FUNCTIONAL OUTCOME OF MICROSURGICAL CLIPPING COMPARED TO ENDOVASCULAR COILING

BY

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Dissertation Submitted In Partial Fulfillment Of The Requirements For The Degree Of Master Of Surgery (Neurosurgery)

UNIVERSITI SAINS MALAYSIA
2011

II. ACKNOWLEDGEMENT

I would like to express my greatest and sincere gratitude to all those who gave me the support to complete my thesis. I am most honored to express my utmost appreciation to my dedicated supervisor, Mr. (Dr) Ramesh Narenthiranathan, Consultant Neurosurgeon of Hospital Kuala Lumpur for providing me the guidance, stimulating suggestions, encouragement and advice in all the time of research and writing of this dissertation.

I would also like to thank my co-supervisor, Associate Professor Dr. Hillol Kanti Pal from Department of Neurosciences Hospital University Sains Malaysia for his invaluable suggestions and practical solutions for my research and writing of this dissertation. I am totally indebted to Professor Dr. Jafri Malin bin Datuk Abdullah, the Head of Department of Neurosciences, School of Medical Sciences, University Sains Malaysia, for his ideas, suggestions, motivation and full support in conducting this study

I also wish to extend my appreciation to Mr. (Dr.) Johari Siregar bin Adnan, Mr. (Dr.) Mohammed Saffari Mohammad Haspani, Mr. (Dr.) Azmin Kass Rosman, Mr. (Dr.) NoorAzman Abdul Rahman and Mr. (Dr.) Azmi Alias, who were ever supportive of me. I would like to offer special thanks to Dr. Liew Boon Seng of Hospital Sungai Buloh for sacrificing his time by going through my data and helping in the analysis. I am also very much obliged to all my fellow colleagues, staffs, specialists and lecturers for their support and efforts in helping me to complete this study.

Last but not least, I would like to thank my family, especially my beloved parents and brothers their immeasurable support all the way from the very beginning of my postgraduate

study. I would like to give my special thanks to my loving wife, Dr. Subashini for her thoughtfulness, patience and encouragement in enabling me to complete this thesis and to my darling children Harish and Tharshana Rani, for being my source of motivation to complete my dissertation.

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IV. ABBREVIATIONS

ACOM aneurysm : Anterior Communicating Artery Aneurysm

BA aneurysm : Basilar Artery Aneurysm

CT : Computed Tomography

DACA aneurysm : Distal Anterior Cerebral artery Aneurysm

EVD : Extraventricular Drain

HKL : Hospital Kuala Lumpur

ICA : Internal Carotid Artery

ISAT : International Subarachnoid Trial

ISUA : International Study of Unruptured Intracranial Aneurysm

MCA aneurysm : Middle Cerebral Artery Aneurysm

mRS : modified Rankin Scale

PCA aneurysm : Posterior Cerebral Artery Aneurysm

PCOM aneurysm : Posterior Communicating Artery Aneurysm

SAH : Subarachnoid Hemorrhage

VA aneurysm : Vertebral artery Aneurysm

VP Shunt : Ventriculo-peritoneal Shunt

WFNS grade : World Federation of Neurosurgeon grade

V. ABSTRAK

OBJEKTIF: Kaedah endovaskular melingkar semakin telah digunakan sebagai alternatif untuk kliping bedah saraf untuk mengubati pendarahan subaraknoid sekunder berikutan kepecahan aneurisma. Tujuan utama kajian ini adalah untuk membandingkan hasil fungsional pada enam bulan selepas pendarahan subaraknoid sekunder berikutan kepecahan aneurisma otak pada subjek yang dirawat dengan kaedah endovaskular melingkar atau kliping bedah saraf. Selain itu, kajian ini juga bertujuan untuk mengenal pasti prediktor dalam jangkamasa rawatan klinikal pendarahan subaraknoid primer.

TATACARA: Hasil analisis retrospektif terhadap kaedah rawatan kepecahan aneurisma telah dilakukan di Hospital Kuala Lumpur selama tempoh 5 tahun (2005-2009). Seramai 268 pesakit yang memenuhi criteria inklusi direkrut untuk kajian ini. Pesakit tersebut dikategorikan kepada dua kumpulan berdasarkan kaedah rawatan mereka untuk kebocoran aneurisma. Nota kes pesakit, laporan filem CT otak dan laporan angiografi dianalisis berkaitan dengan aspek klinikal, data radiologi, pembedahan atau rawatan melingkar endovaskular dan data hasil. Analisis statistik ditentukan dengan menggunakan ujian Chi-Square untuk mengkaji hubungkait antara kedua-dua kaedah rawatan yang dikaji dan hasil rawatan.

KEPUTUSAN: Hasil daripada kajian menunjukkan terdapat lebih ramai subjek perempuan berbanding dengan lelaki dalam populasi kajian (lelaki:perempuan ialah 1:1.4). Purata umur

subjek adalah 50.9 tahun. Didapati 50 pesakit berumur kurang dari 40 tahun (18.7%) manakala 218 pesakit berumur lebih dari 40 tahun (81.3%). 37 pesakit (74%) dari kelompok usia kurang dari 40 tahun telah menunjukkan hasil baik yang signifikan berbanding dengan 125 (57.3%) pesakit di atas 40 tahun ($p = 0.03$). 181 pesakit (67.5%) menunjukkan gred WFNS baik (WFNS1-2) manakala 87 pesakit (32.5%) menunjukkan gred WFNS yang tidak baik (WFNS 3-5) sebelum intervensi. Seratus enam puluh dua pesakit (60.4%) mempunyai hasil fungsional yang baik (gred mRS 0-2) dibandingkan dengan 106 pesakit (39.6%) yang mempunyai hasil mRS yang tidak baik iaitu gred mRS 3-6, malah 50 pesakit meninggal dunia (18.7%) pada waktu kajian susulan pada 6 bulan. Hasil daripada analisis kumpulan WFNS dengan hasil fungsional (mRS) menunjukkan terdapat hubungan yang signifikan ($p<0.01$). Dalam golongan pesakit dengan gred WFNS yang baik, 143 (79%) mempunyai keputusan yang baik dan dalam golongan pesakit dengan gred WFNS yang tidak baik, 68 pesakit (78.2%) mempunyai hasil mRS yang tidak baik. Terdapat 204 (76.1%) pesakit dalam kumpulan kliping dan 64 (23.9%) pesakit dalam kumpulan endovaskular melingkar. Pesakit yang menjalani kaedah endovaskular melingkar, pada awalnya menunjukkan hasil mRS yang lebih baik; iaitu 47 pesakit (73.4%) berbanding dengan 115 pesakit (56.4%) di kumpulan kliping. Perbandingan yang lebih lanjut menunjukkan bahawa 89 (43.6%) pesakit dalam kumpulan kliping mempunyai hasil fungsional (mRS) yang tidak baik berbanding dengan 17 pesakit (26.6%) dalam kumpulan endovaskular melingkar di mana perbandingan ini didapati signifikan ($p <0.05$). Namun, apabila kelas WFNS dijadikan kumpulan kawalan bagi kedua-dua kaedah yang dianalisakan, hasil yang berbeza diperolehi. Dalam kumpulan gred WFNS yang baik, dicatatkan bahawa 98 pesakit (76%) dari 129 pesakit dalam kumpulan kliping mempunyai hasil mRS yang baik, sementara, 45 pesakit (86.5%) dari 52 pesakit dalam kumpulan endovaskular melingkar mempunyai keputusan mRS yang baik ($p = 0.114$). Dalam kategori gred WFNS yang tidak baik, diperhatikan bahawa dalam kumpulan kliping,

58 pesakit (77.3%) dari 75 mempunyai hasil mRS yang tidak baik. Demikian pula dengan kategori gred WFNS yang tidak baik, 10 (83.3%) daripada 12 pesakit dalam kumpulan endovascular melingkar mempunyai keputusan yang tidak baik (p = 1.00). Oleh kerana itu, apabila kelas WFNS dijadikan kumpulan kawalan, didapati tiada hubungan yang signifikan antara kedua-dua kaedah kliping dan melingkar dan juga hasil mRS pada 6 bulan.Selain dari ini kami juga mendapati bahawa keputusan yang baik bagi pesakit di bawah usia 40 tahun and gred Fisher 1-2, sementara pesakit yang memerlukan EVD, jangkitan CSF and radang paru-paru mempunyai keputusan yang tidak baik. Kami menggunakan analisis multiple logistic regression dan dapat menetapkan bahawa mRS yang baik berkaitan dengan WFNS yang baik dan ketiadaan EVD.

KONKLUSI: Keparahan klinikal pendarahan subaraknoid (gred WFNS) adalah prediktor yang paling signifikan untuk hasil fungsional (mRS) pada 6 bulan. Oleh kerana itu, keputusan tentang pilihan kaedah rawatan bagi seseorang individu perlu di ambil kira berdasarkan kepada keadaan pesakit tersebut.

VI. ABSTRACT

Objective: Endovascular coiling has been used increasingly as an alternative to neurosurgical clipping for treating subarachnoid hemorrhage secondary to aneurysm rupture. The purpose of this study was to compare functional outcomes at 6 months post-subarachnoid hemorrhage secondary to cerebral aneurysm rupture in subjects who were either surgically clipped or endovascularly coiled. In addition, the present study aims to identify the predictors in the clinical course of aneurysmal subarachnoid hemorrhage.

Materials and methods: A retrospective case review on the treatment methods of aneurysm rupture in Hospital Kuala Lumpur over the period of five years (2005-2009). A total of 268 patients who fulfilled the inclusion criteria were recruited for this study. These patients were broadly categorized into two groups based on their treatment mode for ruptured aneurysm. The case notes, CT brain films reports and angiography reports were analyzed with respect to their clinical, radiological, surgical clipping or endovascular coiling treatments and outcome data. Statistical analysis was determined using Chi-Square tests to study these associations.

Results:

There was a female predominance with male-to-female ratio 1:1.4. The mean age was 50.9 years old in this series. 50 patients were less than 40 years (18.7%) and 218 patients were more than 40 years(81.3%). 37 patients(74%) in age group less than 40 years had significant good outcome as compared to125(57.3%) patients above 40 years old.(p=0.03). One hundred and eighty one patients (67.5%) presented with Good WFNS (WFNS1-2) and 87 patients (32.5%) presented with Poor WFNS (WFNS 3-5) prior to intervention. One hundred and

sixty two patients (60.4%) had good functional outcome (mRS grade 0- 2) as compared to 106 patients(39.6%) who had poor mRS outcome(MRS 3-6) while 50 patients died(18.7%) during our follow up at 6 months . When we analyzed the WFNS group with functional outcome (mRS), there was significant association ($p<0.01$). In good WFNS, 143(79%) had good outcome and in poor WFNS, 68 patients (78.2%) had poor mRS outcome. There were 204 (76.1%) patients in clipping group and 64 (23.9%) patients in coiling group. Patients who underwent coiling, initially showed a better mRS outcome with 47patients (73.4%) than, 115 patients (56.4%) in clipping. Further comparison showed that 89(43.6%) patients in clipping group had poor functional (MRS) outcome as compared to17 patients (26.6%) coiling, which was significant ($p=0.015$). However when we controlled the WFNS grade of presentation in the treatment groups, we obtained a different result. In good WFNS group, it was noted that 98 patients (76%) out of 129 patients in clipping group had a good MRS outcome while, 45 patients (86.5%) out of 52 patients in coiling group had good mRS outcome ($p=0.114$). In poor WFNS presentation, it was noted that in clipping group, 58 patients (77.3%) out of 75 had poor mRS outcome. Similarly with poor WFNS presentation, 10 (83.3%) out of 12 patient in coiling group had poor outcome. ($p=1.00$). Hence when we control the WFNS group, there was no significant association between treatment group (clipping and coiling) and mRS outcome at 6 months. Further we noted that age less than 40 and Fisher grade of 1-2 have better outcome while patients with EVD, CSF infection and pneumonia have poorer outcome. Using multiple logistic regression analysis we have determined that good mRS outcome is associated with good WFNS and absence of EVD

Conclusion: Clinical severity of the SAH (WFNS grade) was the most significant predictor of functional outcome (mRS) at 6 months. Therefore the decision regarding treatment option needs to be individualized based on the presentation of the patient.

1. INTRODUCTION

Nontraumatic subarachnoid hemorrhage which accounts for 3 – 5% of all strokes, is the second most frequent cause of hemorrhagic stroke, and in more than 85% of cases is caused by a ruptured intracerebral aneurysm. The incidence is at 6–8 cases per 100,000 population (Varelas, 2006). There are various treatment options available for ruptured aneurysms including surgical and endovascular means. Class I evidence for the relative merits of one treatment option over the other is scanty. (Gnanalingham, 2006).

From the era of Dandy until recently, clipping was the most popular treatment. This procedure, which requires craniotomy, aims to prevent rebleeding of the aneurysm by placing a clip across its neck. As such the aneurysm will be excluded from the circulation. Surgical clipping involves the exclusion of re-rupture with a certainty of approximately 98% (Frazer, 2007). In the past decade, endovascular coiling has grown in popularity as an alternative to clipping. This procedure aims to obstruct the aneurysmal lumen with a detachable coil, with the intent to provoke secondary thrombosis of the aneurysm.

This new mode of treatment for intracranial aneurysms has been compared to open surgery in multiple studies. The most recent of these studies, international subarachnoid aneurysm trial (ISAT) was a multicentre randomised trial, which compared neurosurgical clipping with coiling for ruptured anterior circulation aneurysms that were considered suitable for either treatment. Analysis of the outcome at 1-year follow-up revealed a 6.9% absolute risk reduction in dependency or death for the endovascular group in comparison with patients allocated to surgery (Molyneux, 2005). However, a 5 year review of the study noted that the proportion of survivors at 5 years who are independent did not differ between

the two groups; endovascular 83% (626 of 755) and neurosurgical 82% (584 of 713) (Molyneux, 2009).

The definite method of treatment remains debated with conflicting views being constantly published. In addition there is a growing body of evidence suggesting that the most important causal factor for the neuropsychological sequelae of aneurysmal SAH is the hemorrhage itself and associated secondary brain damage, rather than the location of the aneurysm or treatment methods (Frazer, 2007). As such we reviewed the outcome of aneurysm treatment in our centre as both methods of treatment are being practiced here.

We performed a retrospective cohort review on the treatment methods of aneurysm rupture in Hospital Kuala Lumpur over the period of five years (2005-2009). The purpose of this study was to evaluate the outcome of patients with rupture aneurysm who had been treated surgically with clipping or endovascularly with coiling. A total of 268 patients who fulfilled the inclusion criteria were recruited for this study. Their case notes, radiology reports and films were studied specifically on methods of treatment, clinical presentation (WFNS grade) prior treatment, CT Fisher Grade of SAH, angiographic site of aneurysm, clinical vasospasm, requirement of EVD and shunt, pneumonia, CSF infection and subsequent recovery to independence, morbidity and mortality. Apart from that, demographic data including age, gender, ethnicity and duration of illness were also recorded. Statistical analysis (Chi-square and Fisher's exact test) was then performed to determine the association between treatment methods and good functional outcome, morbidity and mortality.

2. LITERATURE REVIEW

2.1 HISTORICAL PERSPECTIVE

Intracranial aneurysms as probable cause of subarachnoid hemorrhage were postulated in the 17th century by Morgagni. He was the first to report the presence of incidental "dilatations" of both posterior cerebral arteries in 1725. Francesco Biumi in 1765 on the other hand was the first to have documented account of an unruptured intracranial aneurysm. In 1814, the first verified account of aneurysmal rupture was reported by Blackall (Greenblatt, 1997).

Most of the reports during this period were based on postmortem findings. There were no treatment options available. However in late 19th century, the concept of carotid artery ligation for intracranial vascular pathology was adopted based on Hunters success in proximal femoral artery ligation for popliteal aneurysm (Prestigiacomo, 2006).

Cooper in 1808 was the first to successfully ligated the carotid artery for an aneurysm of the left cervical carotid artery. In fact even a century later, ligation of cervical artery was still in practice with more sophisticated method and materials. An example will be Neff's clamp that was invented to allow for the development of collateral circulation while occluding and dividing the vessel (Prestigiacomo, 2006; Richling, 2006).

There are many difficulties encountered with the indirect approaches of cervical carotid ligation including thrombotic, embolic phenomenon, infections and poor success rate of aneurysm occlusion. Therefore, more direct, intracranial approaches were sought. The limitation of technology in the 1930s made securing an aneurysm at the neck hazardous, as

only ligatures and silver clips were available for use at that time. Zeller's patient who died from hemorrhage after avulsion of ligated artery by his assistant is an example. (Prestigiacomo, 2006)

Norman McComish Dott was the first surgeon to attempt direct attack on an intracranial aneurysm and introduce wrapping of aneurysm (Choudari, 2004). In 1932, Dott secured bleeding during the exposure of aneurysm of the ICA by placing harvested muscle from patient's thigh on the exposed aneurysm dome. The patient was reported to have made an excellent recovery. The next advance in aneurysm treatment was aneurysm trapping, which was initially described by Walter Dandy in 1936. He performed cervical internal carotid ligation and clipping of the supraclinoid carotid artery for a cavernous aneurysm. (Prestigiacomo, 2006)

The first description of clipping on neck of aneurysm was by Dandy, who placed a silver clip across neck of posterior communicating artery aneurysm and cauterized its dome (Greenblatt, 1997; Bulters, 2010). The next important step in the development of the aneurysm clip was the development of an adjustable clip that could be reopened and repositioned. This was followed by the development of fenestrated clip. Using the fenestrated clip, neck of an aneurysm could be safely clipped without displacing and compromising other vessels in the field.

Currently, modifications to the aneurysm clip are based on metallurgy and different design configurations. Concurrent with the development of the aneurysm clip came many other developments in techniques and parallel technologies like microsurgical techniques which improved the treatment strategy.

There were many attempts to treat aneurysms from the "endovascular side" as early as 1936 when Gardner opened and packed a giant ICA aneurysm with 5 cotton sponges. The patient was well until 2 years later when it became infected (Prestigiacomo, 2006). Mullan in 1965 stereotactically placed wire electrodes into exposed aneurysms and subjected them to an electric current with only partial success (Berenstein, 2006). Gallagher in 1965 described the injection of a horse hair into a surgically exposed aneurysm (pilojection) with only partial thrombosis in most patients (Kamble, 2008)

Despite many approaches at endosaccular occlusion of aneurysms as described earlier, true catheter-based endovascular approaches to vascular diseases of the central nervous system did not take place until 1960. During this period, Luessenhop and Spence were able to cannulate the internal carotid artery and deposited silastic spheres to treat an arteriovenous malformation in the operating room (Guglielmi, 2000 ; Kerber, 2006). Two years later, Rothenberg introduced the concept of using balloons in the treatment of intracranial aneurysms.

In 1971, Serbinenko used balloons for temporary occlusion of brain vessels and carotid cavernous sinus fistulae. By 1974, Serbinenko used detachable balloons filled with a liquid silicone for the treatment of saccular aneurysms of the cerebral arteries (Greenblatt 1997; Guglielmi, 2000). Important milestone was achieved when he reported the successful detachment of balloons within a basilar tip aneurysm and supraclinoid carotid aneurysm (Randall T. Higashida, 2000). In 1985, Braun et al. reported the first intracranial aneurysm treated with coil embolization. In 1988 platinum coils with Dacron fiber were introduced to induce thrombosis for the treatment of vascular malformations and aneurysms (Linxia Gu, 2005).

Guido Guglielmi developed techniques that combined these concepts. He developed the first generation of electrolytically detachable coil. In 1990, the first coil was introduced in a patient for a traumatic carotid cavernous fistula who failed balloon occlusion (Strother, 2001). Since that time, the tremendous advancement in endovascular technology and techniques has challenged the role of microsurgery in the treatment of aneurysms

2.2. EPIDEMIOLOGY OF SAH AND ANEURYSM

SAH represents 2 to 5 percent of all new strokes and affects 21000 to 33000 people each year in the Unites states. Approximately 10,000 per year suffer from SAH in Germany (Bulters 2010).Worldwide incidence is about 10.5 cases per 100,000 person-years. The leading cause of spontaneous (non traumatic) SAH is rupture of aneurysms which account for 85% of all spontaneous SAH, followed by perimesencephalic hemorrhage (10%) and other causes account for the remaining 5%.

Most aneurysms are found in patients aged 40 to 70 years. The incidence increases with age, with a mean age at presentation of 55 years. The prevalence of aneurysm is noted twice as high in oldest age group (75-84 years) as compared to lower age groups. However the incidence of intracerebral hemorrhage due to rupture of these aneurysms is most frequent in the age group of 40 to 60 years.

The relationship between age and risk of rupture is undetermined. An autopsy study by Inagawa fails to demonstrate a relationship between the patient's age and the thickness of the aneurysmal walls (Inagawa, 2009) .Therefore it is likely those factors associated with aging, such hypertension, smoking, and atherosclerotic vessel degeneration, might affect the risk of aneurysm rupture.

While in patients below the age of 40, aneurysms are more common in men, the majority of aneurysm which occurs above the age of 40 predominates in women .The risk for women to develop aneurysm is 1.6 times that of men. The exact etiology is unknown but it

was proposed that the hormonal factors especially after menopause may have a role in the pathogenesis of aneurysmal rupture

The average mortality rate for subarachnoid hemorrhage is 51 percent, with approximately one third of survivors requiring lifelong care. Most mortality occurs within two weeks after the ictus, with 10 percent occurring at home or on transit to hospital and 25 percent within 24 hours. About 46 percent of survivors of subarachnoid hemorrhage may have long-term cognitive impairment, with an effect on functional status and quality of life. The disorder has direct impact on health care resources, most of which are related to hospitalization. (Suarez, 2006)

2.3 PATHOLOGY

The pathogenesis of spontaneous aneurysms are only partially understood Almost all of the aneurysms are located above the carotid siphon on the circle of Willis The most common causes for the development of an aneurysm are hemodynamically induced vascular injuries, atherosclerosis, underlying vasculopathy and high flow states.

Endogenous factors like elevated arterial blood pressure (Inci, 2000), special anatomical relationships given by the Circle of Willis, altered flow conditions, and exogenous factors like cigarette smoking, heavy alcohol and coffee consumption and use of anticoagulant or contraceptive medications have all been found to be associated with the occurrence of cerebral aneurysms (Juvela, 2001; Isaksen, 2002)

Intracranial aneurysms may be classified based on morphology, size, and location and etiology. However commonly intracranial aneurysms are divided into three basic types: saccular, fusiform and dissecting. According to their size, saccular aneurysms can be grouped into three types: small (<10 mm), large (10– 25 mm), giant (>25 mm). According to the neck width they are further classified into small neck (<4 mm) and large neck (>4 mm) (Gasparotti, 2005). They mostly develop spontaneously as solitary (70%–75%) or multiple (25%–30%) vascular lesions located at the Circle of Willis.

Saccular aneurysm

Saccular aneurysms had been described as berry-like vessel outpouchings arising from arterial bifurcations. They account for 66%–98% of intracranial aneurysms (Yong-

Zhong, 1990) in adults and rare in children. The majority of aneurysms (85%) are located in the anterior circulation and only 15% are located in the posterior circulation (Kassell, 1983).

In adults the role of acquired changes in the arterial wall is likely the cause because of exposure to general risk factors responsible for the development of aneurysms like hypertension, smoking and alcohol abuse. These factors might contribute to general thickening of the intimal layer in the arterial wall, distal and proximal to branching sites. Within these "intimal pads" the intimal layer is inelastic and therefore causes increased strain of the more elastic portions of the vessel wall. Further abnormalities in structural proteins of the extracellular matrix contribute to aneurysm formation (Chyatte, 1990; Mizutani, 2000). In addition to above, aneurysms are acquired due to hemodynamic stress on the relatively unsupported bifurcations of cerebral arteries.

Other pathological factors which are associated with formation of aneurysms include increased density of vasa vasorum in proximal segments of atherosclerotic intracranial arteries which has angiogenesis potential. This is augmented by presence of 5-lipoxygenase pathway. 5-lipoxygenase pathway generates LTD4 which binds to endothelial and leads to inflammation of media and subsequently results in aneurysm formation.

The previous theory of a congenital defect in the tunica media through which the inner layer of the arterial wall would bulge was popular in past. These defects are located on the distal carina at the point of branching, at the apex of bifurcation and may also occur at the lateral angles. However the theory is now disputed as media defects noted to occur in the cerebral arteries in many more places than the sites of aneurysms formation. Similar defects have also been observed in the extracranial arteries. It was also noted that if aneurysm has