Correlation of risk factors and ASPECT scores in patients with middle cerebral artery ischaemic stroke in HUSM

by

DR. TEO YIN EIE

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTER OF MEDICINE (RADIOLOGY)

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Supervisor: Dr WIN MAR@ SALMAH JALALUDDIN

DEDICATION

To my beloved husband,

His support and patience accompanying me throughout my master programme.

To my parents,

Who have given me strength to face all kinds of obstacles in life.

To my siblings,

Who accompanied me at all times to share my feelings with.

Biodata Abstrak Penyelidikan

CORRELATION OF RISK FACTORS AND ASPECT SCORES IN PATIENTS WITH MIDDLE CEREBRAL ARTERY ISCHAEMIC STROKE IN HUSM.

Dr Teo Yin Eie

Mmed Radiology

Department of Radiology

School of Medical Sciences, Universiti Sains Malaysia

Health Campus, 16150 Kelantan, Malaysia

Introduction: Stroke has becoming a leading cause of death in recent years. As the population ages, its incidence grows. Studying relationship between various risk factors and severity of stroke by using ASPECTS would be helpful in predicting patients' outcome after suffering a stroke. By realizing the risk factors that contribute to severe stroke, the prevention of these risk factors or their control is of upmost important in management of stroke in primary care. ASPECTS has been shown as a more accurate, reliable, reproducible and objective measures in quantifying the severity of stroke.

Objectives: The aims of this study were to correlate between GCS and ASPECTS. Besides, this study also aims to correlate the risk factors (age, gender, fasting blood sugar level and fasting lipid profile) of acute stroke patients with ASPECTS.

Patients and methods: Patients who were admitted for stroke were identified from medical wards. Their admission GCS, fasting blood sugar, fasting lipid profile and ASPECTS were traced and documented.

Results: There was good positive correlation between GCS and ASPECTS ($r=0.615$, $p<0.001$). On univariate analysis, only GCS was statistically significant (OR 0.076; 95%CI 0.011 to 0.515, $r^2 = -2.58$, $p<0.05$). One unit increament in GCS has 92.4% lesser odds to have worse ASPECTS when other confounders were not adjusted. However, multivariate analysis showed none of the variables was statistically significant.

Conclusion: This study provided a local data regarding stroke in this region of our nation. All risk factors included in this study (age, gender, fasting blood sugar level and fasting lipid profile), showed no correlation with severity of stroke. However, the prevalence of high fasting blood sugar, total cholesterol and LDL level were high among the stroke patients.

Dr. Salmah @ Win Mar : Supervisor

Dr. Sanihah Abdul Halim : Co-Supervisor

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- Radiographers of Hospital Universiti Sains Malaysia

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LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMNS

A & E	Accident and Emergency
ASPECTS	Alberta Stroke Program Early CT Score
ASEAN	Association of Southeast Asian Nation
BIC	Bayesian Information Criterion
CBV	cerebral blood volume
CT	Computed tomography
CTA	CT angiography
CVA	Cerebrovascular accident
DWI	Diffusion-weighted imaging
FBS	Fasting blood sugar
FLP	Fasting lipid profile
GCS	Glasgow Coma Scale
HDL	High Density Lipoprotein
HUSM	Hospital Universiti Sains Malaysia
kV	kilovolt
LDL	Low Density Lipoprotein
mAs	miliampereseconds
MCA	middle cerebral artery
MRI	Magnetic Resonance Imaging
mRs	modified Rankin scale
NIHSS	National Institute Health Stroke Scale
PACS	Picture Archiving and Communication System
CTP	CT perfusion
rtPA	recombinant tissue Plasminogen Activator

Tajuk: Korelasi di antara faktor-faktor risiko dengan skor ASPECT di kalangan pesakit angin ahmar akut arteri serebrum tengah di Hospital USM.

ABSTRAK

Tujuan: Menghubungkan GCS dan faktor-faktor risiko dengan skor ASPECT di kalangan pesakit penyakit angin ahmar di HUSM.

Bahan dan metod: Kami mengambil 148 sampel dari wad perubatan HUSM. Pesakit dengan ciri-ciri klinikal dan menjalani pemeriksaan imbasan CT otak dipilih sebagai sampel. Keputusan kajian darah tentang kandungan gula dan lemak berpuasa diperolehi seperti yang dijalankan dalam wad perubatan. Imej imbasan CT otak setiap pesakit angin ahmar dikaji untuk memperolehi skor ASPECTS individu. Hubungan di antara GCS dan factor-faktor risiko penyakit angin ahmar dengan skor ASPECTS dianalisa dengan cara statistik Correlation dan Regression.

Keputusan: Kami berjaya mengumpul data daripada 148 pesakit di mana 140 adalah pesakit Melayu, 8 adalah pesakit bukan Melayu, 48 adalah lelaki dan 100 adalah perempuan. Kami mendapati hubungan ketara yang positif di antara GCS dengan skor ASPECTS ($r=0.615$, $p<0.001$). Dengan analisa univariate, hanya GCS diakui sebagai penting dari segi statistik(OR 0.076; 95%CI 0.011 to 0.515, $r^2 = -2.58$, $p<0.05$). Dengan penambahan 1 unit GCS, pesakit mempunyai 92.4% kurang kemungkinannya untuk mendapat skor ASPECTS yang buruk dengan syarat faktor-faktor lain tidak dipersesuaikan. Tetapi, analisa multivariate menunjukkan tiada factor-faktor risiko atau GCS diakui penting dari segi statistik.

Konklusi: Kami mencadangkan GCS mempunyai hubungan yang ketara dengan skor ASPECTS dan boleh digunakan untuk meramal skor ASPECTS dengan syarat faktor lain tidak dimasukkan.

Title: Correlation of Risk Factors and ASPECT Score in Patients with Acute Middle Cerebral Artery Ischaemic Stroke in Hospital USM.

ABSTRACT

Purpose: To correlate the GCS and risk factors with ASPECTS among patients with middle cerebral artery territory ischaemic stroke in HUSM.

Materials and methods: In an institutional review board-approved study, the authors obtained 148 samples from medical ward of HUSM. Patients with clinically proven stroke and underwent non-contrast enhanced CT brain were recruited. Fasting blood sugar and fasting lipid profiled were obtained. CT brains were reviewed to obtain ASPECTS of each individuals. Correlation and Regression were used to assess the association and prediction between GCS and various risk factors with ASPECTS.

Results: We were able to obtain 148 patients whom 140 were Malays, 8 were non-Malays, 48 were male and 100 were female. There was good positive correlation between GCS and ASPECTS (r=0.615, p<0.001). On univariate analysis, only GCS was statistically significant (OR 0.076; 95%CI 0.011 to 0.515, r^2 = -2.58, p<0.05). One unit increament in GCS has 92.4% lesser odds to have worse ASPECTS when other confounders were not adjusted. However, multivariate analysis showed none of the variables was statistically significant.

Conclusions: We suggested that GCS is associated significantly with ASPECTS and can be applied to predict ASPECTS when other confounders were not added. The risk factors including age, gender, fasting blood sugar, total cholesterol level, triglyceride level, LDL level and HDL level have no correlation with severity of stroke.

CHAPTER 1

INTRODUCTION

Stroke, also known as cerebrovascular accident, is defined by World Health Organisation (WHO) as “rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin” (Bonita, 1992). The aetiology is due to brain cells death from lack of oxygen supply.

It is classified widely into ischaemic or haemorrhagic according to its aetiology. Ischaemic stroke is caused by blockage of the arterial supply to the brain parenchyma. Haemorrhagic stroke is caused by breakage of artery and subsequently bleeds into the brain parenchyma. Acute ischemia constitutes approximately 80% of all strokes and is an important cause of morbidity and mortality in the United States (Srinivasan *et al.*, 2006). MCA territory is the commonest affected area in comparison to anterior and posterior cerebral artery. It is one of the leading causes of the death worldwide. As the population ages, its significance will grow (Ingall, 2004).

Morbidity and mortality can be reduced by early detection and prompt management. With early presentation, patients with ischaemic stroke can be subjected to intra-arterial thrombolysis or thrombectomy according to current trend in addition to conventional antiplatelets therapy.

Despite these, the mainstay of treatment is prevention. Multiple risks factors contributing to the disease have been identified. Underlying medical conditions such as hypertension, diabetes mellitus, dyslipidaemia and heart disease are documented risk factors. Obesity, sedentary lifestyle, smoking, alcoholism and lack of exercise are examples of conditions leading to stroke gradually and silently. By controlling and reducing the occurrence of the mentioned risk factors along with lifestyle modification and awareness, the prevalence of stroke could be diminished not only in our local population but worldwide.

Despite aware of the risk factors, clinical outcome of stroke depending on the control of the underlying risk factors. Healthcare providers can identify those patients with existing risk factors from early stage to prevent stroke or at least minimize the severity of stroke if it occurs in the future.

Alberta Stroke Program Early CT score (ASPECT) was developed in order to quantify the severity of ischaemic stroke of middle cerebral artery territory (MCA) on non-contrast enhanced CT brain. As the area of infarcted brain tissue is increased, the clinical outcome of patient will be poor. It has been widely used in Western countries but not in our local setting. Local data collection and realizing the correlation of stroke risk factors to ASPECTS are crucial to assess its applicability in local population. It could affect and improve the further plans and management of the stroke patients in the future.

CHAPTER 2

LITERATURE REVIEW

2.1 Epidermiology

According to World Health Organization, every year, 15 million people worldwide suffer a stroke (Organization, 2002). Of these, 5 million die and another five million are left permanently disabled (Organization, 2002). It is among the top four leading causes of death in ASEAN countries (Organization, 2002).

Extrapolation from the Auckland Stroke Study suggests that in a population of 1 million, 1250 people will experience their first-ever stroke each year, and an additional 350 people will have a recurrent episode (Bonita, 1992). 6 months after the stroke, about two-thirds of stroke patients living at home regard themselves as independent and back to their pre-stroke functional status; the remainder, 344 representing about 15% of all acute events in a 1-year period, have residual difficulties with caring for themselves (Bonita, 1992). These reflect that there is still significant impact on quality of life in post-stroke patients.

Stroke has becoming a leading cause of death in recent years. In Malaysia, stroke was the top two leading causes of death reported by Malaysian National Burden of Disease Study (Ng *et al.*, 2014). Stroke is the third largest cause of mortality globally and the 4th in Malaysia (Tharakan, 2012). Stroke is one of the top five leading causes of death and one of the top 10 causes for hospitalization in Malaysia (Loo and Gan, 2012). Stroke is also in the top five diseases with the greatest burden of disease, based on disability-adjusted life years (Loo and Gan, 2012).

Concurrent illnesses like ischemic heart disease, diabetes mellitus type II, hypertension and dyslipidaemia are common. Hypertension was the most commonly identified risk factor (Kothari *et al.*, 1997). Hypertension is the major risk factor for stroke(Loo and Gan, 2012). High blood pressure contributes to more than 12.7 million strokes worldwide (Organization, 2002). Smoking and diabetes mellitus have been shown to be statistically significant in contributing to occurrence of stroke (Zanzmera *et al.*, 2012). Other risk factors like hypertension, coronary disease, dyslipidaemia, transient ischaemic attack and positive family history are also included in the study (Zanzmera *et al.*, 2012).

Its incidence and prevalence increases as the population ages. Stroke incidence rates rise exponentially with increasing age, with a hundred-fold increase in rates from about 3 per 10 000 population in the third and fourth decades to almost 300 in the eighth and ninth decades (Bonita, 1992). The mean age of ischaemic stroke patients admitted to HUSM from April to August 2011 was 54.5 years with 3.3% mortality rate (Loo and Gan, 2012).

Stroke is a common cause of hospitalization and contributing to long term disabilities among the patients. The most common individual complication was pneumonia (12.3%), followed by septicaemia (11.0%), and urinary tract infection (4.0%) (Hamidon and Raymond, 2003). The independent risk factors for complications were diabetes mellitus (OR 2.87; 95%CI 1.06 to 7.78), MCA infarcts (OR 10.0; 95%CI 4.1 to 24.3) and GCS less than 9 (OR 3.8; 95%CI 1.03 to 14.3) (Hamidon and Raymond, 2003).

2.2 Anatomy of middle cerebral artery (MCA)

Pertaining to this study, understanding vascular supply of the brain plays a vital role in determining the territory of each major artery in stroke. Its main blood supply is from the bilateral common carotid arteries and vertebral arteries which derived from the aorta and subclavian arteries respectively (Seeger, 1978). Common carotid artery further divided into internal and external carotid arteries. The internal carotid artery supplies the brain tissue and the external carotid artery supplies the head and neck. Internal carotid artery branches into anterior and middle cerebral arteries which supply their respective territories. Vertebral arteries join to become basilar artery before dividing into right and left posterior cerebral artery supplying the posterior circulation of the brain (Salamon and Huang, 2012). All these constitute the circle of Willis.

Middle cerebral artery (MCA) is the largest and most complex of the cerebral vessels. It has four segments, namely M1 to M4 segment (Figure 2.1).

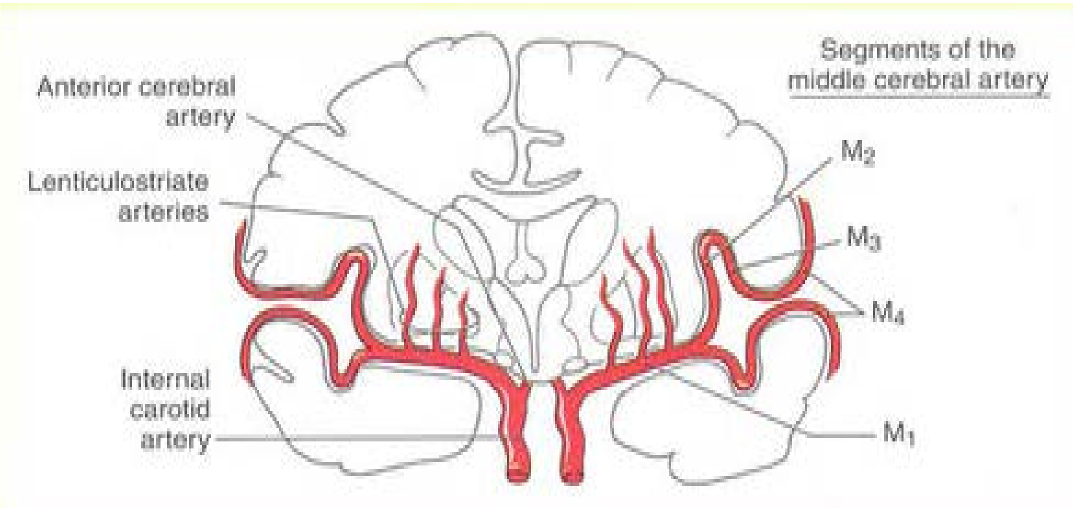

Figure 2.1 Cross-sectional anatomy of MCA (courtesy by https://quizlet.com)

M1 is from the internal carotid artery extends to the lateral fissure where the bifurcation/trifurcation begins. M1 segment also known as horizontal or sphenoidal segment. Its branches includes medial lenticulostriate penetrating arteries, lateral lenticulostriate penetrating arteries, anterior temporal artery, polar temporal artery and uncal artery.

M2 segment originates from bi(tri)furcation to circular sulcus of insula where it makes hairpin bend to continue as M3. It is also known as insular segment. It divides into two main trunks which is superior and inferior trunk. Superior trunk branches include lateral frontobasal artery, prefrontal sulcal artery, pre-Rolandic and Rolandic sulcal arteries. Inferior trunk branches include three temporal branches (anterior, middle, and posterior), branch to the angular gyrus and two parietal branches (anterior and posterior).

M3 segment, is known as opecular segment and its branches are within the Sylvian fissure. M4 segment constitutes several branches emerging from the Sylvian fissure onto the convex surface of the hemisphere and also known as cortical segment.

To be specific, medial lenticulostriate penetrating arteries, lateral lenticulostriate penetrating arteries, which are branches of M1 segment, supply the basal ganglia and internal capsule. Orbitofrontal, prefrontal, pre-Rolandic and Rolandic artery supply the frontal lobe. Anterior parietal, posterior parietal, angular and temporo-occipital artery supply the parietal lobe. Temporopolar, anterior, middle and posterior temporal artery supply the temporal lobe.

MCA supplies the majority of the lateral surface of the hemisphere, except the superior portion of the parietal lobe and the inferior portion of the temporal lobe and occipital lobe. Majority of lateral surface of hemisphere which constitutes cortico-subcortical territory (Figure 2.2), is supplied by M2-M4 segment. M1 mainly supplies the deep territory (Figure 2.2) which includes internal capsule and basal ganglia. Basal ganglia include caudate nucleus, putamen and globus pallidus. Areas supplied by cortico-subcortical and deep territory comprises majority of the entire brain. These area play major functions of the brain including motor, sensory and cognition. Hence, brain cells death from stroke involving MCA territory is debilitating and carries significant morbidity and mortality.

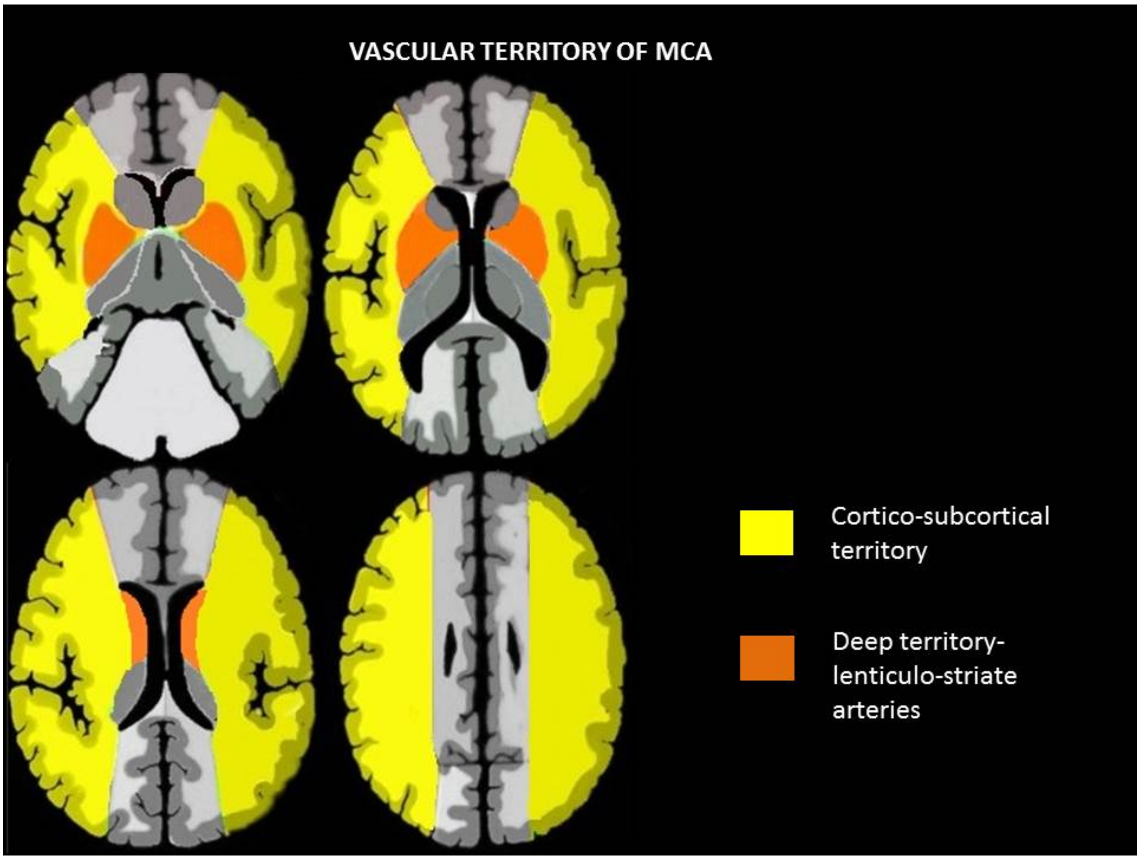

Figure 2.2. MRI of vascular territory of MCA (Popa, 1970). Yellow and orange coloured areas are MCA territory. Non-highlighted area is anterior and posterior cerebral artery territory.

2.3 Fasting blood sugar and fasting lipid profile

As major risk factors for stroke and ischaemic heart disease, diabetes mellitus and dyslipaemia are confirmed via blood investigations. Blood is drawn from patients with at least eight hours of fasting to avoid inaccuracy during serum analysis.

According American Heart Association, the normal fasting blood glucose level of an adult is ranging from 3.9 to 5.5 mmol/L (70 to 100mg/dl). Impaired glucose tolerance is between 5.6 to 7.0mmol/L (101 to 126 mg/dl). To diagnose diabetes, any fasting glucose level above 7.0mmol/L (126 mg/dl) is considered abnormal (Association, 7.5.2012).

Fasting lipid profile includes total cholesterol level, triglyceride level, LDL and HDL levels. Total cholesterol is the summation of LDL, HDL and (0.2 x triglyceride). According to American Heart Association, normal value of total cholesterol is less than 5.0mmol/L (195mg/dl). Normal triglyceride and LDL level is less than 1.7mmol/L (150mg/dl) and 2.6mmol/L (100 mg/dl) respectively (Association, 2012). Triglyceride level of 1.7-2.2 mmol/L is considered borderline high and above 2.2 is confirmed high. For LDL level, 2.6-3.3 mmol/L is considered borderline high and above 3.3 is confirmed high. Both triglyceride and LDL are associated with increased risk of stroke and cardiovascular disease. HDL, which is 'good' cholesterol, should be more than 1.0mmol/L (40 mg/dl). HDL is known to be protective towards coronary heart disease and stroke.

2.4 Diagnosis of stroke and investigation

Diagnosis of stroke is based on history, signs and symptoms and lastly followed by imaging including CT scan and MRI. Unilateral weakness, numbness, and speech abnormality were the most common symptoms recognized as warning signs of stroke by our study (Kothari *et al.*, 1997). Among patients with a final diagnosis of stroke, unilateral weakness was the most common initial symptom at stroke onset noted by the patient (Kothari *et al.*, 1997). The diagnosis of whether or not a stroke has occurred is straightforward if there is a clear history of sudden onset of focal brain dysfunction, or if the symptoms were first noticed on waking, especially if the patient is aged over 50 and has vascular risk factors or disorders (Poungvarin, 1998).

Primary imaging to diagnose a stroke regardless of its subtype is CT scan. CT scan is fast and more readily available than MRI. It is widely applied in our current setting for patient presented with stroke. Magnetic resonance imaging of the brain is superior to CT scanning when the lesion is small or located in posterior fossa, or when the onset is very acute (Poungvarin, 1998). However, it is not as widely available as CT scan in developed countries. It is not cost-effective in developing countries (Poungvarin, 1998).

Sequences of the MRI include T1-weighted imaging, T2-weighted imaging, FLAIR, DWI and ADC mapping. MRI also able to differentiate ischaemic from haemorrhagic stroke. Hypointense areas were seen on T2-weighted MR images in patients with acute hemorrhagic stroke, in contrast to normal to increased signal intensity in those with acute ischaemic stroke (Ebisu *et al.*, 1997). ADC tended to remain decreased in hemorrhagic stroke lesions even 100 days after onset, in contrast to the increased coefficient in nonhemorrhagic stroke lesions at the late chronic stage (31 days or older) (Ebisu *et al.*, 1997).

Other advance imaging like CT perfusion (CTP) and CT angiography (CTA) are also available to identify those patients benefit from thrombolytic therapy. Correlation between CTP/CTA and MRI was excellent for infarct size, cortical involvement and cerebral artery occlusion, and substantial for penumbra/infarct ratio (Wintermark *et al.*, 2007). Hence, decision making on thrombolysis could be relied on any of these modalities.

MR perfusion study is one of the advanced imaging methods. MR perfusion study was compared with CT perfusion by Schaefer. MR and CTP imaging measurements of core/penumbra mismatch for patient selection in stroke trials are highly correlated when CTP coverage is sufficient to include most of the ischemic region (Schaefer *et al.*, 2008). Although MR is currently the preferred imaging method for determining core and penumbra, CTP is comparable and potentially more available (Schaefer *et al.*, 2008). Hence, in the absence of MRI, CTP is adequate to identify salvageable penumbra in acute ischaemic stroke.

Another advanced CT imaging is multiphase CTA. Multiphase CTA generates time-resolved images of pial arteries. Pial arterial filling was scored on a six-point ordinal scale. The score of pial arteries determines the extent of collaterals. Better collateral circulation is associated with less infarct growth and better response to thrombolytic therapy, while poor collateralization is associated with hemorrhage after reperfusion therapy (Almazán, 1970). A study done by Menon has shown that interrater reliability for multiphase CTA was excellent. Ability to predict the clinical outcome by multiphase CTA was better than single phase CTA and CTP (Menon *et al.*, 2015).

2.5 Alberta Stroke Program Early CT Score (ASPECTS)

Unenhanced CT interpretation using the ASPECTS for determining the extent of stroke is a systemic approach in triaging the stroke patients (Demchuk *et al.*, 2005). It is a rapid scoring system to quantify the extent of stroke. Professor Alastair Buchan invented ASPECTS during his 10-year service in Heart and Stroke Foundation in Stroke Research in Calgary, Alberta since 1995.

It offers the reliability and utility of a standard CT examination with a reproducible grading system to assess early ischemic changes on pretreatment CT studies (Pexman *et al.*, 2001). It was compared with the 1/3 MCA rule by study run by Pexman. It has been shown that ASPECTS is superior to the 1/3 MCA rule due to its poorly defined volumetric estimate of the size of cerebral infarction of the MCA (Pexman *et al.*, 2001). ASPECT score has been shown as a more accurate, reliable, reproducible and objective measures in quantifying the severity of stroke in comparison with 1/3 rule (Pexman *et al.*, 2001). The score goes according to areas of stroke involvement in an objective way. Thus, it reduces interobserver discrepancy (Pexman *et al.*, 2001). ASPECTS is a systematic, robust, and practical method that can be applied to different axial baselines. ASPECTS allows a strong and conclusive estimation in the presence of more than one third MCA territory infarction and a cut off point of ASEPCTS < 7 results in best test performance (Pexman *et al.*, 2001).

ASPECTS was originally designed for conventional noncontrast CT to triage acute stroke. However, several recent studies have reported application of ASPECTS to CTA source images and CTP parametric color maps, with data to suggest that the acute ASPECTS is more accurately determined on these advanced CT techniques. For CTP, the cerebral blood volume was used in determining the ASEPCTS. ASPECTS also can be applied onto MRI, by using DWI sequence. Correlation of noncontrast CT, CTA source images, and CT perfusion CBV ASPECTS with final DWI ASPECTS was $r2$ = 0.34, $r2$ = 0.42, and $r2$ =0.91, respectively (Lin *et al.*, 2008). In a retrospective cohort of MCA infarcts imaged less than 3 hours from stroke onset, ASPECTS was most accurately determined on CT perfusion CBV maps (Lin *et al.*, 2008).

Management of stroke is depending on the ASPECTS at presentation. It has been used as an indicator to stratifify patient for intravenous thrombolysis. Tissue plasminogen activator (rtPA) shows favourable outcome among those with score of more than 7 (Demchuk *et al.*, 2005). According to Demchuk, ASPECTS of 8-10 is associated with lower National Institude Health Stroke Scale (NIHSS) and higher Glasgow Coma Scale (GCS) at admission and lower modified Rankin Scale (mRS). It is a good predictor for mortality and early or delayed morbidity (Zanzmera *et al.*, 2012). With good interobserver agreement, this CT score is simple and reliable and identifies stroke patients unlikely to make an independent recovery despite thrombolytic treatment (Barber *et al.*, 2000).

This study looking for association between ASPECTS and its associated factors, we can predict the severity of one’s stroke with underlying medical illnesses. Furthermore, we can strengthen the preventive program and cultivate awareness among the society regarding the importance of the risk factors.

CHAPTER 3

OBJECTIVES

3.1 General objective

To study the relationship of risk factors and ASPECTS in patients with acute middle cerebral artery ischaemic stroke.

3.2 Specific objectives

1. To correlate between GCS and ASPECTS.

2. To correlate the risk factors (age, gender, fasting blood sugar level and fasting lipid profile) of acute stroke patients with ASPECTS.

3.3 Research hypothesis

There is correlation between GCS and ASPECTS.

There is correlation between risk factors (age, sex, fasting blood sugar level and fasting lipid profile) of acute stroke patients with ASPECTS.

CHAPTER 4

METHODOLOGY

4.1 Study design

This was a cross-sectional retrospective study. Data collected from 1st April 2014 till 30th April 2015.

4.2 Study duration

This study took 2-year duration from June 2013-June 2015.

4.3 Reference population

All female and male patients admitted to Hospital Universiti Sains Malaysia (HUSM), Kelantan.

4.4 Source population

Patients more than 18 years old with clinical and CT evidence of acute middle cerebral artery territory ischaemic stroke.

4.5 Study location

Entire study took place in Hospital Universiti Sains Malaysia (HUSM), Kelantan.

4.6 Sampling method

Purposive sampling method was applied. Only patients with clinical presentation of stroke were selected as samples of the study.

4.7 Inclusion criteria

1. First episode of acute MCA territory infarct who presented to HUSM within 48 hours
2. Age>18

4.8 Exclusion criteria

1. Recurrent MCA territory stroke.
2. Associated anterior or posterior cerebral artery infarction, posterior circulation infarction, infarction due to cortical venous thrombosis.
3. Acute stroke with normal CT brain.

4.9 Sample size calculation

Sample size is calculated using Power Sample software.

For specific objective 1: GCS and ASPECTS

2 means formula – GCS

$$n = \frac{2\sigma^2}{\Delta^2} (Z\alpha + Z\beta)^2$$

- α=0.05
- Power of study=80%
- Standard deviation, SD=2.08
- Detectable difference=10
- Sample size=36 (per group) x 2= 72
- Corrected sample size=72+10% dropout=79

For specific objective 2:

Only risk factors age and diabetes were statistically significant from the reference study. Sample size calculation based on these 2 variables is as below:

1. 2 means formula – age

$$n = \frac{2\sigma^2}{\Delta^2} (Z\alpha + Z\beta)^2$$

- α=0.05
- Power of study=80%
- Standard deviation, SD=16.85
- Detectable difference=10
- Sample size=46 (per group) x 2= 92
- Corrected sample size=92+10% dropout=101

2. 2 proportions formula – DM

$$n = \frac{P1(1-P1) + P2(1-P2)}{(P1-P2)^2} (Z\alpha + Z\beta)^2$$

- P1= proportion of non-diabetic patient getting better ASPECT (literature)
- P2= proportion of diabetic patient getting better ASPECT (expert)
- α=0.05
- Power of study=80%
- P1= 0.64
- P2=0.40
- Sample size=67 (per group) x2=134
- Corrected sample size=134+10% dropout=147

From the two mean and two proportion formula calculation, variable diabetes mellitus provides the largest sample size which is 147. Hence, sample size of the study was 147.

4.10 Research tools

This study was carried out by using CT scanner in HUSM. The model is Siemen Somatom Definition AS, 128 slices, 64 detectors. The CT images were reviewed in the computer using PACS.

4.11 Method and procedure

4.11.1 Samples identification

All patients with history, sign and symptoms of stroke presented to A&E department were subjected to plain CT brain. Patients' GCS were documented from physical examination by attending medical officer at A&E department.

They were then admitted to the medical wards of HUSM which are Ward 7 Selatan and 7 Utara respectively. Within 24 hours of hospital stay, fasting blood sugar and fasting lipid profile were routinely taken as part of the management in the wards. No additional intervention involved in this study in the line of management of stroke in this hospital.

4.11.2 Data collection

To collect the data retrospectively, admission records of male and female medical wards were reviewed and patients with reason of admission of stroke/CVA were identified. Fasting blood investigations were searched under database of lab investigation results. The name and registration number of patients with fasting blood taken were written down in tracing folder request forms and sent to record office. Once the needed folders were ready, documented GCS of each patient were written in the data collection sheet.