version at 30-day post-ischemic stroke. Statistical analysis includes univariate, bivariate, and logistic regression multivariate data analysis. The subjects were 84 patients with ischemic stroke. Disability at 30-day post-ischemic stroke occurred in 22 patients (26.2%). Logistic regression multivariate analysis showed that Neutrophil to Lymphocyte Ratio (NLR) (RR: 4.488, CI: 1.873–10.756, p: 0.001) and baseline NIHSS score (RR: 28.563, CI: 2.891–282.181, p: 0.004) together significantly affect the mRS of 30-day post-ischemic stroke. Patients admitted with a higher baseline NIHSS score have a 28.5 fold risk for a worse functional outcome than those with lower baseline NIHSS scores. Stroke severity based on baseline NIHSS score is a determinant factor for disability in patients at 30-day post-ischemic stroke.

Keywords: Disability, Ischemic stroke, modified Rankin Scale (mRS), National Institute of Health Stroke Scale (NIHSS)

ABSTRAK

Lebih dari 50% pasien yang selamat dari stroke mengalami disabilitas kronik. National Institute of Health Stroke Scale (NIHSS) merupakan skor untuk menentukan tingkat defisit neurologi pada pasien stroke yang dapat digunakan sebagai prediktor disabilitas. Penelitian ini dilakukan untuk menganalisis tingkat keparahan stroke berdasarkan skor NIHSS awal sebagai determinan disabilitas 30 hari pasca stroke iskemik. Penelitian dilakukan menggunakan desain kohort retrospektif berdasarkan rekam medis dan stroke registry pasien stroke iskemik di RS Bethesda Yogyakarta. Pada saat admisi dilakukan penilaian faktor-faktor prediktor disabilitas yang dimiliki oleh subjek penelitian. Asemnen skor NIHSS awal diukur 1x24 jam sejak admisi. Disabilitas diukur menggunakan simplified modified Rankin Scale questionnaire (smRSq) versi bahasa Indonesia pada 30 hari pasca stroke iskemik. Analisis statistik meliputi analisis data univariat, bivariat, dan multivariat uji regresi logistik. Didapatkan subjek sebanyak 84 pasien stroke iskemik. Disabilitas pada pasien 30 hari pasca stroke iskemik terjadi pada 22 pasien (26.2%). Analisis multivariat regresi logistik didapatkan bahwa Neutrophil to Lymphocyte Ratio (NLR) (RR: 4.488, CI: 1.873–10.756, p: 0.001) dan skor NIHSS awal (RR: 28.563, CI: 2.891–282.181, p: 0.004) bersama-sama mempengaruhi mRS 30 hari pasca stroke iskemik secara signifikan. Pasien yang datang dengan skor NIHSS awal yang lebih tinggi memiliki risiko 28.5 kali mengalami luaran fungsional buruk dibanding skor NIHSS awal ringan. Tingkat keparahan stroke berdasarkan skor NIHSS awal merupakan faktor determinan disabilitas pada pasien 30 hari pasca stroke iskemik.

Kata Kunci: Disabilitas, National Institute of Health Stroke Scale (NIHSS), modified Rankin Scale (mRS), Stroke Iskemik

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DOI: http://dx.doi.org/10.21776/ub.jkb.2022.032.01.6
INTRODUCTION

Based on World Health Statistics 2020, non-communicable diseases (NCDs) in 2016 contributed 71% of all deaths in the world. Cardiovascular disease, including coronary heart disease and stroke, is the biggest cause of death, reaching 17.9 million (1). Although the mortality rate from ischemic stroke is lower than hemorrhagic stroke, more than 50% of stroke survivors experience chronic disability. The latest data in 2017 shows that stroke is the second highest cause of Disability-Adjusted Life Years (DALYs). Disability, in this case, is in the form of limitations in independently carrying out daily activities, including decreased physical, emotional, and cognition functions. Epidemiology in Indonesia shows that Indonesia is one of the countries in Asia that has the highest death rate due to stroke, namely 193.3/100,000 population per year. It was also found that Indonesia has the highest level of disability due to stroke in Asia, which is 3,382.2/100,000 population.

The high incidence of disability in stroke survivors requires more attention to determine the factors predicting the disability. Several previous studies found functional status predictors in post-ischemic stroke patients, including upper and lower extremity motor skills, age, atrial fibrillation, history of TIA, comorbid factors, less than 12 initial GCS, aphasia, dysphagia, triglyceride levels, and complications (2-5). However, these predictor factors are still broad in scope, and the results are still controversial among studies.

The National Institute of Health Stroke Scale (NIHSS) is a score to determine the level of neurological deficit in stroke patients. The Indonesian version of the NIHSS score has eleven parameter components that are assessed: [1] degree of awareness which is further divided into [1a] level of awareness, [1b] answering questions, [1c] carrying out orders; [2] conjugate horizontal eye movement (GAZE); [3] visual field of view on the confrontation test; [4] facial paresis, [5] arm motor; [6] leg motor; [7] limb ataxia; [8] sensory; [9] aphasia; [10] dysarthria; and [11] neglect/inattention. The NIHSS has a maximum score of 42 and a minimum score of 0 with the interpretation of the results as follows: score <5 mild neurological deficit, score 5-14 moderate neurological deficit, score 15-24 severe neurological deficit, and score 25 represents very severe neurological deficit (6). Several previous studies have also shown that baseline NIHSS scores can predict post-ischemic stroke functional status (7-10). However, some studies find that the initial NIHSS score is not sufficiently accurate to predict the clinical outcome of stroke (11,12). In addition, research on the correlation between the baseline NIHSS score and post-ischemic stroke disability has never been conducted in Indonesia. By finding out the baseline NIHSS score as a determinant of disability, the incidence of disability post-ischemic stroke could be prevented, and patients could return to their activities of daily living (ADL) independently. This study was conducted to measure and analyze the severity of stroke based on the initial NIHSS score as a determinant of 30-day post-ischemic stroke disability.

METHODS

Research Design

This study used an analytical method with a retrospective cohort design. Secondary data were taken from the medical records and stroke registry at the Stroke Center unit of Bethesda Hospital Yogyakarta from January 2020 to October 2020. At the admission, the baseline NIHSS score was assessed, and other accompanying risk factors were observed, including age, gender, onset, type II diabetes mellitus, random blood sugar, dyslipidemia, HDL, LDL, triglycerides, total cholesterol level, white blood cell count, neutrophil lymphocyte ratio, hypertension, atrial fibrillation, ischemic heart disease, dysphagia, muscle strength, hemiparesis, and complication.

Modified Rankin Scale (mRS) is an instrument that is often used to measure disability in post-stroke patients. mRS has 7 points with a score range of 0 to 6. Interpretation is based on the mRS score, ie the patient is considered independent if the mRS score is 0-1 which includes patients without symptoms and not showing significant symptoms of disability. While the patient is said to have a disability if the mRS score obtained is 2-5 consisting of mild, moderate, moderate-severe, and severe disability. An mRS score of 6 indicates a patient who died (13). Assessment of disability was carried out 30 days after ischemic stroke using a simplified modified Rankin Scale questionnaire (smRSq) by Bruno et al., 2010 (14), developed from the traditional unstructured mRS score. This smRSq score has been proven to have higher inter-rater reliability and faster assessment time.

Study Subjects

The sample size was calculated using determined of the open epi version 3.01 statistic program It was found that the total sample size was 76 patients. It is estimated that there will be a patient drop out of 10%. Therefore, the total number of samples was rounded up to 84 ischemic stroke patients. The sample was obtained based on purposive sampling technique.

Subjects were ischemic stroke patients who met the inclusion criteria, namely (i) male and female patients diagnosed with mild to moderate ischemic stroke based on GCS fully alert (GCS score is 15) and NIHSS (score <5 and 5-14), (ii) patients older than 18 years old, (iii) patients with the first-time stroke attack, (iv) patients with onset of hospital admission below 24 hours after ischemic stroke, (v) not referral patients, (vi) patients have a complete medical record and stroke registry data. The exclusion criteria were (i) patients who had a history of permanent disability and/or speech impairment, (ii) forced-discharge patients, (iii) patients who were not assessed for a mRS score at the 30 days post-ischemic stroke, (iv) patients who died during hospitalization.

Statistical Analysis

This study used an analytical method with a retrospective cohort design. Univariate analysis was performed to describ-subject characteristics. Bivariate analysis was used for examining the relationship between independent and confounding variables on the 30-day mRS score. Multivariate analysis of logistic regression to determine the determinants of disability 30 days post-ischemic stroke.

Ethical Clearance

This research has been approved by the Health Research Ethics Committee (KEPK) Bethesda Hospital Yogyakarta through the Ethics Approval number 137/KEPK-RSB/XII/20.
RESULTS
In this study, 84 ischemic stroke patients who met the inclusion criteria were obtained. The subjects were predominantly males (56%), and the highest age range was 61-70 years in 31 subjects (36.9%). Most subjects came to the hospital at intervals of 6-12 hours after the stroke onset. The most common comorbidity was hypertension as in 43 subjects (51.2%). Most patients did not experience dysphagia and complications during hospitalization. Most symptoms of hemiparesis were on the right side, found among 37 subjects (44%). The highest MRC score was 4 in 49 subjects (58.3%), meaning that the patient could move against the examiner’s resistance, but his strength was reduced.

Most of the subjects came with normal blood sugar levels that were below 200 mg/dl (70.2%), HDL levels at 40-59 mg/dl (13.1%), high LDL levels at 130-159 mg/dl (13.1%), high LDL levels at 130-159 mg/dl (13.1%), normal triglycerides (22.6%), normal total cholesterol (38.1%), normal leukocyte count (78.6%), normal neutrophil-lymphocyte ratio (59.5%), and moderate baseline NIHSS score (70.2%). A total of 62 subjects (73.8%) were without any sequelae 30 days after ischemic stroke with a mRS score below 2. Meanwhile, as many as 22 subjects (26.2%) had a poor outcome with a mRS score equivalent or higher than 2. Of the twenty-one characteristics studied, the bivariate analysis revealed that the neutrophil-lymphocyte/NLR ratio (p=0.004) MRC scale muscle strength at admission (p=0.05), baseline NIHSS score (p=0.03), and NLR had a significant relationship with mRS score below 2. Of the twenty-one characteristics studied, the bivariate analysis revealed that the neutrophil-lymphocyte/NLR ratio (p=0.004) MRC scale muscle strength at admission (p=0.05), baseline NIHSS score (p=0.03), and NLR had a significant relationship with mRS score below 2. Meanwhile, as many as 22 subjects (26.2%) had a poor outcome with a mRS score equivalent or higher than 2.

| Table 1. Distribution of characteristics, clinical features of the subjects, and bivariate analysis (n=84)       | Disable | Independent | RR   | CI 95%  | p      |
|--------------------------------------------------------------------------------------------------------------------------------|--------|-------------|------|---------|--------|
| **Age**                                                                                                                                  | 0.703  |
| • 41 – 50                                                                                                                               | 6      | 3           | 9 (10.7%) | 10.7   |
| • 51 – 60                                                                                                                               | 21     | 8           | 29 (34.5%) | 34.5   |
| • 61 – 70                                                                                                                               | 25     | 6           | 31 (36.9%) | 36.9   |
| • > 70                                                                                                                                  | 10     | 5           | 15 (17.9%) | 17.9   |
| Gender                                                                                                                                  | 0.730  |
| • Male                                                                                                                                  | 34     | 13          | 47 (56%)   | 56     |
| • Female                                                                                                                                | 28     | 9           | 37 (44%)   | 44     |
| **Onset (hours)**                                                                                                                       | 0.200  |
| • < 3                                                                                                                                  | 16     | 1           | 17 (10.2%) | 10.2   |
| • 3-6                                                                                                                                   | 17     | 7           | 24 (28.6%) | 28.6   |
| • 6-12                                                                                                                                  | 19     | 9           | 28 (33.3%) | 33.3   |
| • 12-24                                                                                                                                | 10     | 5           | 15 (17.9%) | 17.9   |
| **Type II Diabetes Mellitus**                                                                                                           | 0.766  |
| • Yes                                                                                                                                   | 19     | 6           | 25 (19.8%) | 19.8   |
| • No                                                                                                                                    | 43     | 16          | 59 (70.2%) | 70.2   |
| **Random Blood Sugar Level**                                                                                                            | 0.703  |
| • < 200                                                                                                                                | 42     | 17          | 59 (70.2%) | 70.2   |
| • > 200                                                                                                                                | 16     | 4           | 20 (23.8%) | 23.8   |
| • No data                                                                                                                               | 4      | 1           | 5 (6.0%)   | 6.0    |
| **Dyslipidemia**                                                                                                                       | 0.964  |
| • Yes                                                                                                                                   | 12     | 5           | 17 (20.2%) | 20.2   |
| • No                                                                                                                                    | 37     | 15          | 52 (61.9%) | 61.9   |
| **HDL**                                                                                                                                | 0.745  |
| • < 40                                                                                                                                  | 7      | 2           | 9 (10.7%)   | 10.7   |
| • 40-59                                                                                                                                | 8      | 3           | 11 (13.1%) | 13.1   |
| • ≥ 60                                                                                                                                  | 3      | 0           | 3 (3.6%)   | 3.6    |
| • No data                                                                                                                               | 44     | 17          | 61 (72.6%) | 72.6   |
| **LDL**                                                                                                                                | 0.944  |
| • < 100                                                                                                                                | 4      | 1           | 5 (6.0%)   | 6.0    |
| • 100 - 129                                                                                                                            | 3      | 1           | 4 (4.8%)   | 4.8    |
| • 130 - 159                                                                                                                            | 7      | 4           | 11 (13.1%) | 13.1   |
| • 160 - 189                                                                                                                            | 6      | 1           | 7 (8.3%)   | 8.3    |
| • ≥ 190                                                                                                                                | 3      | 1           | 4 (4.8%)   | 4.8    |
| • No data                                                                                                                               | 39     | 14          | 53 (63.1%) | 63.1   |
| **Triglycerides**                                                                                                                      | 0.275  |
| • < 150                                                                                                                                | 14     | 5           | 19 (22.6%) | 22.6   |
| • 150 - 199                                                                                                                            | 4      | 2           | 6 (7.1%)   | 7.1    |
| • 200 - 499                                                                                                                            | 6      | 0           | 6 (7.1%)   | 7.1    |
| • ≥ 500                                                                                                                                | 0      | 1           | 1 (1.2%)   | 1.2    |
| • No data                                                                                                                               | 38     | 14          | 52 (61.9%) | 61.9   |
| **Total Cholesterol Level**                                                                                                            | 0.300  |
| • < 200                                                                                                                                | 24     | 8           | 32 (38.1%) | 38.1   |
| • 200 - 239                                                                                                                            | 18     | 3           | 21 (25.0%) | 25.0   |
| • ≥ 240                                                                                                                                | 8      | 6           | 14 (16.7%) | 16.7   |
| • No data                                                                                                                               | 12     | 5           | 17 (20.2%) | 20.2   |
baseline NIHSS score is a predictor in assessing post-stroke disability (10,15-18). In their study, Yaghi et al., 2017 (19) showed that the baseline NIHSS score is a predictor in assessing post-stroke disability at 30 days after ischemic stroke. Neutrophil Lymphocyte Ratio (NLR) were the determinants of disability in patients at 30 days after ischemic stroke. This study found that the baseline NIHSS score and Neutrophil Lymphocyte Ratio (NLR) were the determinants of disability in patients at 30 days after ischemic stroke.

**Table 1. Distribution of characteristics, clinical features of the subjects, and bivariate analysis (n=84)**

| White Blood Cell (WBC) count | 0.122 |
|-----------------------------|-------|
| ≤ 4.5                       | 0     |
| 4.5 – 11.5                  | 51    |
| ≥ 11.5                      | 6     |
| No data                     | 5     |

| Neutrophil Lymphocyte Ratio (NLR) | 0.004 |
|-----------------------------------|-------|
| < 3.13                            | 42    |
| ≥ 3.13                            | 16    |
| No data                           | 4     |

| Hypertension | 0.897 |
|--------------|-------|
| Yes          | 32    |
| No           | 30    |

| Atrial Fibrillation | 0.989 |
|---------------------|-------|
| Yes                 | 3     |
| No                  | 59    |

| Ischemic Heart Disease | 0.984 |
|------------------------|-------|
| Yes                    | 6     |
| No                     | 56    |

| Dysphagia | 0.416 |
|-----------|-------|
| Yes       | 1     |
| No        | 61    |

| Muscle Strength (MRC) on Admission | 0.005 |
|-----------------------------------|-------|
| 0                                 | 0     |
| 1                                 | 0     |
| 2                                 | 4     |
| 3                                 | 13    |
| 4                                 | 41    |
| 5                                 | 4     |

| Hemiparesis | 0.061 |
|-------------|-------|
| Left        | 12    |
| Right       | 26    |
| N/A         | 20    |
| No data     | 4     |

| Complication | 0.774 |
|--------------|-------|
| Yes          | 1     |
| No           | 60    |

| Baseline NIHSS Score | 0.003 |
|---------------------|-------|
| ≤ 5                 | 24    |
| 5 - 14              | 38    |

| 30 days mRS Score | 0.004 |
|-------------------|-------|
| < 2               | 22    |
| ≥ 2               | 62    |

The results of the Kolmogorov-Smirnov test (Table 2) show that the baseline NIHSS score and 30-day mRS were not normally distributed (p<0.005). Furthermore, the Mann-Whitney test was conducted and obtained a p-value <0.001, which indicates a significant relationship between the initial NIHSS score and the 30-day mRS. Multivariate analysis of logistic regression (Table 3) showed that NLR (RR: 4.488, CI: 1.873 – 10.756, p: 0.001) and baseline NIHSS score (RR: 28.563, CI: 2.891 – 282.181, p: 0.004) significantly influence mRS 30-day post-ischemic stroke.

**DISCUSSION**

This study found that the baseline NIHSS score and Neutrophil Lymphocyte Ratio (NLR) were the determinants of disability in patients at 30 days after ischemic stroke. Patients who came with a moderate baseline NIHSS score or higher had a risk of 28.5 times more likely to undergo a 30-day post-ischemic stroke disability than patients who had a mild baseline NIHSS score. Previous studies have shown similar results to the results of this study that the baseline NIHSS score is a predictor in assessing post-stroke disability (10,15-18). In their study, Yaghi et al., 2017 (19) showed a correlation between NIHSS scores and infarct volume on Diffusion-weighted imaging (DWI) (p<0.01).
Certain components of the NIHSS score were significantly associated with greater infarct volume, including neglect (p < 0.03), aphasia (p < 0.01), and visual field deficits (p < 0.01). The NIHSS score was also used to determine whether a patient met the inclusion or exclusion criteria for acute stroke therapy, including thrombolysis. Especially in a population of patients with mild ischemic stroke where the decision to treat thrombolysis is controversial (20).

Neutrophil Lymphocyte Ratio (NLR) also had a significant relationship with disability 30 days after ischemic stroke. These results are consistent with previous studies (21-23). Increased levels of NLR have a detrimental effect on the prognosis of the ischemic stroke, where secondary brain injury occurs in the form of the release of oxidative stress and damage to the blood-brain barrier by neutrophil activation, which then causes enlargement of the infarct area. In addition, there is also an increased risk of post-stroke infection (PSI) due to lymphocyte suppression (24). NLR is also associated with several complications of ischemic stroke, including cerebral edema lasting at the first 24-48 hours and an increased risk of hemorrhagic transformation (21). It can be concluded that an increase in the baseline NIHSS and NLR scores together describes how much damage occurs in the brain and indicates a wider cerebral infarction so that it can be a significant determinant of disability in post-ischemic stroke patients (25).

Characteristics of 84 subjects, dominated by men, with the highest age range of 61-70 years with a mean age of ischemic stroke patients 61.86 ± 8.245. This result is in line with a previous study by Samai & Martin-Schild (26). However, several previous studies show that in children and early adulthood, men have a greater risk of stroke. At an older age, the risk of stroke increases in women due to a higher life expectancy and decreased postmenopausal estrogen hormone (27).

Stroke is a multifactorial disease. Comorbidities in the subjects, in sequence, are hypertension (51.2%), dyslipidemia (20.2%), type II diabetes mellitus (19.8%), ischemic heart disease (9.5%), and atrial fibrillation (4.8%). These results are in accordance with previous studies (17,28,29). In this study, disability in patients at 30 days post-ischemic stroke occurred in 22 patients (26.2%), while 73.8% of patients lived independently without any disability. A systematic review study by Carmo et al. (30) concluded that from 212 studies studied, as many as 24%-49% of post-stroke patients have disabilities. The tendency to decrease the incidence of post-stroke disability can be influenced by the subjects of this study that included patients with mild-moderate neurologic deficits who tended to be independent after stroke.

This study is a retrospective cohort and design used secondary data collection. Therefore, the researcher cannot directly control the quality of measurement, recording, and accuracy of the data taken in the past. However, controlled secondary data are an important data source for monitoring, allowing a larger amount of data. The conclusion of this study proves that the severity of stroke based on the initial NIHSS score and NLR is a determinant factor of disability in patients 30 days after ischemic stroke.

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