



Original research article

Association between the frequency of stroke recurrence and cognitive function: a cross-sectional study

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Abstract

Aim: Stroke is a major health burden that causes adult mortality and disability. Cognitive impairment is common after stroke, and this condition can affect the patient's quality of life and independence. In this study, we investigated the association between stroke recurrence frequency and cognitive function.

Methods: The study design was a cross-sectional study. A purposive sampling technique was used to collect data on a total of 69 stroke patients from the University of Muhammadiyah Malang (UMM) Hospital. The inclusion criteria were stroke patients who experienced recurrence, were conscious, and able to communicate at least verbally. The determination of the number of samples was made using G*Power software with an effect size of 0.35, *p*-value of 0.05, and power of 80%. Data was collected using a sociodemographic questionnaire and mini-mental state examination. Data were analyzed using descriptive statistics and Spearman's rho correlation due to the violated normal distribution assumption.

Results: The mean age of the participants was 61.91 (12.65) years, and 84.10% of them had ischemic stroke. The highest incidence of stroke recurrence was the first recurrence (63%), and the majority of respondents had moderate cognitive impairment (52.18%). There is an association between stroke recurrence and cognitive function, with a low correlation ($p = 0.017$, $r = -0.29$).

Conclusions: The results of this study demonstrate that cognitive function will be decreased by stroke recurrence. Healthcare teams should develop strategies and intervention protocols to improve patient compliance in controlling factors that can cause stroke recurrence, so that cognitive function decline can be minimized.

Keywords: Cognitive function; Impairment; MMSE; Recurrence; Stroke

Introduction

Stroke is a major global health issue, and during the past 30 years, its prevalence has significantly increased. Stroke continues to be the second-leading cause of adult mortality and disability worldwide (Markus, 2021; Yi et al., 2020). A stroke, also known as a cerebrovascular accident (CVA), is the sudden onset of a focal neurological deficit that lasts for more than 24 hours. A stroke happens when a thrombus blocks blood vessels that carry oxygen and nutrients to the brain, or when there is a rupture in a particular area of the brain. It is typically described as a neurological deficiency caused by a vascular source of acute localized injury to the central nervous system (CNS) (Kariasa et al., 2019; Parmar, 2018; Sacco et al., 2013; Setyowati et al., 2021).

According to the WHO, there are 13.7 million new instances of stroke every year, and 5.5 million deaths due to stroke (Kemenkes, 2021). In South America, stroke incidence rates

range from 0.35 to 1.83 per 1000 per year, and from 1.74 to 6.51 per 1000 people (Saposnik et al., 2003). The prevalence and incidence of stroke are lower than in developing countries (Saposnik et al., 2003). With its frequency rising, stroke is now the sixth most prevalent cause of death in the United States (Anand et al., 2021). In the meantime, the frequency in low and middle-income nations has doubled. In Asia, the annual incidence of stroke ranges from 116 to 483 per 100,000, with hypertension being the most common risk factor (Turana et al., 2020). In 2018, stroke prevalence in Indonesia ranked third behind heart disease and cancer. It is one of the illnesses with the highest treatment expenses, according to the Indonesian Ministry of Health (Kemenkes, 2021).

The two types of stroke recognized by the International Classification of Diseases-11 (ICD-11) are ischemic and hemorrhagic. Ischemic stroke is described as an episode of neurological dysfunction caused by a focal cerebral, spinal, or retinal infarction-related episode of neurological impairment with symptoms lasting more than 24 hours. Whereas a transient

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ischemic attack (TIA) is described as a “transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemic without acute infarction”. TIAs are frequently described as a mini-stroke, and their symptoms are momentary (*i.e.*, lasting from minutes to hours but less than 24 hours). The two kinds of hemorrhagic stroke are subarachnoid hemorrhagic stroke (SAH) and intracerebral hemorrhagic stroke (ICH). Compared to patients who encounter hemorrhagic stroke, patients who experience ischemic stroke typically have a higher probability of survival (Norrving et al., 2013; Parmar, 2018; Pinzon and Viaya, 2020).

Stroke patients commonly experience some long-term stroke complications such as musculoskeletal, psychosocial, and late medical consequences. According to Chohan et al. (2019), cognitive impairment is one type of late medical consequence that could affect stroke survivors' quality of life. Post-stroke cognitive impairment occurs frequently in patients after stroke, the possible mechanisms are infarcts, and reduced hippocampal volume is independently associated with memory decline (Sun et al., 2014). Stroke influences the cognitive domain, which encompasses attention, memory, language, and orientation (Aam et al., 2020; Al-Qazzaz et al., 2014). Cognitive deficits may manifest in different ways, including confusion, memory problems, decreased mental ability, impulsiveness, distractibility, impaired judgment, executive dysfunction, and anosognosia (patient's inability to recognize his/her impairment) (Stroke Recovery Association, 2022). Within a year of the stroke, 20% to 30% of stroke patients experience cognitive impairment and memory loss (Al-Qazzaz et al., 2014; Pinzon and Vijaya, 2020). Late medical complications can also appear weeks to months after hospital discharge (Chohan et al., 2019). A meta-analysis study found a pooled prevalence of cognitive impairment was 53.4% (including, mild cognitive impairment = 37.4%, and major cognitive impairment = 16%) measured within 1.5 years post-stroke (Aam et al., 2020).

Although evidence of cognitive deterioration in stroke survivors has been reported, to our knowledge, there are limited studies that discuss the frequency of stroke recurrence and impaired cognitive function. Therefore, the purpose of this study is to ascertain whether there is a relationship between frequency of stroke recurrence and cognitive performance using primary data obtained through interviews and examinations of stroke patients in hospitals. It was hypothesized that there would be an association between the frequency of stroke recurrence and cognitive function.

Material and methods

Research design

The study design was a cross-sectional study. It was accepted by the research and ethical committee of the Medical Faculty of the University of Muhammadiyah Malang (UMM) number E.5.a/038/KEPK-UMM/II/2020.

Setting and participants

Data were collected from April 2020 to February 2021 at the UMM Hospital, East Java, Indonesia. The sample was estimated using G*Power 3.1.9.4 software, with a medium effect size of 0.35, p -value of 0.05, and power of 80%. Based on the calculation results, a minimum sample of 61 participants was obtained, but we added it to 69 participants to avoid a loss of follow-up from participants (Vetter and Mascha, 2017). The sampling technique was purposive sampling. The inclusion

criteria were stroke patients who had experienced recurrence, were conscious, able to communicate at least verbally, and willing to be respondents. The exclusion criteria were patients diagnosed with stroke for the first time. Before we collected the data, all respondents and their families received an explanation about the study and signed the informed consent.

Measurement and data collection

The independent variable in this study was stroke recurrence frequency, which has an interval data scale. The dependent variable was cognitive function. We collected sociodemographic data (including age, gender, level of education, occupation), and level of stress. For stroke disease characteristics, we only have data about stroke types. Patients did not have data regarding location of stroke and revascularization treatment. All patients received oral medicine as their therapy and performed outpatient treatment in the hospital's polyclinic. Furthermore, we used the mini-mental state examination (MMSE) questionnaires to examine the cognitive function, because MMSE is the most used screening tool for cognitive impairments after stroke (Khaw et al., 2021). A previous systematic review found that the MMSE is the most widely used cognitive screening tool for stroke, despite its lack of criterion validity (Merriman et al., 2019). The MMSE consists of 11 commands that must be answered and carried out by the respondent, which include aspects of orientation, registration, language, attention, calculation, and memory recall. The MMSE has reliable reliability, good sensitivity, and specificity for detecting a cognitive decline in patients (Devenney and Hodges, 2017; Khairunnisa et al., 2013; Nurfiandi and An, 2019; Widyanoto et al., 2021). Stroke recurrence is seen from the results of a doctor's examination. The MMSE instrument's reliability and validity test findings show an overall validity and have Cronbach's alpha value of 0.763 (Layla and Wati, 2017). MMSE has a range score of 0–30 and is categorized into (1) <10: severe cognitive impairment, (2) 10–20: moderate, (3) 21–24: mild, (4) 25–30: normal. A cutoff of <24 is used to define cognitive impairment (Khaw et al., 2021; Nakling et al., 2017).

In this research, we also measured stress scores using the international stress management association (ISMA) questionnaire, because psychological functions, for instance, stress can affect one's cognitive function so that the person experiences a decrease in memory (Purnama et al., 2020). We collected data using the international stress management association (ISMA) questionnaire, which consists of 25 items and a scoring scale of mild: <4, moderate: 5–13, and severe >14–15 (ISMA Organization, 2017).

Data analysis

Spearman's rho correlation test was used to analyze the purpose of this study, namely the relationship between stroke recurrence and cognitive function, because based on the normality test the data results are not normally distributed (p -value 0.00). We used Pearson and Spearman correlation test to analyze the association between the sociodemographic data with stroke recurrence and cognitive impairment. The sociodemographic parameters were described using descriptive statistics, such as frequency distributions, percentages, means, and standard deviations. A p -value of 0.05 or less was regarded as significant in all statistical analyses. In the Spearman test, the value of the strength of the relationship (r) and the direction of the relationship (positive or negative) will also be seen. All data were analyzed using SPSS software version 23.

Results

Demographic and clinical characteristics of participants

The mean age of the participants was 61.91 (± 12.65) years, with the majority in the late elderly age category. Males made up 52.18% of the study participants. The majority of respondents had a bachelor's education (28%), were retired from work, or worked as a housewife (53.61%). Ischemic stroke was diagnosed in 84.10% of patients with recurrent stroke, and 75.37% of patients had moderate stress (Table 1). Based on participant characteristics, age has a significant association with cognitive impairment, and stroke type has a significant

association with both variables (stroke recurrence and cognitive impairment).

Association between stroke recurrence and cognitive function

The highest prevalence of stroke recurrence was the first recurrence (63%), and the majority of respondents had similar percentages in mild and moderate cognitive dysfunction [24 (34.80%), 24 (34.80%), respectively] with an average MMSE score of 21.41 (± 4.34). There was a negative low correlation between stroke recurrence and cognitive function (with a significant MMSE domain were orientation to place and recall), it means that higher frequency of stroke recurrence, the cognitive function will decrease (Table 2).

Table 1. Participant characteristics and their correlation with cognitive and stroke recurrence

Characteristics	Mean (SD)	n (%)	Significance with	
			Recurrence stroke	Cognitive
Age	61.91 (± 12.65)		0.632*	0.004*
Gender			0.211**	0.059**
Male		36 (52.18)		
Female		33 (47.82)		
Age category			0.927**	0.046**
Early adulthood (26-35 years)		1 (1.45)		
Late adulthood (36-45 years)		6 (8.70)		
Early elderly (46-55 years)		16 (23.19)		
Late elderly (56-65 years)		25 (36.23)		
Elderly (>65 years)		21 (30.43)		
Level of education			0.782**	0.123**
Primary school		13 (18.85)		
Junior high school		8 (11.59)		
High school		20 (28.98)		
College		28 (40.58)		
Occupation			0.469*	0.277*
Civil servant		5 (7.25)		
Private workers		8 (11.59)		
Entrepreneur		13 (18.85)		
Unemployed		5 (7.25)		
Health workers		1 (1.45)		
Others (housewife, retired)		37 (53.61)		
Stroke type			0.013*	0.032*
Hemorrhagic stroke		11 (15.90)		
Ischemic stroke		58 (84.10)		
Level of stress (ISMA)			0.757**	0.098**
Mean stress score	8.70 (± 3.94)			
Mild		8 (11.59)		
Moderate		52 (75.37)		
Severe		9 (13.04)		

Note: * Pearson correlation; ** Spearman correlation. Abbreviation: International Stress Management Association (ISMA).

Table 2. Stroke recurrence, cognitive function, and statistical test results

Characteristics	Mean (SD)	n (%)	Significance <i>p</i> -value (<i>r</i>)
Stroke recurrence			0.017 (−0.29)
First recurrence		63 (91.30)	
Second recurrence		1 (1.45)	
Third recurrence		1 (1.45)	
Fourth recurrence		3 (4.34)	
Sixth recurrence		1 (1.45)	
MMSE score	21.41 (±4.34)		
Domain of MMSE			
Orientation to time			0.311 (−0.12)
Orientation to place			0.019 (−0.28)
Registration			0.564 (0.71)
Attention and calculation			0.161 (−0.17)
Recall			0.026 (−0.27)
Language			0.389 (−0.11)
Impaired cognitive function			
Normal		19 (27.50)	
Mild		24 (34.80)	
Moderate		24 (34.80)	
Severe		2 (2.90)	

Abbreviation: The mini-mental state examination (MMSE).

Discussion

The mean age of stroke survivors was 61.91 (±12.65). These findings are in line with previous studies (Liu et al., 2020; Zhuo et al., 2020), stroke patients are predominantly aged >55 years and the risk of stroke increases with age. At the age of 45–55 years, the prevalence increased by 20%, at the age of 55–64 years by 32%, and at the age of 65–74 years by 83%. Age-related alterations in the micro and macro circulation's structure and function will result in microvascular and neurovascular damage and stroke (Setyowati et al., 2021). There is a positive correlation between age and recurrence ischemic stroke (Juli et al., 2022). However, our result showed no association between age and stroke recurrence. The current research also revealed no association between level of stress with stroke recurrence and cognitive impairment. This is inconsistent with study by Purnama et al. (2020) that showed a close relationship between stress and cognitive impairment in post-stroke patients.

The majority of respondents experienced the first recurrence, with the largest type of stroke being ischemic. According to a prior study, patients with ischemic stroke (63.3%) experience recurrence more frequently than those with hemorrhagic stroke (Pinzon and Vijaya, 2020). According to a systematic review, stroke survivors had a higher prevalence of stroke recurrence (33%) than those with hemorrhagic stroke (26.3%) (Rao et al., 2016). As stated by Setyowati et al. (2021), the incidence of ischemic stroke is 81.25%. The risk of stroke recurrence will increase by 1.2% in the first 30 days, 3.4% within 90 days, 7.4% within 1 year, and 19.4% within 5 years (Stahmeyer et al., 2019). Research by Ramdani (2018) shows that the first recurrence in the >12 months period was 45.2%, in the 7–12 months period 41.1%, and 31.7% of respondents experienced a recurrence <6 months. Another study confirmed that 1 out of 10 stroke survivors had stroke recurrence within 6–12 months of the first stroke (Pinzon and Vijaya, 2020).

In this research, we assessed cognitive impairment using the MMSE questionnaire. There are several cognitive screening tools besides MMSE, such as the Montreal Cognitive Assessment (MoCA), Loewenstein Occupational Therapy Cognitive Assessment (LOTCA), and the Cognistat Assessment (Merriman et al., 2019). According to Khaw et al. (2021), the MMSE and MoCA are the most used screening tools for cognitive impairments after stroke, but a systematic review by Merriman et al. (2019) found that the MMSE is the most widely used cognitive screening tool, despite its lack of criterion validity, whereas the MoCA has good predictive validity in assessing overall cognition post-stroke. MMSE and MoCA are short-assessment cognitive tools that are widely used in neurology. However, a new study by Benaim et al. (2022) found that MMSE and MoCA are unsuitable for many post-stroke patients. For instance, a patient with motor aphasia cannot answer the MMSE and MoCA questions assessing anterograde amnesia or time orientation. Thus, Benaim et al. (2022) developed the Cognitive Assessment scale for Stroke Patients (CASP) to minimize the limitations of both instruments. Therefore, for future research, researchers can combine several instruments to achieve more valid results.

The results of our study show that there is an association between the prevalence of stroke recurrence and cognitive function. The higher the prevalence of stroke recurrence, the less cognitive function will decrease. Based on patient characteristics, age and type of stroke significantly affect or relate to cognitive function. Along with increasing age, there will be a decrease in performance of cognitive tasks. Cognitive activities require quick processing or transformation of information to make a decision, including measures of processing speed, working memory, and executive cognitive function (which includes decision-making, problem-solving, planning and sequencing of responses, and multitasking) (Dumas, 2017; Murman, 2015). The ischemic cardioembolic and large vessel subtypes of stroke were associated with significant immediate deficits in global cognition as compared to hemorrhagic stroke

(Levine et al., 2018). Nearly four times as many people worldwide suffer from ischemic strokes than hemorrhagic strokes, and 25–30% of ischemic stroke survivors experience acute or delayed vascular cognitive impairment (Kalaria et al., 2016).

Memory loss and cognitive impairment are common after stroke; more than 70% of stroke survivors develop cognitive impairment in the first year (Lee et al., 2021). A study by Renjen et al. (2015) revealed that 72% of patients have cognitive impairment after stroke, with risk factors including old age, male sex, low education, hemorrhages, and recurrence or severe stroke. Blood flow is impaired by stroke, which also causes excitotoxicity, calcium overloading, oxidative stress, dysfunction of the blood-brain barrier (BBB), microvascular injury, hemostatic activation, injury-related inflammation, immune responses, and cell death involving neurons, glia, and endothelial cells. Vasogenic edema is brought on by microvascular injury and interruption of the BBB, which might happen days later and may potentially result in bleeding. To reduce harm and enhance results, the tissue may also go through a broad variety of reparative and remodeling responses, including angiogenesis. These processes slow down as people age, causing irreparable parenchymal damage that worsens cognitive impairment (Kalaria et al., 2016).

To function normally, the brain requires sufficient blood flow to deliver nutrients and oxygen to the cortical neurons. A stroke damages specific neuroanatomical regions (right hemisphere cortex, left hemisphere cortex, or subcortex, then localizes further to the frontal lobe, temporal lobe, parietal lobe, and thalamus), causing the part of the brain that lacks blood supply to die and harm multiple cognitive functions. In addition, ischemic stroke patients had a considerable reduction in gray matter volume. The thalamus was the primary area with reduced gray matter volume. Thalamic damage following an ischemic stroke may cause abnormalities in several cognitive areas, which may eventually show up as a dementia diagnosis (Al-Qazzaz et al., 2014). The severity of cognitive deterioration or recovery after stroke fluctuates depending on each individual's premorbid capacity. Educational, occupational, lifestyle, medical comorbid, and other factors unique to each person may have an impact on the behavioral and clinical symptoms of neuropathological loads (Shin et al., 2019; Suda et al., 2020). Moreover, cognitive impairment does not follow a linear time course after stroke; short-term studies may over-diagnose cognitive post-stroke dysfunction (Renjen et al., 2015). Therefore, perhaps further follow-up or longitudinal study can reveal in more detail the impact of stroke recurrence on cognitive decline.

Implications and limitations

The findings in this study show that stroke recurrence will decrease cognitive function. Stroke patients are at risk of expe-

riencing cognitive impairment, but this impact can be minimized if the patient adheres to therapy so that the frequency of relapse is reduced. Therefore, the role of health care teams is needed to motivate patients to comply with stroke treatment and implement a good lifestyle. To our knowledge, few studies have explored the association between stroke recurrence and cognitive function. However, our study has some limitations. First, in measuring cognitive function, the researcher only used the MMSE instrument, without combining it with other instruments that have higher sensitivity – for instance MoCA and CAPS. Second, we didn't use the probability sampling technique, so the results have low external generalizability. Third, we have limited data due to stroke characteristics; in the current research we only have stroke type. Finally, we used a cross-sectional design thus we did not know the cause-effect relationship between both variables in this study. Therefore, further research can use different study designs and explore more disease and sociodemographic characteristics.

Conclusions

This study indicates that the higher the frequency of stroke recurrence, the more cognitive function will decrease. The study also showed that different types of stroke were associated with stroke recurrence, for example stroke recurrence is more common in ischemic stroke. Therefore, healthcare teams should conduct a periodic cognitive assessment, and develop strategies and interventions to improve patient compliance in controlling factors that can cause stroke recurrence, so that cognitive function decline can be minimized, because this disorder can cause impaired patient independence. Stroke patients who have decreased cognitive function also need to be stimulated so that cognitive damage does not become worse.

Ethical aspects and conflict of interests

The authors have no potential conflict of interest regarding this research, authorship, or publication.

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Author contribution

NA, RDA: made substantial contributions to the conceptualization and design, data collection, analysis, or interpretation of the results. NA, RDA, OF, EW, LS: developed the text or critically reviewed it for significant intellectual content. NA, OF, TO: final checks and submission.

Vztah mezi frekvencí recidivy mrtvice a kognitivními funkcemi: průřezová studie

Souhrn

Cíl: Cévní mozková příhoda je velkou zdravotní zátěží, která způsobuje úmrtnost a invaliditu dospělých. Kognitivní porucha je po mrtvici běžná a tento stav může ovlivnit kvalitu života a nezávislost pacienta. V této studii jsme zkoumali souvislost mezi frekvencí recidivy mrtvice a kognitivními funkcemi.

Metodika: Tato studie je průřezová. Ke sběru dat o celkem 69 pacientech s mrtvicí z nemocnice University of Muhammadiyah Malang (UMM) byla použita účelová technika odběru vzorků. Kritériem pro zařazení byli pacienti s cévní mozkovou příhodou, kteří zaznamenali recidivu, byli při vědomí a byli schopni komunikovat alespoň verbálně. Stanovení počtu vzorků bylo provedeno pomocí softwaru G*Power s velikostí účinku 0,35, *p*-hodnotou 0,05 a silou 80 %. Data byla sbírána pomocí sociodemografického dotazníku a minipsychologického vyšetření. Data byla analyzována pomocí deskriptivní statistiky a Spearmanovy rho korelace kvůli porušení předpokladu normálního rozdělení.

Výsledky: Průměrný věk účastníků byl 61,91 (12,65) let a 84,10 % z nich mělo ischemickou cévní mozkovou příhodu. Nejvyšší výskyt recidivy cévní mozkové příhody byl první recidivou (63 %) a většina respondentů měla středně těžkou kognitivní poruchu (52,18 %). Existuje souvislost mezi recidivou mozkové mrtvice a kognitivními funkcemi s nízkou korelací ($p = 0,017$, $r = -0,29$).

Závěr: Výsledky této studie ukazují, že kognitivní funkce budou sníženy recidivou mrtvice. Zdravotnické týmy by měly vyvinout strategie a intervenční protokoly pro zlepšení dodržování kontrolních faktorů pacienta, které mohou způsobit recidivu cévní mozkové příhody, aby bylo možné minimalizovat pokles kognitivních funkcí.

Klíčová slova: kognitivní funkce; MMSE; mozková mrtvice; postižení; recidiva

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