Role Of Span-75 In Determining Prognosis Of Non-Thrombolysis Acute Ischemic Stroke Patients

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Citation : Sutanto Anyeliria, Simanungkalit Astra Dea. Role Of Span-75 In Determining Prognosis Of Non-Thrombolysis Acute Ischemic Stroke Patients
Medicinus. 2019 October; 7(7):209–215
Keywords : acute ischemic stroke, non-thrombolysis, prognosis, SPAN-75 index
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Online First : October 2020

Abstract

Introduction: The SPAN-75 index is a modification of the SPAN-100 index as a prognostic tool in acute ischemic stroke patients. Previous studies were using SPAN index in cases of ischemic stroke patients treated with rTPA and in cases of intracerebral hemorrhage.

Aim: To determine the role of the SPAN-75 index as a prognostic scoring in patients with acute ischemic stroke who did not get thrombolysis therapy.

Method: The subjects were acute ischemic stroke patients at Siloam Hospitals Lippo Village who were not treated with thrombolysis therapy and had no disability before stroke onset during January to April 2019. Subjects were classified into a positive and negative of SPAN-75 index group. Disability due to stroke was assessed with Modified Rankin Score (mRS) at the time of admission and discharged from the hospital. This prospective study was analyzed by the Kruskal-Wallis test.

Result: Forty subjects (average age of 57 years old) consisted of 31 negative and 9 positive of SPAN-75. Based on the Kruskal-Wallis test, the SPAN-75 index was positively associated with a more severe degree of stroke disability at the time of admission ($p = 0.002$), but not related to the change in the degree of disability when the patient was discharged from the hospital ($p = 0.807$). Age ($p = 0.445$) and gender ($p = 0.578$) had no significant relationship with the degree of disability of acute ischemic stroke.

Conclusion: The SPAN-75 index is related to the degree of disability of acute stroke patients at the time of admission

Background

Stroke is the second most common cause of death worldwide with annual mortality reaching 5.5 million people.[1] Stroke is caused by a multifactorial etiology, both modifiable and non-modifiable risk factors.[2] High degree of stroke severity (NIHSS> 8) and age over 65 years are the main predictors that cause poor outcome in patients with ischemic stroke. [3] The scoring system commonly used in assessing the severity of acute stroke is the NIHSS (NIH Stroke Scale), which consists of 11 variables, with each variables are assessed with a score of 0 - 4. The NIHSS classify strokes into 5 categories, (1) without symptoms of stroke, (2) minor stroke, (3) moderate stroke, (4) moderate-severe stroke, and (5) severe stroke. [4] Stroke Prognostication using Age and NIH Stroke Scale (SPAN) was created in 2012 by

Saposnik et al [5] with the aim of being a prognostic tool in acute stroke patients who received intravenous thrombolysis therapy with rtPA (recombinant tissue plasminogen activator). The SPAN index is calculated by adding the age of patients with NIHSS scores, then classified into two categories, namely, SPAN-100 is positive in patients with SPAN-100 scores greater than or equal to 100, and SPAN-100 is negative if the SPAN score is below 100. The SPAN-Index 100 were created with the rationale: (1) age and severity of stroke are the two most important prognostic factors in acute stroke, (2) patients over 80 years of age and high NIHSS scores (≥20) have a worse prognosis, and (3) the need for a simple index that is easier to apply than the scoring that is now available.[5] Several studies have shown that the SPAN-100 index can assess the prognosis of stroke patients receiving rtPA therapy. [5-7]

Stroke not only causes a high mortality rate but also causes significant morbidity, around 50% of stroke patients will experience chronic disability. [1] The degree of disability or dependence for carrying out daily activities in stroke patients is generally assessed using mRS (Modified Rankin Scale). The mRS degree consists values from 0 to 6 which represent degrees of disability from asymptomatic to death. [8] Research conducted by Fabiana et al showed the SPAN-100 index could predicted functional output (mRS) in stroke patients receiving tPA intravenous thrombolysis. [9] Based on previous research, a positive SPAN-100 index was very difficult to achieve, even with a high NIHSS score. [7] Therefore in 2015 Escabillas et al modified the SPAN-100 index (modified SPAN-100 index) by lowering the positive threshold value from 100 to 75. The study showed a negative SPAN-75 index related to ICHS (Intracerebral Hemorrhage Score) and a lower amount of cerebral hemorrhage. [10] Most studies focused more on examining the SPAN index on the output of stroke patients receiving rt-PA as well as in cases intracerebral hemorrhage [10,11,] so the role of the SPAN index in determining the prognosis of patients not treated with rtPA remains unclear. Until now there has been no research that examines the role of SPAN-75 in determining the prognosis of acute stroke patients. In this study we assessed the role of the SPAN-75 index in determining the prognosis in acute stroke patients who were not receiving rtPA therapy.

Methods

Study design and population

This study was an observational prospective cohort study in patients with acute ischemic stroke who did not receive rtPA at Siloam Hospitals Lippo Village during January-April 2019 timeframe. Severity of symptoms and disability were assessed twice with NIHSS and mRS within 5 to 10 days in-patient care on hospital admission and discharge. Exclusion criteria were patients who experienced hemorrhagic transformation, had a history of previous stroke, had a disability before the onset of stroke, and went home on their own request before the treatment period was completed. The diagnosis of acute ischemic stroke was established by a neurologist with clinical judgement and non-contrast brain CT scan. Patient with SPAN index more than 75 were considered SPAN-75 positive while less than 75 were considered SPAN-75 negative. In the statistical analyses, factors considered potiential confounders were education, age, comorbidities and number of previous stroke.

Statistical analysis

Statistical analysis was performed using PASW (Predictive Analytic Software) Statistics 25 (SPSS Inc., Chicago, Ill., USA). All data were checked for normality. Categorical variables were presented as frequency and percentage, while continuous data were expressed as mean and standard deviation or as medians and interquartile distances accordingly. Bivariate analysis was carried out using Kruskal-Wallis H analysis test, p-values ≤0.05 were considered significant. Our missing data analysis procedures used missing at random (MAR) assumptions. We used the MICE (multivariate imputation by chained equations) method of multiple multivariate imputation in STATA.

Results

The number of research subjects in this study were 40 subjects with NIHSS values at admission in minor, moderate, moderate-severe, and severe strokes respectively were 8 (20%), 30 (75%), 1 (2.5%), and 1 (2.5%) subject. In addition, NIHSS scores at

discharges were 15 (37.5%), 24 (60%), 1 (2.5%), and 0 (0%). The mRS at admissions with scores of 0 to 6 in a row were 0 (0%), 9 (22.5%), 13 (32.5%), 11 (27.5%), 6 (15%), 1 (2.5%), and 0 (0%), while for MRS at discharge were 0 (0%), 10 (25%), 20 (50%), 7 (17.5%), 2 (5%), 1 (2.5%) and 0 (0%).

As many as 31 subjects (77.5%) were in the negative SPAN-75 group and 9 subjects (22.5%) were in the positive SPAN-75 group. Based on sex, the sample in this study consisted of 16 male (40%), (12 in the SPAN-negative group, 4 in the SPAN-positive group) and 24 female (60%) (19 in the SPAN-negative group, 5 in the group SPAN-positive). The average age of the total sample of the study was 57 years. In the SPAN-75 negative group, the average age was 51 years old, while in the SPAN-75 positive group the average age was 75 years old.

The median NIHSS scale at admission was 11 in the positive SPAN-75 group and 7 in the negative SPAN-75 group. The median value of mRS at admission was 3 at SPAN-75 positive and 2 at SPAN-75 negative. In both groups there were no subjects with a scale of mRS 0 and 6. In the SPAN-75 negative group, 9 subjects (29%) experienced improvement and 22 subjects (71%) with no changes, whereas in the positive SPAN-75 group, there were 3 subjects (33.3%) with improvement, and 6 subjects (66.7%) with no changes. No deterioration in the degree of mRS was found in either the negative or positive SPAN-75 group.

Discussion

The SPAN-100 index was introduced in 2013 by Saposnik et al [5] to help determine the treatment of stroke patients. The SPAN-100 index is calculated by adding the patients' age with NIHSS, with a value above or equal to 100 is classified as positive SPAN-100 and a value below 100 is classified as negative SPAN-100. [5] Although other scoring systems have better prognostic strength and accuracy, [12] the SPAN-100 index is more practically applied in helping determine which patients have a better prognosis if thrombolytic or endovascular therapy is performed. In 2017, Escabillas et al modified the SPAN-100 index to SPAN-75 on the basis of the difficulty of achieving a positive SPAN-100 value even with a high NIHSS score.[10]

This study assessed the role of SPAN-75 in determining the prognosis of acute ischemic stroke patients who were not treated with rTPA. The results showed that SPAN-75 had no significant relationship to the disability of patients when they were discharged from hospitals, which were assessed with mRS ($p > 0.05$). This was probably due to the short duration of follow-up (5-7 days), so that the mRS tended to have not experienced changes in either the SPAN-75 negative group or the SPAN-75 positive group. This possibility is consistent with the study of Nedeltchev et al which showed that the degree of the new mRS would show a significant change within 3 months after the patient was discharged from the hospital.[13] Research conducted by Abilleira et al also showed the SPAN-100 index showed a significant relationship with the degree of mRS after 3 months .[6]

In the other hand, the study result showed a significant relationship between positive SPAN-75 value and a higher degree of mRS ($p < 0.05$). This result was in accordance with several previous studies which showed that age and severity of stroke, the two variables that make up the SPAN-75 index, were the main factors which affect the disability of acute stroke patients. [14,15] Previous studies have shown that age over 65 years significantly increased the rate of disability in acute stroke patients as measured by the degree of mRS. [14] Demchuk et al conducted a study which showed that patients with mild strokes (NIHSS score 1-5) compared with more severe strokes (NIHSS scores 11-15,16-20,> 20) were associated with milder degrees of mRS (0-5). [15] Other research also shows that the transition of mRS degrees also correlates with changes in NIHSS scores. [16]

The results of the analysis in this study showed that age was not directly related to the degree of mRS at admission or the change in mRS when the patient was discharged, even if added to the NIHSS score variable, which formed the SPAN-75 variable, showed a significant relationship with mRS at admission . This result was likely due to the uneven distribution of subjects in which the subjects below the

age of 45 years old were only 25% (n = 10) of the total sample, compared to subjects aged over 45 years who fill 75% (n = 30) of the total sample. Sex was also not associated with the degree of mRS either at the time of admission or changes in mRS when the patient went home (p <0.05). This result was different from previous studies [14], where female sex tended to have worse degrees of mRS (> 2). This result was likely due to a small sample (n = 40) and a too short degree of follow-up of mRS.

Limitations

Limitations of our study are the short duration of follow-up so that significant changes in mRS degrees might be difficult to be achieved. Our study did not examine factors that increase the risk of positive SPAN-100 such as hypertension, atrial fibrillation, congestive heart failure, and smokers.[5]

Fundings

None

Conclusion

The SPAN-75 index is related to the degree of stroke disability in patients with acute non-thrombolysis ischemic stroke at admission but is not related to changes in the degree of disability when the patient is discharged from the hospital. There is no significant relationship between age and sex with the degree of stroke disability at the time of admission or at discharge.

TABLES

Table 1. Characteristics of study subjects (n=40)

	n	%
Age (years)		
≤65	30	75
>65	10	25
Sex		
Male	16	40
Female	24	60
NIHSS (NIH Stroke Scale)		
Admission		
Minor stroke (1-4)	8	20
Moderate stoke (5-15)	30	75
Moderate-severe stroke (16-20)	1	2.5
Severe stroke (21-42)	1	2.5
Discharge		
Minor stroke (1-4)	15	37.5
Moderate stoke (5-15)	24	60
Moderate-severe stroke (16-20)	1	2.5
Severe stroke (21-42)	0	0
MRS (Modified Ranking Scale)		
Admission		
Score 0 (Without symptoms)	0	0
Score 1 (Without significant disability)	9	22.5
Score 2 (Mild disability)	13	32.5
Score 3 (Moderate disability)	11	27.5
Score 4 (Moderate-severe disability)	6	15
Score 5 (Severe disability)	1	2.5
Score 6 (Died)	0	0
Discharge		
Score 0 (Without symptoms)	0	0
Score 1 (Without significant disability)	10	25
Score 2 (Mild disability)	20	50
Score 3 (Moderate disability)	7	17.5
Score 4 (Moderate-severe disability)	2	5
Score 5 (Severe disability)	1	2.5
Score 6 (Died)	0	0

Tabel 2. Bivariat analysis at admission

	mRS at admission n(%)					Total	p value
	1	2	3	4	5	n (%)	
Age (years)							
≤65	7 (17.5)	11 (27.5)	7 (17.5)	4 (10)	1 (2.5)	30 (75%)	0.146
>65	2 (5)	2 (5)	4 (10)	2 (5)	0 (0)	10 (25%)	
Gender							
Pria	2 (5)	7 (17.5)	3 (7.5)	3 (7.5)	1 (2.5)	16 (40%)	0.431
Wanita	7 (17.5)	6 (15)	8 (20)	3 (7.5)	0 (0)	24 (60%)	
SPAN-75							
Negative SPAN-75	9 (22.5)	12 (30)	7 (17.5)	3 (7.5)	0 (0)	31 (77.5%)	**0.002**
Positive SPAN-75	0 (0)	1 (2.5)	4 (10)	3 (7.5)	1 (2.5)	9 (22.5%)	

Tabel 3. Bivariat analysis at discharge

	mRS evaluation at discharge n (%)			Total	p value
	Improvement	No change	Deterioration	n (%)	
Age (years)					
≤65	8 (20)	22 (55)	0 (0)	30 (75%)	0.445
>65	4 (10)	6 (15)	0 (0)	10 (25%)	
Gender					
Pria	4 (10)	12 (30)	0 (0)	16 (40%)	0.578
Wanita	8 (20)	16 (40)	0 (0)	24 (60%)	
SPAN-75					
Negative SPAN-75	9 (22.5)	22 (55)	0 (0)	31 (77.5%)	0.807
Positive SPAN-75	3 (7.5)	6 (15)	0 (0)	9 (22.5%)	

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