

Wu Yee Sun College 2018/19 MBChB Final Year Project - Stroke

STROKE

Background

Stroke is defined as the hypoperfusion of brain tissues, leading to cellular hypoxia and damage. The two common types of stroke are ischaemic and haemorrhagic strokes (WHO, 2010).

According to the Global Burden of Disease report published by WHO in 2008, 30.5 million of people worldwide suffered a stroke. The number of new cases for first-ever stroke in 2000 and 2002 were 3.8 million and 15.3 million respectively, showing an increasing trend in worldwide prevalence (Yu, R, Chau, PH, McGhee, SM, et al., 2012).

In Hong Kong, an increasing trend in the prevalence rate of stroke among population aged 65 or above is illustrated and the rate increased from 2.8% in 1998 to 4.2% in 2004 (Census and Statistics Department, 2005). Including all new, recurrent and old strokes, the number of stroke episodes recorded from 1999 to 2007 was 166,355. A decreasing trend in the incidence of new strokes is observed across both sexes, with the rate reducing from 526.4 per 100,000 persons in 1999 to 353.5 per 100,000 persons in 2007 for men and 440.1 per 100,000 persons to 279.4 per 100,000 persons in 2007 for women respectively. However, the incidence of recurrent and old strokes remains relatively stable (Woo, 2014).

Stroke carries significant morbidity and mortality rate. It is the fourth leading cause of death in Hong Kong, accounting for approximately 3,000 deaths per year (Centre for Health Protection, 2018). The mortality rate of stroke varies among different age groups and the rate is higher in the age group of 65 or above, contributing to 86% of the deaths of stroke in 2009 (Department of Health of HKSAR, 2011). Despite the steady number of absolute deaths from stroke between 2001 to 2018, the age adjusted mortality rate from stroke decreased from 63.5 per 100,000 in 2001 to 49.2 per 100,000 in 2009 (Department of Health of HKSAR, 2011).

The total burden of disease from stroke can be measured in terms of disability-adjusted life years, which is the sum of burden from premature death and the burden of disability. In total, 119,000 years of healthy life were lost due to stroke for people aged 65 or above in Hong Kong in 2006, with the years lost due to disability accounting for 90% of the years lost (Yu, R, Chau, PH, McGhee, SM, et al., 2012).

With high prevalence and morbidity, stroke creates burden to the health care services economically. According to the database of the Hospital Authority, the number of bed days due to stroke in public hospitals was 420,767 in 2006, spending an annual cost of 1,388 million for in-patient stroke cases. Including an estimated cost of 71 million in private sectors, the cost of hospitalization

due to stroke was 1,460 million annually. In addition, 67 million was spent in outpatient stroke services per year. With the high morbidity, rehabilitation services are also one of the major components in the burden from stroke, with 147.8 million spent annually (Yu, R, Chau, PH, McGhee, SM, et al., 2012).

In short, stroke has high prevalence and incidence in Hong Kong, with major mortality and morbidity, creating a huge burden to the health care services.

Literature review

Patients suffering from stroke are often exposed to different risk factors which increase the chance of stroke. Some of the risk factors of stroke include: hypertension, atrial fibrillation, cigarette smoking, history of transient ischemic attack (Wolf, Abbott & Kannel, 1991; Wolf, D'Agostino, Kannel, Bonita & Belanger, 1988; Stegmayr & Asplund, 1995). For example, Wolf, Abbott & Kannel noted that atrial fibrillation was the only mechanism causing 76% of cases of anterior-circulation stroke in a study of 156 stroke patients.

To minimize the risk of developing stroke, lifestyle modification is of utmost importance. As hypertension is one of the most significant risk factors, lifestyle modifications to prevent and control hypertension should be considered in terms of primary prevention. Lifestyle modifications for lowering blood pressure (BP) including weight reduction, low salt diet and exercise are recommended for patients with borderline BP values (Sarikaya, Ferro & Arnold, 2015). From the study conducted by Sarikaya, Ferro & Arnold, there is evidence that the reduction of systolic BP was associated with stroke reduction by 25%. Apart from lifestyle modification, medical measures such as anti-hypertensive drugs are indicated for those with a high vascular risk profile. Rothwell pointed out that higher variability of BP is associated with higher stroke risk and for example, calcium antagonists can be used for efficacious reduction of BP (Rothwell, 2010).

For patients with atrial fibrillation, the CHA₂DS₂-VASc score is used to predict the risk of stroke. From a study conducted by Chen, Zhang, et al, CHA₂DS₂-VASc score can be used to predict stroke and thromboembolism and it has the important advantage of identifying extremely low-risk patients with atrial fibrillation (Chen, 2013). With the score, appropriate management may be given to atrial fibrillation patients and current NICE guidelines suggests anticoagulation with vitamin K antagonists or novel oral anticoagulants for patients with a score >2 to reduce the risk of stroke (NICE, 2014).

Cigarette smoking is another risk factor of stroke. To prevent people from being exposed to this risk factor of stroke, implementing a smoking cessation programme is one of the means to reduce risk of stroke. There is evidence that the risk for ischemic stroke is largely diminished from two to four years after cessation of smoking (Kawachi, Colditz, Stampfer, et al., 1993). The Quitline programme and smoking cessation clinic are operated to encourage smoking cessation (Abdullah, Lam, Chan, et al., 2004).

Patients with previous transient ischemic attack have a higher risk of developing stroke. A study conducted by the Foothills Hospital Medical Center of Canada shows that patients with a history of transient ischemic attack or minor stroke have 10% risk for developing new ischemic lesions on MRI. Therefore, taking a full history is essential to evaluate the risk factors of developing stroke. However, patients often may not be able to inform physicians that they have a past medical history of transient ischemic attack. Nonetheless, symptoms consistent with transient ischemic attack can be obtained from the patients. Common associated symptoms include: severe headache, sudden loss of vision, sudden numbness, sudden weakness, vomiting and seizures.

Neuroimaging plays a role in identifying silent brain infarcts. Silent brain infarcts are lesions associated with mild decline in cognitive function without clinically diagnostic symptoms. According to the study done by the University of Washington in 2002, silent brain infarcts which can be identified on MRI are associated with increased risk of developing subsequent stroke in patients with no brain infarcts initially. MRI also provides prognostic information for subsequent infarcts by the degree of white matter changes.

Regarding to secondary causes of developing stroke, patients with blood pressure higher than 220/120 mmHg have increasing risk in having hemorrhagic stroke. While increase in total cholesterol, plasma lipoprotein level and decrease in high density lipoprotein are also associated with increasing risk of developing ischemic stroke. To identify these groups of patients, regular follow-up and regular blood tests should be taken to assess their control and progression in blood pressure and lipid levels. Biomarkers play a limited role in identify patients with stroke. Current available biomarkers such as D-dimer, fibrinogen, C-reactive protein, brain natriuretic peptide help to assess the likelihood of stroke by evaluating the coagulation system and cardiac function, but the sensitivity and specificity of these markers remains low and are not routinely used in clinical diagnosis of stroke.

While interventional and pharmacological management for acute treatment as well as secondary treatment of stroke has been more well-defined due to the abundance of research and

guidelines from various societies, the optimal approach of non-pharmacological measures is less clear.

A systematic review and meta-analysis by Heron et al. aimed to review the effectiveness of secondary prevention with lifestyle interventions. The review failed to find any significant results regarding the use of lifestyle interventions to modify vascular risk factors and risk of recurrent stroke.

It should be noted, however, that there are significant limitations to the systematic review, and more definitive studies are required to conclude whether lifestyle modifications are effective in secondary prevention of stroke. First of all, only 4 studies were included in the systematic review, containing 380, 28, 314, 52 patients respectively. Follow-up periods of all 4 studies were no longer than 2 years. Given the relatively low incidence of recurrent stroke and the short follow-up, it is expected that the review would be in lack of power and may fail to demonstrate any significant result.

Other issues in the reviews include the lack of consistency in approach and intensity of lifestyle interventions. Lifestyle intervention is a broad term and encompasses numerous interventions. If we were able to test different interventions in an isolated manner, we are more likely to identify measures with greater effect sizes and what interventions genuinely work. Similarly, a well-defined intensity of intervention would make results more conclusive and reliable.

Besides, outcome measures were also inconsistent, which led to difficulties in combining the results in the meta-analysis.

On the contrary, the methodology of the review is also prone to leading to false conclusions. It is noted that the primary outcomes are several vascular risk factors while the actual incidence of recurrent stroke is only a secondary outcome. Whether or not reducing vascular risk factors through lifestyle interventions translates to actual benefit of reduced risk of recurrence, and if so, in what magnitude is the risk reduced, are unclear.

All in all, there has been numerous limitations in the studies on arriving at a definitive conclusion. More studies are required to further evaluate whether lifestyle modifications are effective on secondary prevention of stroke.

Interview: Hospital Doctor

Interview on how primary care should be strengthened to help to reduce the burden with Dr Chan, a Medical trainee

Q: What is the current stroke management at HA hospitals?

A: The acute management of stroke at wards are orchestrated by neurologists assessing the patient and providing medical treatment. A dedicated stroke nurse carries out risk stratification and ward nurses provide nursing care. A radiologist is involved to interpret urgent imaging, most often CT scans. Neurosurgeons are consulted if surgical intervention is required. There are stroke management protocols, but they are not standardized in HA because not every hospital offers 24-hour TPA (thrombolytic) service. Whereas rehabilitation is multidisciplinary involving neurologists, physiotherapists, occupational therapists, nursing staff and rehabilitation hospital staff.

Q: I understand that QEH has a 24-hour TPA service, do you mind elaborating a bit on that?

A: At QEH, starting from 2008, there is a 24-hour intravenous thrombolytic therapy for acute ischemic stroke which is in collaboration with ICU and Departments of Accident and Emergency, Neurosurgery, Surgery, and Radiology. The Stroke Advance Practice Nurse is on call 24 hrs a day, and during outside office hours, assessments can be made by on-site medical specialists with the support by off-site neurologists who reviewed CT scans via remote access. The establishment of the 24-hour TPA service has been useful and able to provide immediate care for stroke patients.

Q: What is your insight on how primary care can be strengthened to help reduce the burden of stroke at HA hospitals?

A: Primary care can be strengthened by providing universal 24-hour thrombolytic service at all HA hospitals. However, having a neurology specialist on call every night for TPA is difficult considering the manpower shortage in HA, so developing a streamlined triaging system is of utmost importance.

Just some ideas: A few hospitals can share an on-call neurologist to provide emergency TPA treatment. Triage starts in AED. If imaging can be swiftly done and patient can be stabilized, they can be transferred to the nearest centre with emergency thrombolysis service if their hospital doesn't have it (better trauma diversion between cluster hospitals). A dedicated doctor or nurse can be assigned as coordinator to assess indications and stability of patients.

Another option would be the better and widespread use of the telestroke system so as to allow video conferencing between on-site stroke nurses and off-site neurologists to determine the eligibility for

thrombolysis based on clinical and radiological findings that can be seen through cellular devices. This can help alleviate the neurologists' workload for being on call all the time as well.

One more thing, the limitation of the current 24-hour TPA service may be contributed to the delay in patient delivery, which may be due to patients being uneducated to recognize stroke symptoms. Hence, more work can be done at a primary level to spread the awareness of stroke in the community. With patients being able to recognize stroke symptoms at an earlier onset and call for help immediately, this can help increase the chance and success of TPA service.

Interview: General Practitioner

We have also interviewed a general practitioner, Dr. Ng and invited him to share about his thoughts.

Primary prevention

Dr. Ng: I think the focus would be on patient education and risk factors screening. Doctors should proactively encourage patients to work on optimizing the modifiable risk factors (i.e. diet, smoking) of stroke in their daily consultation, and practise anticipatory care. Government can provide subsidies for general practitioners in the private sector to screen for some chronic disease risk factors (i.e. performing blood tests for lipids) and this would facilitate better identification. However, appropriate subsidies should be provided to drive this practice.

Secondary prevention

Dr. Ng: For patients that already harbour significant risk factors, for instance atrial fibrillation, doctors can provide appropriate medication. This should be carefully tailored to each patient's profile by considering other co-morbidities and co-existing risk factors. Condition such as carotid artery stenosis is also reasonable to screen for in primary care, but again government should provide subsidies. For alarming presentations such as transient ischemic attack, medications and appropriate referrals must be promptly considered.

Tertiary prevention

Dr. Ng: Doctors can work with the patient on rehabilitation and remind the patient on important items such as how to prevent falls and maintaining mobility post-stroke. Nevertheless, it can sometimes be hard for a general practitioner to provide holistic care, because stroke patients require multidisciplinary care, such as physiotherapy and occupational therapy on top of having a family doctor. However, they might not be readily accessible in terms of location (i.e. elderly can't travel very far) and availability in some of the current community settings. Recent proposal of district health

centres can possibly tackle this problem, but most importantly government needs to make them accessible for this target group.

Discussion

As of the increasing trend in chronic illnesses in our locality, the Food and Health Bureau has recently set up the District Health Centre (DHC) in Kwai Tsing in view of relieving the burden in hospitals. This is a pilot Health Centre aimed to provide primary healthcare for the public suffering from chronic illnesses. The Kwai Tsing DHC will be a hub comprising a Core Centre serving as the DHC headquarters, supplemented by five Satellite Centres in Kwai Tsing sub-districts and a network of medical and healthcare practitioners providing multiple access and service points. The basic services provided by the DHC includes primary, secondary and tertiary prevention services.

With the aim of preventing recurrence of stroke at the level of primary health care, the DHC intends to work on different levels to provide a holistic approach in aiding the patients, and educating them for self-management of health. First of all, the DHC's primary prevention would be to prevent any new cases or recurrence of stroke by promoting healthy lifestyles. Secondly, the secondary prevention would be to screen for high risk groups and to identify individuals likely to develop stroke, with treatment given in advance in order to preventing stroke from occurring. An early detection could undoubtedly lead to better prognosis, and is key in primary healthcare. Thirdly, tertiary prevention services include post-stroke rehabilitation services that aims to improve prognosis and to maintain an independent lifestyle where self-management of health is possible. The details of such preventative approaches to improve primary care management of stroke would be discussed below.

As previously discussed, patient education is of utmost importance in order to achieve successful primary prevention, as well as timely treatment of stroke. This does not only limit itself to lifestyle modifications like cessation of smoking and low fat diet, but also the public's recognition of stroke symptoms if they happen to occur. As TPA therapy is only indicated for a few hours after onset of symptoms, stroke patients must be immediately delivered to the hospital. For medical practitioners, this entails that the onset of symptoms is key to deciding between TPA therapy and other modalities of treatment, this is also supplemented by clinical and radiological findings. The implementation of telestroke system can also help to assist clinicians in managing stroke should they not be available on site.

Although there is no reliable evidence that suggests primary prevention by lifestyle modification can work, it is often the part of the treatment to manage significant comorbidities of

stroke, such as atrial fibrillation, coronary artery disease, and hypertension. Examples include giving statins to lower the cholesterol levels in blood and giving warfarin to patients with atrial fibrillation. However, giving warfarin also gives rise to an increased risk of haemorrhagic stroke. The use of CHA₂DS₂-VASc score consists of a few elements which overlaps with HAS-BLED score, which is a scoring system used for calculating the 1 year risk of major bleeding in patients taking anticoagulants with atrial fibrillation. The overlapped criteria includes: age >65, hypertension, previous history of stroke.

On the other hand, screening and identification of high risk groups ensure effective secondary prevention. Similar to most diseases, stroke can be preventable through early diagnosis and treatment of high risk conditions such as atrial fibrillation, history of transient ischaemic attack, high level of total cholesterol and plasma lipoprotein, low level of high density lipoprotein and hypertension. DHC facilitates early detection of high risk patients as they can be screened out in multiple different settings including referral by DHC Service Providers, Satellite Centers and DHC staff in outreach activities. DHC then enables efficient and proper preventive management via a chain of readily accessible service packages such as drug counselling and medication consultation. Such packages including health assessment are under governmental subsidies which, according to Dr Ng, can be a driving force for more extensive coverage and better identification of high risk patients. Tests for blood lipid profile and consultation for pre-existing high risk conditions such as atrial fibrillation can be costly and will deter individuals with potential risk from receiving proper diagnosis and treatment. Extensive subsidies for the high risk group allows more patients to be favored and promotes stroke prevention through the necessary means including higher patient drug compliance which accounts for better disease progression control.

As seen from the interview with Dr. Ng, it is critical to provide holistic care as tertiary prevention for patients post-stroke with physiotherapy, occupational therapy, and patient education. With all things considered, the treatment regime should be guided by the expertise of the primary physician of the patient after obtaining the full picture. Guidelines are in place to provide physicians with a framework, but after all, medicine is still an art endeavoring to tailor to patients' personal needs.

Conclusion

Stroke is a prevalent health problem around the world and in Hong Kong. It is associated with significant morbidity and mortality and this places tremendous economic burden on public and private health care services with regards to hospitalisation and rehabilitation services.

Several risk factors of stroke and strategies to monitor, control or recognise them to prevent stroke have been discussed with respect to current literature. Borderline hypertensive patients should undergo lifestyle modifications while patients with higher vascular risk profile should be given anti-hypertensive medication on top of lifestyle modifications. Patients with atrial fibrillation should be assessed with the CHA₂DS₂-VASc score to determine the need for anticoagulation. Cigarette smoking cessation should be undertaken by patients with help of cessation programmes. Previous history of transient ischemic attack should be obtained to recognise the increased risk of stroke in particular patients. Regular blood testing and follow-up should be performed for assessing control and progression of dyslipidemia.

The hospital doctor we interviewed suggests that 24-hour TPA service could be made universal across all HA hospitals by devising a smoother triaging system, sharing of on-call neurologists between few hospitals and the use of telestroke systems to alleviate the burden of stroke at HA hospitals. With regards to primary care, he recommends patient education of stroke symptoms for earlier recognition and presentation. The general practitioner we interviewed similarly suggests stroke risk factor education and screening with governmental subsidisation on the primary level. On a secondary level, he endorses medication control and specialist referral. For tertiary prevention, he suggests a multidisciplinary approach to rehabilitation which might be challenging currently due to the inaccessibility of such services in local communities.

The Government's DHC proposes to deliver services such as health promotion, health assessment, chronic disease management and community rehabilitation. Health promotion includes programmes that facilitate lifestyle modifications, smoking cessation, alcohol prevention, management of chronic diseases such as hypertension and diabetes. Health assessment allows early identification of risk factors, diagnosis of chronic disease and prompt referral to doctor for disease control. Chronic disease management slows progression and decreases disease complications. Community rehabilitation services increases local accessibility of such services. These services are mainly consistent with the literature and doctors' opinions, making the DHC a feasible option for the prevention of stroke in the primary setting.

However, we believe that a few additional services can be considered as well. Stroke symptoms education should be emphasised through talks or pamphlets for earlier recognition of stroke to decrease the time to treatment. Stroke-specific risk assessment should be performed with referral of high-risk patients. Assessment of stroke complications for patients who suffered from stroke in a manner similar to diabetic complications screening can be performed. Finally, governmental subsidisation for risk factor screening can provide greater incentive for the public to undergo screening. With these additional services and expansion of the government's DHC to more areas, greater primary, secondary and tertiary prevention of stroke may be achieved and the burden on the public and private healthcare services may be decreased.

References

Abdullah, A. S. M., Lam, T. H., Chan, S. S. C., & Hedley, A. J. (2004). Which smokers use the smoking cessation Quitline in Hong Kong, and how effective is the Quitline?. *Tobacco Control*, 13(4), 415-421.

Abdullah, A. S. M., Hedley, A. J., Chan, S. S., Ho, W. W., & Lam, T. H. (2004). Establishment and evaluation of a smoking cessation clinic in Hong Kong: a model for the future service provider. *Journal of Public Health*, 26(3), 239-244.

Allen K, Hazelett S, Jarjoura D, et al. (2009) A randomized trial testing the superiority of a postdischarge care management model for stroke survivors. *J Stroke Cerebrovasc Dis* 18(6):443–452.

Bladin CF, Alexandrov AV, Bellavance A, et al. Seizures after stroke: a prospective multicenter study. *Arch Neurol* 2000; 57:1617.

Boysen G, Krarup LH, Zeng X, et al. (2009) ExStroke Pilot Trial of the effect of repeated instructions to improve physical activity after ischaemic stroke: a multinational randomised controlled clinical trial. *BMJ* 339:b2810.

Chen, J. Y., Zhang, A. D., Lu, H. Y., Guo, J., Wang, F. F., & Li, Z. C. (2013). CHADS2 versus CHA2DS2-VASc score in assessing the stroke and thromboembolism risk stratification in patients with atrial fibrillation: a systematic review and meta-analysis. *Journal of geriatric cardiology: JGC*, 10(3), 258.

Heron, Neil, et al. "Secondary Prevention Lifestyle Interventions Initiated within 90 Days after TIA or 'Minor' Stroke: a Systematic Review and Meta-Analysis of Rehabilitation Programmes." *British Journal of General Practice*, vol. 67, no. 654, 2016, doi:10.3399/bjgp16x688369.

Karapanayiotides T, Piechowski-Jozwiak B, van Melle G, et al. Stroke patterns, etiology, and prognosis in patients with diabetes mellitus. *Neurology* 2004; 62:1558.

Kawachi, I., Colditz, G. A., Stampfer, M. J., Willett, W. C., Manson, J. E., Rosner, B., ... & Hennekens, C. H. (1993). Smoking cessation and decreased risk of stroke in women. *Jama*, 269(2), 232-236.

Legislative Council of the Hong Kong Special Administrative Region of The People's Republic of China. (2018). *Legislative Council Panel on Health Services: District Health Centre in Kwai Tsing District*. Hong Kong.

Longstreth WT Jr, Dulberg C, Manolio TA, et al. Incidence, manifestations, and predictors of brain infarcts defined by serial cranial magnetic resonance imaging in the elderly: the Cardiovascular Health Study. *Stroke* 2002; 33:2376.

National Institute for Health and Care Excellence. (2014). *Atrial fibrillation: management*. Retrieved from National Institute for Health and Care Excellence:
<https://www.nice.org.uk/guidance/cg180/chapter/1-Recommendations#interventions-to-prevent-stroke-2>

Rothwell, P. M. (2010). Limitations of the usual blood-pressure hypothesis and importance of variability, instability, and episodic hypertension. *The Lancet*, 375(9718), 938-948.

Stegmayr, B., & Asplund, K. (1995). Diabetes as a risk factor for stroke. A population perspective. *Diabetologia*, 38(9), 1061-1068.

Sarikaya, H., Ferro, J., & Arnold, M. (2015). Stroke prevention-medical and lifestyle measures. *European neurology*, 73(3-4), 150-157.

Tanne D, Tsabari R, Chechik O, et al. (2008) Improved exercise capacity in patients after minor ischemic stroke undergoing a supervised exercise training program. *Isr Med Assoc J* 10(2):113–116.

Toledano-Zarhi A, Tanne D, Carmeli E, Katz-Leurer M (2011) Feasibility, safety and efficacy of an early aerobic rehabilitation program for patients after minor ischemic stroke: a pilot randomized controlled trial. *Neuro Rehabilitation* 28(2):85–90.

Whiteley W, Tseng MC, Sandercock P. Blood biomarkers in the diagnosis of ischemic stroke: a systematic review. *Stroke* 2008; 39:2902.

Wolf, P. A., D'Agostino, R. B., Kannel, W. B., Bonita, R., & Belanger, A. J. (1988). Cigarette smoking as a risk factor for stroke: the Framingham Study. *Jama*, 259(7), 1025-1029.

Coutts SB, Hill MD, Simon JE, et al. Silent ischemia in minor stroke and TIA patients identified on MR imaging. *Neurology* 2005; 65:513.

Wolf, P. A., Abbott, R. D., & Kannel, W. B. (1991). Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke*, 22(8), 983-988.

Yaghi S, Elkind MS. Lipids and Cerebrovascular Disease: Research and Practice. *Stroke* 2015; 46:3322.

Yu, R, Chau, PH, McGhee, SM, et al. Trends of Disease Burden Consequent to Stroke in Older Persons in Hong Kong: Implications of Population Ageing. Hong Kong: The Hong Kong Jockey Club. 2012

Woo, J., Ho, S., Goggins, W., Chau, P., & Lo, S. (2014). Stroke incidence and mortality trends in Hong Kong: Implications for public health education efforts and health resource utilisation. *Hong Kong Medical Journal = Xianggang Yi Xue Za Zhi*, 20(3 Suppl 3), 24-29.