FACTORS ASSOCIATED WITH OUTCOMES IN SURGICALLY MANAGED RUPTURED CEREBRAL ANEURYSMS

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ABSTRAK

Latar Belakang: aneurisme serebrum pecah merupakan satu keadaan yang membahayakan nyawa dan memerlukan rawatan perubatan segera. Di Malaysia, satu kajian oleh bahagian neurosurgikal Hospital Umum Sarawak dari tahun 2000-2002 telah menunjukkan purata sebanyak 2 kes aneurisme sebulan dengan kematian pembedahan sebanyak 20% dan kematian pengurusan pesakit sebanyak 25%. Kegagalan dalam mengenali penyakit sebegini, kelewatan pesakit dimasukkan ke pusat perubatan neurosurgikal dan kekurangan kemudahan boleh menpengaruhi hasil rawatan dalam pesakit-pesakit ini. Tujuan kajian ini adalah untuk mengkaji semula epidemiologi aneurisme serebrum pecah yang menjalani pembedahan di rantau ini dan mengenal pasti faktor-faktor yang boleh menpengaruhi hasil rawatan di kalangan pesakit-pesakit ini selepas pembedahan.

Bahan dan Kaedah: Kajian retrospektif satu pusat dengan menyemak rekod-rekod perubatan telah dibuat melibatkan 105 pesakit yang telah menjalani pembedahan "clipping" di Hospital Sultanah Aminah, Johor Bahru bermula dari Julai 2011 sehingga Januari 2016. Maklumat pesakit termasuk, data demografi, Glasgow Come Scale(GCS) pesakit sebelum pembedahan, World Federation of Neurosurgical Societies Scale (WFNS) pesakit dan masa antara serangan pendarahan subaraknoid sehingga pembedahan. Gred klinikal pesakit yang baik ditakrifkan sebagai WFNS gred I-III manakala gred lemah sebagai WFNS gred IV dan V. Hasil rawatan pesakit dinilai pada masa discaj dan enam bulan selepas pembedahan mengunakan skor "modified Rankin'scale (mRS)". Skor mRS 0 sehingga 2 dikumpulakan dalam ke dalam skor memuaskan (favourable) manakala skor mRS 3 sehingga 6 dalam kumpulan tidak memuaskan(unfavourable). Hanya kes-kes pendarahan subaraknoid yang melibatkan aneurisme

serebrum peach pada saluran darah bahagian depan otak yang menjalani pembedahan "clipping" dimasukkan dalam kajian ini. Data yang dikumpul dianalisis dengan mengunakan SPSS. Analisis univariat dan multivariat dibuat dan nilai $p < 0.05$ diambil sebagai kepentingan statistik.

Keputusan: Sebanyak 105 pesakit telah dikumpulkan terdiri daripada 42.9% lelaki dan 57.1% perempuan. Purata GCS pesakit yang telah menjalani pembedahan "clipping" ialah 13 dengan majoriti terdiri daripada kumpulan gred klinikal bagus(78.1%). Purata masa diambil dari serangan subraknoid sehingga pembedahan dibuat ialah 5.3 hari di mana katogori awal(sehari sehingga 3 hari) sebanyak 45.3%, pertengahan (4 hari sehingga 10 hari) sebanyak 56.2%, dan katogori lewat(melebihi 10 hari) sebanyak 9.5%. Sebanyak 59.0% pesakit mencapai hasil rawatan memuaskan manakala 41.0% dalam golongan tidak memuaskan dengan kadar kemation sebanyak 10.5% pada masa discaj. Selepas enam bulan pembedahan(n=94), pesakit yang mencapai hasil rawatan memuaskan ialah 71.3% berbanding dengan 28.7% yang tidak memuaskan dengan kadar kematian sebanyak 3.2%. Dalam analisis univariat, pesakit yang menjalani pembedahan awal, pesakit dengan GCS bagus dan pesakit yang mempunyai gred klinikal yang bagus adalah dikaitkan dengan hasil rawatan yang memuakan. Dalam analisis multivariat, pesakit lelaki berusia muda dengan gred klinikal bagus adalah dikaitkan dengan hasil rawatan memuaskan pada masa discaj apabila factor-factor lain telah diselaraskan. Pada enam bulan selepas pembedahan, analisis multivariat menunjukkan pesakit lelaki yang memiliki gred klinikal bagus dikaitkan dengan hasil rawatan yang memuaskan.

Kesimpulan: Dalam kajian ini, kami membuat kesimpulan bahawa pesakit lelaki berusia muda dengan gred klinikal yang bagus adalah dikaitkan dengan hasil rawatan memuaskan pada masa

discaj dan enam bulan selepas pembedahan. Kajian ini tidak menunjukkan kaitan dari segi masa pesakit menjalani pembedahan, saiz aneurisme dan jangka masa pembedahan dengan hasil rawatan pesakit selepas pembedahan. Usia yang semakin meningkat juga tidak dikaitkan dengan hasil rawatan pembedahan dari segi janka masa panjang.

Kata Kunci: aneurism pecah, gred WFNS, skor mRS, masa pesakit menjalani pembedahan, Hospital Sultanah Aminah,

ABSTRACT

Background: Ruptured cerebral aneurysm is a life-threatening condition that requires urgent medical attention. In Malaysia, a prospective study by Hospital Sarawak Neurosurgical center in year 2000-2002 revealed an average of 2 cases of intracranial aneurysm per month with an operative mortality of 20% and management mortality of 25%. Failure to recognize, delay in admission to neurosurgical center and lack of facilities may lead to poor surgical outcome of these patients. The purpose of the study is to review the epidemiology of the ruptured cerebral aneurysm who underwent surgical clipping in this region and to identify the predicting factors that influence the prognosis and outcome of these patients.

Material and method: A single center retrospective study with review of medical records was performed involving 105 patients who were surgically treated for ruptured intracranial aneurysm in Hospital Sultanah Aminah, Johor Bahru from July 2011 until January 2016. Information collected including the patient's demographics data, Glasgow Coma Scale (GCS) prior to surgery, World Federation of Neurosurgical Societies Scale (WFNS) of the patients and timing between SAH ictus and surgery. Good clinical grade is defined as WFNS grade I-III while poor grade as WFNS grade IV and V. The outcomes at discharge and after 6th months of surgery were assessed using modified Rankin's Scale (mRS). mRS scores of 0 to 2 were grouped into "favourable" and mRS scores of 3 to 6 were grouped into "unfavourable". Only cases of proven ruptured aneurysmal SAH involving anterior circulation and underwent surgical clipping were included in the study.   Data collected were analyzed using SPSS. Univariate and multivariate analysis were performed and p value of < 0.05 was taken as statistical significance.

Result: A total of 105 patients were included which consisted of 42.9% male and 57.1% of female patients. The mean GCS of the patient subjected for surgical clipping was 13 with majority fall into the good clinical grade (78.1%). Mean timing of surgery after SAH was 5.3 days and was further categorized into early (day 1 to day 3, 45.3%), intermediate (day 4-day 10, 56.2%) and late (after day 10, 9.5%). Total favourable outcome achieved` at discharge was 59.0% as compare to 41.0% of unfavourable outcome with an overall mortality rate of 10.5%. At 6th month of review (n=94), the patient with favourable outcome constituted 71.3% as compared to 28.7% with unfavourable outcome. The mortality at 6th month was 3.2%. On univariate analysis, early surgical clipping, patient with better GCS and good clinical grade had significant better outcome at discharge. Timing of surgery and clinical grade remained significant predictors for outcome at 6th month base on univariate study. On multivariate analysis, younger age male patient with good clinical grade is associated with favourable outcome at discharge when other factors were adjusted. Multivariate analysis done for outcome at 6th month showed only male patient and good clinical grade was associated with favourable outcome.

Conclusion: In our study, we conclude that younger male patient with good clinical grade are associated with favorable outcome at discharge and at 6th month post-surgery. We do not find timing of surgery, size of aneurysm and duration of surgery to be associated with the outcome of the patient post clipping. Increasing age is not associated with surgical outcome in longer term of patient's follow up.

Key words: ruptured aneurysm, WFNS grading, mRS scoring, timing of surgery, Hospital Sultanah Aminah,

1. INTRODUCTION & LITERATURE REVIEW

Aneurysmal subarachnoid haemorrhage (SAH) is a catastrophic condition (1, 2) affecting 30,000 individuals in the United States every year. This condition produces the significant impact on mortality and morbidity(3). Majority of individuals (60%) either die or suffer permanent disability, 50% of survivors with favourable outcome experience considerable neuropsychological dysfunction. In Japan, mortality rate for post clipping for ruptured aneurysm was 9.6 % and 0.2 % for unruptured(4). Despite advances in surgical techniques and perioperative management, the mortality and morbidity associated remain high(5). Most of the patients died as a result of the initial bleed or its complications such as rebleeding and delayed cerebral ischaemia due to vasospasm(6). Some established risk factors for poor outcome after SAH based on studies from western country include increasing age, female, hypertension, smoking, excess alcohol consumption, poor clinical condition at admission, and certain aneurysm characteristics such as posterior circulation aneurysms and large aneurysms((7, 8). In Malaysia, this condition is commonly seen however there is not much of local information published(9). A prospective study by Hospital Sarawak Neurosurgical center in year 2000-2002(9) revealed an average of 2 cases of intracranial aneurysm per month presented to their center. The center manage to achieve an operative mortality and management of 20% and 25% respectively(9). On average, Hospital Sultanah Aminah Johor Bahru received around 2-3 cases of patient with ruptured aneurysm per month. It is the sole government neurosurgical center covering the entire southern peninsular Malaysia with an estimated population of 3 million. Despite study from International Subarachnoid Aneurysm Trial(ISAT) has demonstrated that endovascular coiling of ruptured intracranial aneurysm has benefits over surgical clipping in

those patients suitable for either treatment(10), surgical clipping is the only therapeutic option in this center due to unavailability of interventional radiologist. However, the latest six-year results from The Barrow Ruptured Aneurysm Trial (BRAT) suggest little difference in outcome between the two treatments for anterior circulation aneurysms (11). Multiple predicting factors of outcome of patient with ruptured aneurysm have been discussed in various international studies however there is no local data is available (9). Recent observational study by Mayank et al.(12) published in Indian Journal of Neurosurgery showed that apart from the clinical grade at presentation, gender, age, and interval of surgery do not have significant impact over the outcome of clipped aneurysm patients. Failure in recognition, delay in admission to neurosurgical center and lack of facilities are the factors contributing to the outcome of the patients. The purpose of the study is to review the epidemiology of the surgically clipped ruptured cerebral aneurysm in this region and to identify the predicting factors that influence the prognosis and outcome of these patients. Reliable knowledge on ruptured cerebral aneurysm will help in future planning, screening and prevention strategies as well as in predicting the prognosis of each patient.

2. ETHICAL APPROVAL

JAWATANKUASA ETIKA & PENYELIDIKAN PERUBATAN
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Tarikh : 7hb Oktober 2015

LAI CHUANG CHEE
HOSPITAL SULTANAH AMINAH

Tuan/Puan,

NMRR-15-1321-25646(IIR)
A STUDY LOOKING AT THE FACTORS ASSOCIATED WITH OUTCOMES IN
SURGICALLY MANAGED RUPTURED CEREBRAL ANEURYSM IN HOSPITAL
SULTANAH AMINAH, JOHOR BAHRU (HSAJB)

Lokasi Kajian: HOSPITAL SULTANAH AMINAH

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4.   Adalah dimaklumkan bahawa kelulusan ini adalah sah sehingga **6hb Oktober 2016**. Tuan/Puan perlu menghantar dokumen-dokumen seperti berikut selepas mendapat kelulusan etika . Borang-borang berkaitan boleh dimuat turun daripada laman web MREC (http://www.nih.gov.my/mrec).

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III. Laporan mengenai "All adverse events, both serious and unexpected"/Protocol Deviation atau Violation kepada Jawatankuasa Etika & Penyelidikan Perubatan, KKM jika berkenaan.
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5. Sila ambil maklum bahawa sebarang urusan surat-menyurat berkaitan dengan penyelidikan ini haruslah dinyatakan nombor rujukan surat ini untuk melicinkan urusan yang berkaitan.

Sekian terima kasih.

BERKHIDMAT UNTUK NEGARA

Saya yang menurut perintah,

(DATO' DR. CHANG KIAN MENG)
Pengerusi
Jawatankuasa Etika & Penyelidikan Perubatan
Kementerian Kesihatan Malaysia

CC

Pengarah
Hospital Sultanah Aminah

THE FACTORS ASSOCIATED WITH OUTCOMES IN SURGICALLY MANAGED

RUPTURED CEREBRAL ANEURYSM

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ABSTRACT

Background: Ruptured cerebral aneurysm is a life-threatening condition that requires urgent medical attention. In Malaysia, a prospective study by Hospital Sarawak Neurosurgical center in year 2000-2002 revealed an average of 2 cases of intracranial aneurysm per month with an operative mortality of 20% and management mortality of 25%. Failure in recognition, delay in admission to neurosurgical center and lack of facilities may lead to poor surgical outcome in these patients. The purpose of this study is to identify the factors that significantly predict the outcome of patients undergoing surgical clipping of ruptured aneurysm in the local population.

Material and method: A single center retrospective study with review of medical records was performed involving 105 patients who were surgically treated for ruptured intracranial aneurysm in Hospital Sultanah Aminah, Johor Bahru from July 2011 until January 2016. Information collected included patient's demographics data, Glasgow Coma Scale (GCS) prior to surgery, World Federation of Neurosurgical Societies Scale (WFNS) of the patients and timing between SAH ictus and surgery. Good clinical grade was defined as WFNS grade I-III while poor grade as WFNS grade IV and V. The outcomes at discharge and after 6th months of surgery were assessed using modified Rankin's Scale (mRS). mRS scores of 0 to 2 were grouped into "favourable" and mRS scores of 3 to 6 were grouped into "unfavourable". Only cases of proven ruptured aneurysmal SAH involving anterior circulation and underwent surgical clipping were included in the study. Data collected was analyzed using SPSS. Univariate and multivariate analysis was performed and p value of < 0.05 was taken as statistical significance.

Result: A total of 105 patients were included which consisted of 42.9% male and 57.1% of female patients. The mean GCS of the patient subjected for surgical clipping was 13 with a majority falling into the good clinical grade (78.1%). Mean timing of surgery after SAH was 5.3 days and this was further categorized into early (day 1 to day 3, 45.3%), intermediate (day 4-day 10, 56.2%) and late (after day 10, 9.5%). Total favourable outcome achieved` at discharge was 59.0% as compare to 41.0% of unfavourable outcome with an overall mortality rate of 10.5%. At 6th month of review (n=94), the patient with favourable outcome constituted 71.3% as compared to 28.7% with unfavourable outcome. The mortality at 6th month was 3.2%. On univariate analysis, early surgical clipping, patient with better GCS and good clinical grade had significant better outcome at discharge. Timing of surgery and clinical grade remained significant predictors for outcome at 6th month base on univariate study.   On multivariate analysis, younger age male patient with good clinical grade is associated with favourable outcome at discharge when other factors were adjusted. Multivariate analysis done for outcome at 6th month showed only male patient and good clinical grade was associated with favourable outcome.

Conclusion: In our study, we conclude that younger male patient with good clinical grade are associated with favorable outcome at discharge and at 6th month post-surgery. We do not find timing of surgery, size of aneurysm and duration of surgery to be associated with the outcome of patient post clipping. Increasing age is not associated with surgical outcome in longer term of patient's follow up.

Key words: ruptured aneurysm, WFNS grading, mRS scoring, timing of surgery, Hospital Sultanah Aminah,

1. INTRODUCTION

Aneurysmal subarachnoid haemorrhage (SAH) is a catastrophic condition (1, 2) affecting 30,000 individuals in the United States every year. Majority of individuals (60%) either die or suffer permanent disability; 50% of survivors with favorable outcomes experience considerable neuropsychological dysfunction. In Japan, mortality rate for post clipping for ruptured aneurysm was 9.6 % and 0.2 % for unruptured(4). In Malaysia, this condition is commonly seen however there is not much local information published(9).

A prospective study by Hospital Sarawak Neurosurgical center in year 2000-2002(9) revealed an average of 2 cases of intracranial aneurysm per month presented to their center. The center manage to achieve an operative mortality and management mortality of 20% and 25% respectively(9). On average, Hospital Sultanah Aminah Johor Bahru received around 2-3 cases of patient with ruptured aneurysm per month. It is the sole government neurosurgical center covering the entire southern peninsular Malaysia with an estimated population of 3 million. Multiple predicting factors of outcome of patient with ruptured aneurysm have been discussed in various international studies however there is no local data is available(9).

Failure to recognize, delay in admission to neurosurgical center and lack of facilities are the factors contributing to the outcome of the surgically clipped patients.   The purpose of the study is to review the epidemiology of the surgically clipped ruptured cerebral aneurysm in this region and to identify the predicting factors that influence the prognosis and outcome of these patients.

2. METHODOLOGY

A single center retrospective study with review of case notes was performed involving 105 patients who were surgically treated for ruptured intracranial aneurysm from July 2011 until January 2016. Information collected including the patient's demographics, types of symptoms, Glasgow Coma Scale (GCS) prior to surgery, timing between SAH ictus and surgery, duration of surgery, location of aneurysm, and maximum size of the aneurysm. Preoperative patient's neurological condition was classified using the World Federation of Neurosurgical Societies' Scale (WFNS grades I-V, Table 1) (4)and subclassified into good clinical grade (WFNS 1-III) and poor grade (WFNS IV and V) (13). The outcomes at discharge and after 6th months after surgery were assessed using modified Rankin's Scale (mRS score 0-6, Table 2). A dichotomized mRS score based on other aneurysm studies (4, 14, 15) were used as a clinical outcome measurement of the patient post clipping. mRS scores of 0 to 2 were grouped into "favourable" and mRS scores of 3 to 6 were grouped into "unfavourable". Data collected were analyzed using SPSS and the association between predictor factors and outcome were studied using univariate and multivariate logistic regression where p value of < 0.05 is to be considered statistically significant.

Only cases of angiographically proven ruptured aneurysmal SAH involving anterior circulation who underwent surgical clipping were included in this study. Case of non-aneurysmal SAH or SAH with negative CT or MR angiogram or cerebral angiogram, aneurysms combined with arteriovenous malformation (AVM), mycotic aneurysm or unruptured aneurysm were all excluded from the study. Out of 128 cases that met the criteria, 23 of these were excluded from

the study due to incomplete information and loss of follow up. This series represents 105 cases of ruptured aneurysm from single center treated with surgical clipping.

In this institution, spontaneous SAH was diagnosed mainly by CT brain and rarely some by analysis of cerebrospinal fluid via lumbar puncture. Cerebral aneurysms were further diagnosed via CT angiogram, MR angiogram or digital subtraction angiogram and these patients were admitted under neurosurgical care. They were started with nimodipine for 21 days and phenytoin for seizure prophylaxis. Those patients with hydrocephalus were treated with external ventricular drainage (EVD) and those who developed huge haematoma underwent urgent decompression. In view of absence of neurointerventionist and limited resources, surgical clipping was selectively performed in this institution and mainly concentrated on the patient with good WFNS grade. The surgery was scheduled mainly weekdays during office hour where the surgeon and the staff were better prepared. Clipping was performed by consultant neurosurgeon using mainly Leica OH 5 microscope or occasionally with Carl Zeiss NC31. Surgical clips available including Aesculap standard clips, miniclips, and Mizoho Sugita clips. Post-surgical clipping, the patients were admitted to High Dependency Unit (HDU) with triple "H" therapy(16) for at least 72 hour. The patients with poor GCS recovery post clipping were subjected to tracheostomy and those with EVD dependent were subjected to permanent cerebral spinal fluid diversion. Clinical conditions of the patients were obtained upon discharged and at 6th month post-surgery. Data collected were analyzed using SPSS. Univariate and multivariate analysis were performed and p value of < 0.05 was taken as statistical significance.

3. RESULT

a) Demography of study data

Base on table 3, a total of 105 patient's medical records were reviewed and included into this study which consisted of 45(42.9%) male and 60 (57.1%) of female patients. The patient age ranged from 25 to 75 with a mean (SD) of 51(11.84) years. Majority of the patients were at the age group of 51-60(32.4%). The commonest presenting symptom was headache which occurred in 73.3% of cases. This was followed by reduced consciousness in 15% and seizure in 7%. Other symptoms of presentation including neck pain, photophobia, weakness and cranial nerve deficits which accounted for 6%. The mean GCS (SD) of the patient subjected for surgical clipping was 13(2.3) with majority fall into the group of WFNS grade 2 (41.0%), followed by WFNS grade 1 (21.0%) and WFNS grade 3(16.2%). Only 15.2% of the patients with the WFNS of grade IV and 6.7% of grade V were subjected to surgery in our observation. Mean (SD) timing of surgery after SAH was 5.3 (3.6) days and was further categorized into early (day1 to day3), intermediate (day 4-day 10) and late (after day 10) according to Taha et al.(17). Majority patients were treated in the intermediate group (n = 59) followed by early (n = 36) and late (n = 10). Average size of the aneurysm clipped was 6.4mm with the range from 3mm to 21mm. The commonest site of aneurysm arising from Anterior communicating artery (31.4%) followed by middle cerebral artery (26.7%). The aneurysm arisen from internal cerebral artery, anterior cerebral artery and posterior communicating artery contributed 12.4% respectively and lastly from the distal anterior cerebral artery at 4.8%. The documented duration of surgical clipping ranged from 170 to 630 minutes with the mean (SD) of 322.8(88.9) minutes.

b) Outcomes of the patient underwent surgical clipping

Majority of the post-surgical clipping patient upon discharge achieved an outcome of mRS Score of 2 (32.4%) followed by mRS score 1 (24.8%) and mRS 3 (20.0%) as shown in table 4. Mortality of the patient post clipping (mRS 6) was 10.5% at discharge. Hence, the total favourable outcome achieved at discharge was 59.0% as compare to 41.0% of unfavourable as depicted in table 4. At 6th month of review (n = 94) as tabulated in table 5, the patient with favourable outcome was 71.3% as compared to 28.7% of unfavourable.   There were 13.8% of patient with mRS score of 0, 26.6% of patient with mRS score 1, 30.9% of patient with mRS score 2 and 20.2% of mRS score 3. Mortality (mRS score 6) of 3.2% was observed after 6 months.

c) Predicting factors for favourable outcomes

Univarate logistic regression was done for each of the predicting factor that may be associated with the outcomes of patient with surgically clipped aneurysm at discharge as shown in table 6. Early surgery (p = 0.015) and better GCS (p < 0.001) had a significant higher odds to favourable outcome of the patient with surgically clipped aneurysm at discharge. Patient with WFNS grade I (p = 0.004) and WFNS grade II (p = 0.014) had significant favourable outcome compared to WFNS grade V at discharge. Good clinical grade patient had 11.4 times higher odds for having favourable outcome as compare to poor grade (95% CI: 3.5-37.3, p < 0.001). Age, gender, size of aneurysm and the duration of surgery has no statistical significance on the outcome of the patient at discharge. GCS, WFNS grading and timing of surgery remained significant predicting factors (p < 0.05) for outcome of the patient at 6th month post-surgery as depicted in table 7.

On multivariate analysis tabulated in Table 8, increased in one year of age for surgical clipping has 0.95 times lower odds of having favourable outcome at discharge (95% CI :0.92-1.00, p =0.028) when adjusted for gender, clinical grade and timing of surgery. Male gender had 2.9 times higher odds of having favourable outcome at discharge (95% CI: 1.09-7.72, P= 0.033) and good clinical grade had 11.67 times higher odd of having favourable outcome (95% CI: 3.010-44.02, p < 0.001) when other factors were adjusted. Multivariate analysis were done for similar factors for the outcome at 6th month showed only male patient (p = 0.039; OR = 3.19) and good clinical grade (p = 0.005, OR = 6.45) were associated with favourable outcome when other factors were adjusted.

4. DISCUSSION

a) Demography of aneurysm surgery

Ruptured cerebral aneurysm is a life-threatening condition that requires urgent medical attention (1, 2). On average, almost 2 patients per month were subjected for surgical clipping for ruptured aneurysm in this center. Majority of the patient are female ranging from the age of 51-60 year old. This is in correlation with the drop in estrogen level during post-menopausal period among the woman as suggested by Ghods et al.(18). Estrogen has been shown to promote normal physiologic vascular endothelial function and reduction of estrogen level leads to compromised arterial integrity and hence the development of aneurysm(18). Female patients tend to have poorer outcome probably due multiple comorbid and late presentation to the hospital. In this center, majority of surgery was done at the interval of day 4 to day 10 due to time taken for proper investigation and imaging as well as limited operating theater time.

b) Outcomes of surgical clipping

Our center manages to achieve 59% of favourable outcome at discharge and 71.3% at 6th month post-surgery. We observe a 10% increase in favourable outcomes comparing the both time frame. This is possibly due to good post-operative care by multidisciplinary team namely the rehabilitation medicine department, physiotherapy and occupational therapy as well as medical department. Functional recovery after all stroke patients is estimated to be completed within 12.5 weeks after proper acute treatment and all stages of rehabilitation(19) hence explained the increment of favourable outcomes at 6th month.

c) Predicting factors for favourable outcomes

Multiple studies have been conducted to determine the outcome of patient post-surgical clipping however different centers yield different results. A few predicting factors associated with unfavorable outcome have been proven by Axel J et al.(7) including worse WFNS grades of the patient on admission, larger aneurysm size and increased age. Study from Lintigua et al.(1) showed that rebleeding(20) and intracerebral haematoma are common cause that leads to death or devastating neurology. Taha et al.(17) concluded that timing of surgery does not affect outcome of patients however study by Sanne M et al.(21) support for early aneurysm treatment in both coiling and clipping in subarachnoid hemorrhage patients.

In our study among local population, we demonstrated patients with good clinical grade (WFNS I-III) are associated with favourable outcome at discharge and at 6th month post-surgery. Hutchinson PJ et al. (22) reported as high as 60% patients with poor clinical grade will become dependent or die while Qiao et al.(23) reported that many neurosurgeons are reluctant to treat the patients with poor clinical grade due to higher mortality and disability as well as medical cost. Poor clinical grades are associated with poorer GCS and hence patient will have poorer surgical outcome. An observational study by Helbok et al. (24) suggest that patients with poor clinical grade are associated with global cerebral edema after initial SAH and resulting in metabolic distress. The initial bleeding is associated with rapid increase in intracranial pressure and thus a reduction in cerebral blood flow(25) leading to decreased substrate delivery to the brain during a time of increased demand.

In our study, male patients are associated with favourable outcome at both discharge and 6th month post-surgery. Poorer outcome in female possibly explained by the significant higher vasospasm that lead to cerebral infarction which was demonstrated in the study by Rosenrln et al.(26) . However the recent study by Duijhuisen et al.(27) documented no difference of outcome between male and female.

In multivariate regression, we did not find timing of surgery to be significantly associated with the outcome in post clipping patient at both discharge and at 6th month post-surgery when other factors were adjusted. Recent study by Zhao et al.(15) and N Ross et al.(13) also concluded that timing of surgery is not significantly associated with the clinical outcome of the patient post-surgery. Early surgery may increases the periprocedural complication due to swollen, hyperaemic and poorly auto-regulated brain which is more prone for laceration, contusion and infarction due to retraction(28). Despite that, it is proven than early surgery prevents the risk of rebleeding that usually occurs in the first 6 hour after initial SAH(29) thus allowing aggressive medical management via triple 'H' to be started promptly to prevent vasospasm and delayed ischaemic neurological deficits. Study by Timothy j et al.(20) showed that treatment of ruptured aneurysm within 24hours is associated with improved clinical outcome compared to treatment > 24 hours.

Our study found that advancing age is a predictor factor for poor outcome at discharge which is also report by Pradeep et al. (30) and N Ross et al(13). Younger age patient has better outcome because of the fact that they have better regenerative capacity and neural plasticity as compared