

Factors associated with outcomes in ruptured aneurysmal patients: Clinical Study of 80 Patients

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Abstract: Background: Due to insufficient data in the literature, the optimal timing for surgical intervention for ruptured intracranial aneurysms is still controversial. Some practitioners advocate early surgery, but others not. It is important to identify other factors that can be used to predict poor prognosis in ruptured intracranial aneurysm patients. Objective: To determine the influence of timing of clipping surgery, and other factors on the outcomes of ruptured intracranial aneurysms in Hunt & Hess I~III grade patients. Method: We have performed a retrospective study involving 80 patients who were surgically treated for ruptured intracranial aneurysm between 2007 and 2012. The patient population consisted of 50(62.5%) females and 30(37.5%) males, with an age range of 12 to 75 years old, mean age 52.33 ± 10.63 years. We measured association between the Glasgow Outcome Scores and Sex, timing of clipping surgery, aneurysm location and pre-operative patient's neurological condition using famous Hunt and Hess grade system. Results: We did not find any correlation between the outcomes of ruptured intracranial aneurysm patients and timing (early, intermediate, late stage) of clipping, sex, aneurysm location. Whereas there is a significant correlation between patients outcomes and pre-operative patient neurological condition (Hunt & Hess grade). Conclusion: Timing of Surgery (early, intermediate, late) does not affect outcomes in low Hunt and Hess grade patients I~III. Whereas neurological condition (Hunt & Hess) has strong impact on postoperative outcomes. Others factors like sex, Age, Aneurysm location have no effect on outcomes in ruptured intracranial aneurysms.

Key words: Subarachnoid hemorrhage, Aneurysm, Timing, Hunt & Hess, Outcomes.

Introduction

Management of ruptured intracranial aneurysms is indispensable to prevent the risk

of re-bleeding especially the first four weeks after the aneurysmal rupture, with a cumulative risk of 30% without intervention.

The treatment options for securing the aneurysm is either to coil the aneurysm by packing it with platinum coils or by direct open surgery and application of a surgical clip. The optimal treatment for an aneurysm depends on the condition of the patient, the anatomy of the aneurysm, the ability of the surgeon, and must be weighed against the natural history of the condition.

Many factors had been studied to investigate the relation between the outcome in patients who performed clipping ruptured aneurysm with time of surgery, Sex, Hunt and Hess grade and location of aneurysm. The timing of definitive management of acutely ruptured intracranial aneurysms (endovascular coiling or craniotomy and clipping) has been the subject of considerable debate[1][2]. Some authors advocated conservative treatment for all ruptured intracranial aneurysm patients till their condition is stable and perform late surgery, but some reports no significant different between early or late surgery in the outcomes[3].

In literature the concept of early stage surgery is defined between 1~3 days post subarachnoid hemorrhage (SAH), late surgery, defined as >10 days post SAH. Some few studies raise what called "ultra-early" aneurysm treatment, within 24 hours of SAH[4][5][6].

Cerebral vasospasm, also known as delayed ischemic neurologic deficit (DIND), A delayed ischemic neurologic deficit following SAH. Clinically characterized by confusion or decreased level of consciousness sometimes with focal neurologic deficit like speech or

motor. Typical at risk period is quoted as days 3-14 post-SAH. Always resolved by day 12 post-SAH. Because cerebral vasospasm never occur before day 3[7], many studies advocate early surgery treatment especially in good medical and neurological condition patients, Hunt and Hess ≤ 3 . Early surgery facilitates treatment of vasospasm which peaks in incidence between days 6-8 post SAH by allowing induction of arterial hypertension and volume expansion without danger of aneurysmal rupture, and in the same time allows lavage to remove potentially vasospasmogenic agents from contact with vessels.

To evaluate the most factors effecting the outcome of post-surgical clipping of intracranial aneurysm patients, we study some factors like: Sex, Hunt-Hess grade, timing of surgery and location of aneurysm and their influence on Glasgow outcome scores of hospitalization patients. It is important to identify factors that can be used to predict poor prognosis in ruptured intracranial aneurysm patients.

Method

We have performed a retrospective study involving 80 patients who were surgically treated for ruptured intracranial aneurysm between 2007 and 2012. The patient population consisted of 50(62.5%) females and 30(37.5%) males, with an age range of 12 to 75 years old, mean age 52.33 ± 10.63 years. We measured associations between the Glasgow Outcome Scores and Sex, timing of clipping surgery, aneurysm location and pre-operative patient's neurological condition using famous Hunt and Hess grade system. For patients

selection, Symptoms, aneurysm location, pre-operative patient's neurological condition (Hunt & Hess) see Table I.

Patients' inclusion criteria:

1 - Patients with subarachnoid hemorrhage due to ruptured of intracranial aneurysm (RIA), approved by Computerized Tomographic Angiography (CTA), magnetic resonance angiogram (MRA) and Digital Subtraction Angiography (DSA).

2 - Patients treated only by surgical clip placement.

3 - The Glasgow Outcome Scale is defined in our study as the outcome on the day of discharge from hospital [8].

4 - Timing of surgery is defined in our study as: Early stage surgery: 1~3 days, intermediate stage surgery: 4~10 days and late stage surgery: more than 11 days.

5 - Hunt and Hess Grade System is used to describe pre-operative neurological condition of ruptured aneurysm patients [9].

Excluding criteria:

1 - Subarchnoid hemorrhage due to

another cause like:trauma, arteriovenous malformation(AVM), pretruncal nonaneurysmal SAH and Vasculitis or vasculopathy.

2 - Anuerysms combined with arteriovenous malformation (AVM).

3 - Patients treated endovascularly.

4 - Incidentally discovered unruptured intracranial aneurysms.

5 - Patients with multiple systemic disease especially with coagulation disorders like: thrombocytopenia or liver dysfunction.

6 - patients with uncompleted information.

7 - Rebleeding Patients

7 - Hunt & Hess IV and V except for large hematoma needs emergency evacuation.

In this research to determine the relative risk affect the prognosis and outcome of post-surgical clip placement patients with four independent variables: Sex, Hunt & Hess, aneurysm location and timing of surgery, SPSS 16.0: Kruskal-wallis, Chi-Square Tests were performed; significant difference when $P < 0.05$.

TABLE I

Sex Cases (%)	Onset Symptoms Cases (%)	Hunt & Hess Cases (%)	Aneurysm Location Cases (%)
Female 50(62.5)	Headache 53(66.25)	I~III 64(80)	LMCA 20(25)
Male 30(37.5)	Syncope 22(27.5)	IV 11(13.75)	RMCA 11(13.8)
	Coma 2(2.5)	V 5(6.25)	LICA 3(3.8)
	Seizure 1(1.25)		LPCoMA 9(11.3)
	Aphasia & Hemiparesis 2(2.5)		RPCoMA 7(8.8)
			ACoMA 21(26.3)
			RACA 2(2.5)
			LChA 2(2.5)
			RChA 1(1.3)
			LOphA 2(1.3)
			BTA 2(2.5)
			RACA+RICA 1(1.3)

Abbreviation: AChA: anterior choroid artery, ACA: anterior cerebral artery, AComA: anterior communicating artery, BTA: basilar tip artery, MCA: middle cerebral artery, ICA: intracranial carotid artery, OphA: ophthalmic artery, PComA: posterior communicating artery.

the outcomes of ruptured intracranial aneurysm patients and timing (early, intermediate, late stage) of clipping, sex, aneurysm location. Whereas there is a significant correlation between patients outcomes and pre-operative patient neurological condition (Hunt & Hess grade), Table II. Outcomes in patients according to timing of surgery, Table III.

Results

We did not find any correlation between

TABLE II
Correlation between GOS and sex, Hunt & Hess, aneurysm location and timing

	variable	cases	X ²	P
Glasgow Outcome Scale (GOS)	Sex:		2.37	0.122
	Male	30		
	Female	50		
	Hunt & Hess:		15.052	0.01
I~III	64			
IV	11			
V	5			
Aneurysm Location:	LMCA	20	19.628	0.051
	RMCA	11		
	LICA	3		
	LPCoMA	9		
	RPCoMA	7		
	AComA	21		
	RACA	2		
	LACHA	2		
	RACHA	1		
	LOphA	1		
	BTA	2		
	RACA+RICA	1		
	Timing:	1~3d		
4~10d		21(26.2)		
>11d		5(6.2)		

TABLE III
Outcomes in patients according to timing of surgery

Outcomes	Timing			Total Cases (%)
	1~3d Cases (%)	4~10d Cases (%)	Cases (%)	
Death	3(60.0)	1(20.0)	1(20.0)	5(6.2)
Persistent Vegetative State	3(100.0)	0(0.0)	0(0.0)	3(3.8)
Severe Disability	7(58.3)	4(33.3)	1(8.3)	12(15.0)
Moderate Disability	18(75.0)	5(20.8)	1(4.2)	24(30.0)
Good Recovery	23(63.9)	11(30.6)	2(5.6)	36(45.0)
Total	54(67.5)	21(26.2)	5(6.2)	80(100.0)

Discussion

Many factors had been studied to investigate the relation between the outcome in patients who performed clipping ruptured aneurysm with time of surgery, Sex, Hunt and Hess grade and location of aneurysm.

The most controversial factor is timing of surgery. The timing of definitive management of acutely ruptured intracranial aneurysms (endovascular coiling or craniotomy and clipping) has been the subject of considerable debate [1][2]. In literature the concept of early stage surgery is defined between 1~3 days post subarachnoid hemorrhage (SAH), late surgery, defined as >10 days post- SAH. Some few studies raise what called "ultra-early" aneurysm treatment, within 24 hours of SAH[2][3][10][11].

By the late 1980s, several reports suggested that early surgery was safe with good outcomes[12][13][14], especially in patients with good neurologic condition (Hunt and Hess (H&H) grade ≤ 3). Early surgery eliminates the risk of re-bleeding which occurs most frequently in the period immediately following SAH, and allows lavage to remove

potentially vasospasmogenic agents from contact with vessels. However, early treatment (particularly of poor-grade patients) may increase the periprocedural complications beyond the rates reported in the International Cooperative Trial[3][15][16], and the acutely swollen, soft, hyperemic, poorly autoregulating brain was considered more prone to laceration, contusion, and infarction secondary to retraction [14][17]. The risk of intra-operative rupture is higher with early surgery, and possible increase incidence of vasospasm following early surgery from mechanotrauma to vessels, thus delayed ischemic neurological deficits can be started promptly[18][19][20].

Period in 4 to 10 days after occurrence of SAH also has been reported as a risky time for surgery[3]. In one study by Dorhout Mees et al. They found Clipped patients had no higher risk of delay cerebral ischemia when treated between 5 to 10 days if they compared to patients who treated with coils[21].

In one prospective study found the timing of surgery is no longer an important factor influencing surgical outcome in treating

supratentorial circulation aneurysms[22]. Cerebral ischaemia due to non-surgical causes (such as “vasospasm”) no longer seems to be the important issue governing the timing of surgery[23][24]

Some authors advocated conservative treatment for all ruptured intracranial aneurysm patients till their condition is stable and perform late surgery, but some reports no significant different between early or late surgery in the outcomes[3].

In our study we did not find any correlation between timing of surgery (early:1~3d,intermediate:4~10d, late:>11d) and postoperative outcomes in the patients with good neurological conditions (Hunt & Hess ≤ 3) $P > 0.05$.

In 2002, de Gans et al. performed a systematic review, 1 randomized clinical trial and 10 observational studies, met the inclusion criteria. Meta-analysis suggests that outcomes were better after early or intermediate surgery than after late surgery for patients in good clinical condition at admission[25]

We think the Hunt & Hess grade on admission correlates with the risk of CVS. In our institute our strategy to eliminate the risk of peri/postoperative Vasospasm and re-bleeding of the aneurysm: Pre/post-operative strategy :Smooth muscle relaxants, calcium channel blockers(CCBs),which have neuro-protection more than preventing vasospasm, the most used agent is nimodipine (Nimotop) 60 mg/iv/24h.The most seen side effect is systemic hypotension: which may be mitigated by IV volume expansion.

Triple-H therapy which includes: hypervolemia, hypertension and

hemodilution[26]. For hypervolemia the target is euvolemia or very slight hypervolemia the most used agents: colloid: albumin, low molecular weight dextran, keep systolic blood pressure (SBP) between 160~180mmHg in all cases pre and postoperative.

During operation, in case swelling of the brain, to avoid excessive brain retraction, surgical exposure requires sufficient bony removal, we use hyperventilation, CSF drainage(ventriculostomy, lumbar spinal drainage and intra-operative drainage) and diuretics mannitol with Decadron, furosemide and continuous irrigation of the operation field with normal saline (NS), nimotop can have some effect on vasospastic vessels,we do not use papaverine because its side effects like hypotension ,bradycardia and even death[27][28].

The Hunt and Hess grade and World Federation of Neurological Surgeons (WFNS) scale are commonly used to predict mortality after aneurysmal subarachnoid hemorrhage, these scales are also used for prognostication purposes. Hunt & Hess in their experience the survival for patients admitted at grade 1, 2, or 3 was 70%, for grade 4 or 5 have historically fared poorly and many often were excluded from aggressive treatment. Le Roux et al demonstrated that 86% of patients with Hunt and Hess grades 1–3 return to independent function. This rate was 96% for the grade 1 patients[29].Many studies indicates that very poor prognosis for high Hunt & Hess grade, in our study we find when patient with high Hunt&Hess grade the Glasgow Outcome Scale (GOS) will be low. No matter the timing of the clipping surgery, the most important factor is

the neurological condition of the patient. For I~III grade the we advocate surgery no matter with time, but early surgery can eliminate the risk of re-bleeding, In a study of 33 patients who re-bled, the highest risk of re-bleeding occurred in the first 6 hours following SAH[30]. For IV~V grade are excluded from our surgical clipping ,and are treated either conservatively or endovascular using Guglielmi detachable coil (GDC) embolization .In the patients who are treated conservatively many techniques are use to improve outcome like: control elevated Intracranial pressure (ICP), prophylaxis of delay ischemic neurological deficit (DIND), triple -H therapy. Exceptions were made for patients with multiple, repeated bleeding episodes and those with significant mass effect from a hematoma.

The GDC system was first made available for approved use in 1995. This device has since gained widespread acceptance as an alternative treatment technique for intracranial aneurysms. Weir RU et al found[31]Patients who are acutely ill with high Hunt and Hess grades after SAH can undergo successful coil embolization despite their poor medical condition and a high frequency of vasospasm. Many of these patients have a good clinical outcome.

Conclusion

Timing of Surgery (early, intermediate, late) does not affect outcomes in low Hunt and Hess grade patients I~III. The most advantage of early surgery is preventing re-bleeding, which is has high morbidity and mortality[32]. The most important factor that influencing on

Glasgow Outcome Scale is the neurological condition (Hunt & Hess) of ruptured intracranial aneurysms patients. Urgent preoperative resuscitation, early surgery, and aggressive treatment of vasospasm to improved the outcome in patients with good grades[29]and conservative treatment or GDC system coiling for high grade Hunt & Hess grade IV~V[31].

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