Prevalence, risk factors and secondary prevention of stroke recurrence in eight countries from south, east and southeast asia: a scoping review

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ABSTRACT

Introduction: In most Asian countries, stroke is one of the major causes of mortality. A stroke event is life-changing for stroke survivors, which results in either mortality or disability. Therefore, this study comprehensively focuses on prevalence, risk factors, and secondary prevention for stroke recurrence identified in South, East, and Southeast Asian countries. Methods: This scoping review uses the methodological framework of Arksey and O’Malley. A comprehensive search of academic journals (English) on this topic published from 2007 to 2017 was conducted. A total of 22 studies were selected from 585 studies screened from the electronic databases.

Results: First-year stroke recurrence rates are in the range of 2.2% to 25.4%. Besides that, modifiable risk factors are significantly associated with pathophysiological factors (hypertension, ankle-brachial pressure index, atherogenic dyslipidaemia, diabetes mellitus, metabolic syndrome, and atrial fibrillation) and lifestyle factors (obesity, smoking, physical inactivity, and high salt intake). Furthermore, age, previous history of cerebrovascular events, and stroke subtype are also significant influence risk factors for recurrence. A strategic secondary prevention method for recurrent stroke is health education along with managing risk factors through a combination of appropriate lifestyle intervention and pharmacological therapy.

Conclusion: To prevent recurrent stroke, health intervention should be geared towards changing lifestyle to embody a healthier approach to life. This is of great importance to public health and stroke survivors’ quality of life.

KEY WORDS:
Stroke recurrence, prevalence, risk factors, secondary prevention

INTRODUCTION

The American Heart Association (AHA)/American Stroke Association (ASA) have provided an updated definition of stroke. The disease which is broadly characterised as a central nervous system (CNS) infarction included ischaemic stroke (IS) and silent infarction, as well as intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH). CNS infarction is defined as “brain, spinal cord, or retinal cell death attributable to ischaemia, based on neuropathological, neuroimaging, and/or clinical evidence of permanent injury”.

Worldwide, stroke is the second leading cause of death after ischaemic heart disease. Stroke attributes to 5.7 million deaths per year and will be ranked as the top four leading causes of death globally in 2030. In most Asian countries, stroke is one of the major causes of death. A stroke event is life-changing for stroke survivors in relation to their physical mobility, behaviour, emotional patterns, and communication skills. Moreover, stroke survivors are at high risk of stroke recurrence.

Stroke recurrence is defined as a new neurological deficit, including ischaemic or haemorrhagic stroke, which occurs any time after the index stroke. It is evident that stroke recurrence is in effect a new neurological deficit or a deterioration of an existing deficit. Serious complications can arise from one or more episodes of stroke recurrence that results in either mortality or increased disability.

This review comprehensively focuses on evidence on prevalence, risk factors, and secondary prevention for stroke recurrence identified in countries from South (India), East (China, Taiwan, Japan, Korea), and Southeast Asia (Malaysia, Singapore, Thailand). Our review studied in South, East, and Southeast Asia serves as a precursor to our future study which will be focusing in Malaysia. These countries are earmarked due to their similarity in ethnicity, culture, dietary cultures which can be seen amongst Malaysian population. Therefore, this scoping review’s results act as a foundation in investigating various aspects of stroke recurrence.

MATERIALS AND METHODS

Scoping review’s purpose is “to map rapidly the key concepts underpinning a research area and the main sources and types of evidence available especially when an area is complex or has not been reviewed comprehensively before”. This scoping review covers the relevant available literature on stroke recurrence. This study was conducted to outline prevalence, risk factors, and secondary prevention of stroke recurrence in countries from South (India), East (China, Taiwan, Japan, Korea), and
Southeast Asia (Malaysia, Singapore, Thailand). There is currently no existing guideline for scoping reviews. The methodological framework by Arksey and O’Malley was used for the scoping review, which involved five stages, namely (1) identifying the research questions; (2) identifying relevant studies; (3) study selection; (4) charting the data; and (5) collating, summarising, and reporting the results. A flow diagram referring to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2009) showed the flow of articles from search to its final selection.

**Identifying the research questions**
The review questions were: (1) What is the prevalence of stroke recurrence in South, East, and Southeast Asian countries?; (2) What are the risk factors associated with stroke recurrence?; and (3) What is the secondary prevention of stroke recurrence?

**Identifying relevant studies**
Search in electronic databases (MEDLINE Complete at EBSCOhost, Scopus, ScienceDirect, and PubMed) was conducted. In addition, relevant research websites such as World Health Organizations (WHO) were explored thoroughly. A comprehensive search of academic journals (English) published on this topic from 2007 to 2017 was conducted. All types of studies, except systematic reviews or review papers, were included in the search. Inclusion criteria was applied to South, East, and Southeast Asian countries. After independent examination by the researchers on eligibility via titles, abstracts, and keywords, a total of 22 studies were selected for this review from 585 studies screened from electronic databases. Key search terms used for searching articles are recorded in Table I.

**Study selection**
After careful consideration, the reviewed studies were selected if information about: (1) South, East, and Southeast Asian countries; (2) profile of participants (i.e., gender, age, and ischaemic stroke patient); (3) stroke recurrence rate; (4) risk factors or factors associated with stroke recurrence; and (5) secondary prevention of stroke recurrence, were provided.

**Charting the data**
The country(-ies), author(s), year of publication, type(s) and purpose(s) of study, number of participants, and findings on prevalence, risk factors, and secondary prevention of stroke recurrence relating to South, East, and Southeast Asian countries are summarised in Table II.

**Collating, summarising, and reporting the results**
Evaluations of the review on prevalence, risk factors, and secondary prevention of stroke recurrence are illustrated in the Table II.

**RESULTS**
A total of 585 titles were identified during the search. As shown in Figure 1, 22 articles were selected and included at the final stage of screening procedure in this review. 

Majority of these research are prospective observational studies (14 studies, 63.6%) while the others are retrospective studies (five studies, 22.7%).

**Prevalence of Stroke Recurrence**
Fourteen studies in this review examined stroke recurrence rate among stroke patients reported across South, East, and Southeast Asian populations. First-year stroke recurrence rates are in the range of 2.2% to 25.4%. Meanwhile, recurrence rate with various time intervals of follow-up was reported by 2.7% patients within 30 days after their stroke, whereas 3.9% to 16.1% patients reported it in 90 days. Recurrence rate within two years after stroke was reported to be 12.9% in ischaemic stroke patients. In addition, the rate of stroke recurrence has been reported to be approximately 16% after five years of initial stroke.

**Risk Factors of Stroke Recurrence**
Stroke recurrence and its associated risk factors have been investigated in this review. After evaluating several studies, risk factors for recurrence after stroke were documented into unmodifiable and modifiable risk factors. Identification of these risk factors is crucial to prevent recurrent stroke and could be predictors of early stroke recurrence.

**Unmodifiable Risk Factors**

**Age**
The association between age and stroke recurrence was examined in three studies. Age was independently associated with recurrence of stroke within one year after the onset. A hospital-based study by Fu et al. suggested that risk factors for stroke recurrence vary between younger and older patients. Indeed, a study revealed that older patients had an increased risk of mortality in post stroke outcomes due to stroke recurrence, which includes all categories of stroke.

**Gender**
Only one study reported on gender; nonetheless, it failed to demonstrate any significant association between gender and stroke recurrence.

**Previous history of cerebrovascular events**
This refers to patients with a history of stroke, including ischaemic stroke (IS), intracerebral haemorrhage (ICH), or subarachnoid haemorrhage (SAH), circulatory ischaemia, transient ischaemic attack (TIA), carotid stenosis or intracranial large artery stenosis (ILAS). These health conditions were identified as independent risk factors for recurrent stroke. In another study, Fu et al. confirmed that relationship between previous history of cerebrovascular events and stroke recurrence was significantly associated among older stroke patients compared to younger ones.
Stroke subtype
The association between stroke subtype and stroke recurrence was examined in several studies. Ischaemic stroke subtypes were revealed to be significant independent predictors of stroke recurrence.14 Moreover, large-artery atherosclerosis (LAA) subtype was commonly higher in patients with stroke recurrence than in those without it. The difference, nevertheless was statistically, it showed no significance between different subtypes of ischaemic stroke patients.7

Modifiable Risk Factors Pathophysiological Factors Hypertension
The majority of the studies were concerning the association between hypertension and stroke recurrence, yet the results were different and inconsistent. A positive association between hypertension and stroke recurrence was found in four studies.7,12,19,22 In contrast, hypertension was not a significant risk factor for recurrent stroke in stroke patients.17,18 Wang et al. demonstrated a significant association between hypertension and stroke recurrence in only the small-artery occlusion (SAO) subtype, but not in other subtypes such as LAA, cardioembolic, and stroke of other determined and undetermined causes.15 Therefore, hypertension may not contribute to stroke recurrence equally in all subtypes of ischaemic stroke.

Ankle-brachial pressure index (ABI). Abnormal ABI was associated to atherothrombosis. Only one study looked into the association between abnormal ABI and stroke recurrence. The result showed that it was a significant independent predictor for stroke recurrence in patients with mild stroke.14

Atherogenic dyslipidaemia (AD) and hyperlipidaemia
AD is defined as having low high-density lipoprotein cholesterol (HDL-C) (<40 mg/dl) and high triglycerides (≥200 mg/dl) levels in both men and women.20 The relationship between AD and stroke recurrence was examined in three studies. Zhao et al. found that ischaemic stroke patients with AD had significantly higher risk of stroke recurrence than those without it and the risk was more pronounced among stroke patients of LAA subtype.20 In other words, recurrence in stroke patients can be predicted by low levels of HDL-C and elevated levels of serum triglyceride. The results were consistent with other studies whereby low HDL-C levels were considered as a significant risk factor for stroke recurrence.27 Besides that, a few studies had shown that hyperlipidaemia was demonstrated to be a risk factor for subsequent stroke and other vascular events.5,22

Diabetes mellitus
The association between diabetes mellitus and stroke recurrence was discovered in nine studies.1,5,12,13,15,17-19,22 The results demonstrated that diabetes mellitus was an independent risk factor for recurrent stroke in stroke patients.5,13,15,17,19,22 Nonetheless, Pan et al. determined that this association was only found in the SAO subtype and, not in other stroke subtypes.5 In addition, evidence showed that it was not a strong risk factor in young men.17 Nevertheless, the results were inconsistent as Chen et al. discovered that diabetes mellitus was not a significant risk factor for stroke recurrence.18

Metabolic syndrome (MetS)
MetS is defined according to the International Diabetes Federation (IDF) criteria. Individuals are considered to have MetS if they have central obesity (waist circumference ≥90 cm for Asian men or ≥80 cm for Asian women), in addition to any two of four additional factors such as elevated triglyceride levels (≥150 mg/dl), decreased HDL-C levels (<40 mg/dl in males; <50 mg/dl in females), elevated blood pressure, and elevated FPG levels (≥100 mg/dl).1 The association between MetS and stroke recurrence was determined in two studies. Kono et al. found that MetS was associated with stroke recurrence;11 nonetheless, Mi et al. discovered the reverse.1

Atrial fibrillation (AF)
Relationship between AF and stroke recurrence was evaluated in five studies.12,13,15,18,19 A significant association between AF and stroke recurrence was determined in these studies.12,13,15,18 Nevertheless, Chen et al. found contradictory results.18

Lifestyle factors
Obesity. The association between obesity and stroke recurrence was observed in two studies. Obesity or body mass index (BMI) greater than or equal to 25 kg/m² was determined to be an independent predictor for stroke recurrence.14,15

Smoking. The impact of smoking on stroke recurrence was examined. The study by Xu et al. showed that smoking was significantly associated with stroke recurrence.15

Physical inactivity
Two studies examined the relationship between physical inactivity and stroke recurrence as their relationship has not yet been renowned. Physical inactivity was found to be significantly associated with stroke recurrence.14,24

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Table I: Key terms in the scoping review

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Abbreviations:
- ABI: Ankle-brachial pressure index
- BMI: Body mass index
- HDL-C: High-density lipoprotein cholesterol
- LDL-C: Low-density lipoprotein cholesterol
- IS: Ischaemic stroke
- mRS: Modified Rankin Scale
- SAH: Subarachnoid haemorrhage
- AD: Atherogenic dyslipidaemia
- CHD: Coronary heart disease
- HS: Haemorrhagic stroke
- ICH: Intracerebral haemorrhage
- MetS: Metabolic syndrome
- NIHSS: National Institute of Health Stroke Scale
- TIA: Transient ischaemic attack
- AF: Atrial fibrillation
- FPG: Fasting plasma glucose
- LAA: Large-artery atherosclerosis
- ILAS: Intracranial large artery stenosis
- MI: Myocardial infarction
- PSD: Poststroke dementia
High salt intake
The association between high salt intake and stroke recurrence was evaluated in two studies. \(^{14,24}\) Higher salt intake was significantly associated with higher stroke recurrence. \(^{14,24}\)

Secondary Prevention of Stroke Recurrence
The primary concept for secondary prevention is through modification of risk factors. If modification of risk factors is not properly managed, risk of stroke recurrence is high. Thus, to prevent stroke recurrence effectively, optimal management of risk factors, especially the modifiable ones at a certain level is important for the outcome and quality of life among stroke patients. An integration of appropriate pharmacological treatment and lifestyle modification was emphasized to prevent recurrent stroke and vascular consequences. \(^{22,23,25}\)

Healthy lifestyle interventions can be achieved by controlling body weight, increasing daily physical activity, reducing salt intake, smoking cessation, alcohol reduction, and lastly modifying dietary patterns such as low saturated fat intake, caloric restriction, and increase potassium-rich foods. \(^{22,23,24}\)

Other than that, persistent health education was the strongest associated factor in secondary stroke prevention. \(^{22}\) Lastly, the findings in Suanprasert and Tantirithisak stated that folic acid and statin therapies were important for stroke recurrence protection. \(^{7}\)

DISCUSSION
Stroke is one of the major causes of death in most Asian countries. According to Nomura et al., stroke continues to be one of the leading causes of death in Japan. \(^{23}\) Stroke also causes higher risk of physical disability among stroke survivors. \(^{7}\) Moreover, stroke recurrence may increase the disability of patients, even leading to possible mortality. \(^{7}\) Two types of strokes reacted differently, for example, ischaemic stroke patients had a higher recurrence rate and late mortality whereas haemorrhagic stroke patients had a higher early mortality rate. \(^{21}\)

In this review, the recurrence rate is about 1 in 4 persons within one year. And as time goes on, their chance of getting recurrent stroke will decrease. Therefore, it is imperative that stroke survivors are preventing another stroke by adhering to secondary stroke prevention strategies during the highest risk time.

The high recurrence rate could be due to the increased prevalence of recurrent risk factors such as dyslipidaemia, diabetes mellitus, and obesity. \(^{14}\) In addition, race could also be a possible reason for high rates of stroke recurrence. It had been demonstrated by Sacco et al. that Asian populations such as Chinese, Koreans, and Japanese tend to have a higher stroke incidence and stroke recurrence compared to Western populations. \(^{27}\)

Identifying risk factors for subsequent stroke events in stroke survivors would vary depending on different geographical regions. \(^{13}\) In this review, the risk factors of stroke recurrence are divided into unmodifiable risk factors which are age and previous history of cerebrovascular events, while the modifiable risk factors include hypertension, ABI, AD, diabetes mellitus, MetS, AF, obesity, smoking, physical inactivity and high salt intake.

Age had been determined as an immutable risk factor for stroke recurrence in which older patients had a higher risk of stroke recurrence. \(^{7}\) Well-controlled systolic and diastolic blood pressure reduced the incidence of stroke recurrence. \(^{25}\) For example, by controlling blood pressure stroke patients were able to halve the risk for stroke recurrence. \(^{12}\) In addition, the study found out that stroke patients with AD were more prone to have type 2 diabetes mellitus, and higher BMI and fasting plasma glucose values; therefore, IS patients with AD had significantly higher risk of stroke recurrence than those without. There was clear evidence that HDL-C helped in preventing atherosclerosis and acted as an antioxidant. \(^{19}\) Thus, stroke survivors are recommended to increase HDL-C levels.

Indeed, stroke patients with diabetes mellitus appeared to be older, many were female, and most were obese and had more vascular risk factors (namely previous stroke history, hypertension, dyslipidaemia). \(^{14}\) These may be due to diabetes mellitus being associated with endothelial dysfunction and increased platelet aggregation. Diabetes glucose control was recommended among diabetic stroke patients to reduce microvascular and possibly macrovascular complications. \(^{25}\)
Although many traditional risk factors for stroke recurrence have been identified, other new modifiable risk factors remain to be explored. For instance, MetS provided a new focus. Patients with MetS were more likely to be female, younger, and non-smokers, and rarely have a previous history of AF compared to stroke patients without a metabolic syndrome. Besides that, obesity was a newly identified risk factor which made it a new content for the study of stroke recurrence. Therefore, controlling body weight was important as a long term lifestyle changes. 

Evidence showed that risk for recurrence was detected to be slightly higher in current smokers compared to non- or former smokers. Thus, smoking cessation was recommended for patients with stroke. In addition, increase in exercise helps to prevent stroke recurrence by improving insulin sensitivity and increasing HDL-C levels in stroke patients. Furthermore, moderate intensity physical activities were recommended for most days of the week, which should last for at least 30 minutes to have a good effect on vascular health, including anti-inflammatory and antioxidant effects.

High prevalence of stroke recurrence highlighted the importance of secondary prevention. Secondary prevention refers to standard therapeutic guideline for patients with stroke as these patients have another recurrent stroke or other vascular events within a few years. It was observed that recurrence rates were significantly higher in stroke patients who failed to execute secondary preventive treatment. Better control and early awareness of risk factors could bring about effective stroke recurrence prevention.

Persistent health education among patients with a more educated profile instead of income or occupation would adhere to better self-management of the disease due to higher rates of awareness, control of cardiovascular risk factors, and lifestyle behaviours. Nevertheless, usually education does not make any difference after young adulthood. Therefore, a successful intervention to reduce stroke recurrence is to develop and implement stroke education programmes through appropriate techniques to deliver the messages effectively.

Interestingly, a study in Thailand showed that folic acid was associated with decreased incidence of recurrent stroke. This makes therapeutic modification of stroke possible, using dietary supplements like folic acid, and vitamins B6 and B12 that reduces homocysteine levels in stroke patients.

Finally, this scoping review noticed that there was limited evidence on prevalence rates, risk factors, and secondary prevention of stroke recurrence among other Asian countries besides those countries in this review. Therefore, future collaborative researches are necessary to address the overall prevalence rates and guidelines of secondary prevention in terms of lifestyle modification based on Asian populations.

CONCLUSION

In conclusion, screening for stroke recurrence risk factors will help in decreasing the burden of cerebrovascular diseases in the community, especially when stroke incidence in low- middle income countries in Asia is on a rising trend. Health system planning on controlling risk factors for stroke recurrence protects and reduces recurrent stroke attacks. To prevent recurrent stroke, health intervention should be geared towards changing lifestyle to embody a healthier approach to life. This is of great importance to public health and quality of life of stroke survivors.

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