Prognostic Factors of Hunt and Hess Grade V Subarachnoid Hemorrhage Patients

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Prognostic Factors of Hunt and Hess Grade V Subarachnoid Hemorrhage Patients

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This certifies that the Master's Thesis (Doctoral Dissertation) of Namkyu You is approved.

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ABSTRACT

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Objective: This study was designed to identify the prognostic factors of patients with Hunt and Hess grade (HHG) V aneurismal subarachnoid hemorrhage (SAH).
Patients & Methods: Between March 1996 and June 2007, 81 patients presented with HHG V were selected. We reviewed the clinical record and images of them retrospectively. Median post-treatment follow up period was 17.0 months (range: 1 – 119). Clinical outcome was assessed using modified Glasgow Outcome Scale. Possible prognostic factors were analyzed. Binary logistic regression analysis was performed.
Results: Thirty two patients were male, and 49 patients were female. The median age was 55.5 years old (range: 27–81). Twenty three patients were Fisher group 3 and the remaining 58 patients were group 4. Twenty three patients suffered from repeated SAH before admission. The locations of aneurysms were anterior cerebral artery in 25, internal carotid artery in 21, middle cerebral artery in 25, and vertebrobasilar-posterior cerebral artery in 10 patients. Fifty nine patients had small, 21 had large, and 2 had giant aneurysms. The improvement of HHG was identified on 41 patients; from HGG V to IV in 37 patients, to HHG III in 2 patients, and to HHG II in 2 patients. Microsurgery was performed on 51 patients and endovascular treatment was performed on 30 patients. Early surgery was performed on 46 patients, intermediate surgery (between days 4 – 10) was performed on 24 patients, and delayed surgery was performed on 11 patients. The clinical outcome was good in 21, fair in 14, poor in 25, and dead in 21 patients. The statistically significant prognostic factors were the improvement of HGG before surgery and young age. The causes of unfavorable outcome might be brain damage by initial hemorrhage, treatment-related complications, and rebleeding of aneurysm.
Conclusion: Although poor clinical grade on arrival, active management should be performed on younger patients and the patients with improved HHG

Key words : Subarachnoid hemorrhage, Hunt and Hess grade V, prognostic factor

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I. INTRODUCTION

Subarachnoid hemorrhage (SAH) is one of the hemorrhagic strokes and it accounts for 6~8% of all strokes[1]. Most common cause of spontaneous SAH is aneurismal rupture of intracranial arteries, known as aneurismal SAH[2]. It has various clinical courses, from full recovery to death. Initial hemorrhage and brain damage play great role in the clinical course and recovery[3]. Measuring severity of SAH is considered important in managing patients and deciding treatment modality, so most neurosurgeons use both radiologic grading system, Fisher Grade, and clinical grading system, Hunt and Hess grade (HHG, Table 1.)[4, 5] .

Table 1. Hunt-Hess Grade system for Subarachnoid Hemorrhage

Grade	Definition
0	Asymptomatic (Unruptured)
I	Asymptomatic or mild headache, nuchal rigidity, No neurologic deficit (except cranial nerve palsy)
II	Cr. N. palsy(e.g. III, IV), moderated to severe H/A, nuchal rigidity
III	Drowsiness, confusion, or mild focal deficit
IV	Stupor or mild to moderate hemiparesis, possible. Early decerebrate rigidity and vegetative disturbance
V	Deep coma, decerebrate rigidity, moribund

Prognosis of poor HHG patient was evaluated in several studies, and results of intensive care to poor grade patients were reported. Poor grade patients include HHG IV and V. HHG V is most severe clinical feature of SAH patients and the worst prognosis can be expected. This study was designed to identify the prognostic factors of patients with HHG V aneurismal subarachnoid hemorrhage (SAH).

II. MATERIALS AND METHODS

From March 1996 to June 2007, 1388 patients who were diagnosed with ruptured aneurysm and treated with craniotomy or endovascular surgery at a single institute were reviewed retrospectively. Total of 81 patients had been presented with HHG V. Mean post-treatment follow up period was 17.0 months (range: 1 – 119). Clinical outcome was assessed with modified Glasgow Outcome Scale. Good and fair clinical outcome was grouped as favorable outcome then poor and dead outcome was as unfavorable outcome. Possible prognostic factors were analyzed; Sex, age, Fisher group, location of aneurysm, size, number of bleeding, change of HHG before treatment, delayed ischemic deficit, hydrocephalus, intracerebral hemorrhage, low density on initial CT, timing of surgery, and treatment modalities. Binary logistic regression analysis about the favorable and unfavorable outcome was performed using the statistic program, SPSS v 18.0 (Copyright © SPSS Inc).

III. RESULTS

Of the 81 evaluable patients, 32 patients were male, and 49 patients were female. The mean age was 55.5 years old (range: 27–81). Fisher group 3 on initial CT scan was 23 and the remaining 58 patients were Fisher group 4. There were repeated hemorrhages in 23 patients before their admission to the hospital. The locations of aneurysms were in anterior cerebral artery in 25, internal carotid artery in 21, middle cerebral artery in 25, and vertebrobasilar-posterior cerebral artery in 10 patients. The size of aneurysm was classified by its dimension. Small size was less than 10mm in the longest axis. Large size aneurysm was 10~25mm size. Giant aneurysm was more than 25mm. There were 59 small aneurysms, 21 large aneurysms and 2 giant aneurysms. The improvement of HHG after arrival had been observed in 41 patients; from grade V to IV was 37 patients, to grade III was 2 patients, and to grade II was 2 patients. Delayed ischemia was developed in 11 patients. Hydrocephalus was found in 42 patients. Intracerebral hemorrhage was accompanied in 47 patients. Infarction was present in 9 cases. Low density lesion on initial CT scan was found in 9 patients, 1 of good outcome group and 8 of poor outcome group. Microsurgical obliteration of aneurismal sac was performed on 51 patients and endovascular treatment was performed on 30 patients. Early surgery was performed on 46 patients, intermediate surgery (between days 4 – 10) on 24 patients, and delayed surgery on 11 patients. The clinical outcome was good in 21, fair in 14, poor in 25, and dead in 21 patients. The causes of unfavorable outcome were initial severe brain damage in 39, treatment-related complications in 4, and rebleeding of aneurysm in 3 patients. Different factors between favorable and unfavorable groups were age of the patients, improvement of clinical grade after initial hemorrhage, and low density lesion on CT (Table2.)

Table 2. Clinical profiles of 81 Hunt and Hess grade 5 patients according to the clinical outcome. P-values was taken by independent sample t-test between favorable and unfavorable groups.

Factors	Favorable (N = 35)	Unfavorable (N = 46)	p-value
Sex			
Male	14	18	p=0.938
Female	21	28	
Age			
20-29	1	1	p=0.015
30-39	4	3	
40-49	5	5	
50-59	17	13	
60-69	7	19	
70-79	1	4	
80-89	0	1	
Fisher Grades on initial CT			
1	0	0	p=0.319
2	0	0	
3	12	11	
4	23	35	
Aneurysm Site			
Left	7	10	p=0.501
Midline	14	14	
Right	14	22	
Location 1			
Anterior circulation	32	39	p=0.358
Posterior circulation	3	7	
Location 2			
ACA	14	11	p=0.934
ICA	10	11	
MCA	8	17	
VB-PCA	3	7	

Size (diameter, mm)			
Small (< 10)	28	31	
Large (10 – 25)	7	12	p=0.096
Giant (>= 25)	0	3	
Bleeding number			
1	23	35	
2	11	10	p=0.35
3	1	1	
Change of HHG			
Improved	26	15	p<0.05
Unchanged	9	31	
Delayed ischemic deficit			
Yes	6	5	p=0.433
NO	29	41	
Hydrocephalus			
Yes	11	31	p=0.35
NO	24	15	
Intracerebral hemorrhage			
Yes	18	29	p=0.488
NO	17	17	
Low density lesion on initial CT			
Yes	1	8	p=0.04
NO	34	38	
Timing of surgery			
Early	22	24	
Intermediate	9	15	p=0.406
Delayed	4	7	
Treatment			
Microsurgery	25	26	p=0.168
Endovascular	10	20	

ACA: anterior cerebral artery, ICA: internal carotid artery, MCA: middle cerebral artery, HHG: Hunt and Hess grade
* indicates the significacy of p-value

However our result of binary logistic regression of this study revealed two significant predictable factors (Table 3).

Table 3. Results of the logistic regression test of prognostic factors.

Factor	p-value	Exp (B)
Age	p = 0.035	1.058
Improvement of HHG*	p = 0.007	0.158

* HHG = Hunt and Hess grade

Those were the improvement of HHG before surgery, and younger age. Age of HHG V patient might incased the risk of unfavorable outcome by 5.8% per years. And the improvement of HHG before surgery might decrease the risk by 15.8%.

IV. DISCUSSION

Aneurismal SAH is one of severe forms of hemorrhagic strokes. HHG system was first suggested by Hunt et al in 1968 and is used widely to assess the severity of SAH patients[5]. Patients who are graded by HHG system proceed to several clinical courses and their severity correlate with their HHGs. However in severe case of aneurismal SAH such as HHG IV and V, the outcome is unpredictable. Generally poor grade (HHG IV and V) patients, who are reported to occupy from 20 to 30 percent of all aneurismal SAH patients by Le Roux[6], had the worst outcome. Wilby et al commented that poor grade patients are associated with high mortality[7]. HHG IV and V were studied together in several studies and it was found that HHG V patients had worse prognosis and outcome than grade IV. Zentner et al reported that HHG IV patients benefit from early surgery compared to grade V[8].

A clinical feature of HHG V patient is coma status or decerebrate rigidity. Initial SAH causes increased intracerebral pressure (IICP) and decreased cerebral blood flow (CBF), which lead to cerebral dysfunction and moreover permanent brain damage. Clinical features of poor grade patients could represent severity of initial hemorrhage but they are not enough to predict final outcomes. HHG is based on clinical features, meaning that it has insufficient predictability, as reported by Steudal et al, that HHG alone is not sufficient basis for decision making because some comatose patients even in mid-brain syndrome profit from an early operation[3].

In order for accurate prognosis, more relevant factors are needed. We suggested some statistically significant predictable factors for a positive outcome per independent sample T test analysis. They are improvement HHG before surgery, younger age, and no low density on initial brain CT scan.

Improvement of HHG before surgery was the most powerful predictable factor in our study. HHG represents cerebral dysfunction, therefore improvement may mean recovery of cerebral function. Before aneurysm obliteration, CBF enhancement is recommended to be restricted because in order to enhance CBF, increase of blood pressure is needed, which leads to higher risk of rebleeding. Therefore, it can be concluded that effect of treatment for recovery of cerebral function before aneurysm occlusion is insignificant. HHG improvement means that the brain damage was not completely irreversible in the first place, thus leading to a positive prognosis. We suggest that close monitoring after hospitalization to all grade V patients should be necessary to observe changes in HHG. Improvement of HHG will help determine timing of surgery. Sasaki et al stressed that close monitoring for HHG change over the first 24 hours after hospitalization is mandatory in patients whose poor grade is primarily due to SAH, because it can help determine the appropriateness of surgery[9]. Le Roux et al insisted that aggressive management of SAH including surgical aneurysm obliteration should not be denied solely on the basis of the neurological condition on admission[10] .

Younger age patients had better outcome than older age patients. Younger age patients were observed with more favorable outcome in general. This can be supported by Hutchinson et al's study, which reported that age over 65 patients had less favorable outcome than age under 65 patients[11]. Older age patients generally have more systemic disease in heart, lung and kidney and they may prohibit treatment to achieve proper ICP and CBF[12]. These diseases may increase risk of extracranial organ dysfunction and attribute to worse outcome of patients. However Laidlaw et al insisted that elderly poor grade patients had similar outcome to younger patients, although good grade patients had better outcome in the younger group than the elderly group[13,14,15]. And they also reported that rebleeding occurred in 9% of the elderly series despite of early surgery. Clinical course of old aged poor grade patients will need further investigation.

Low density lesion on Brain CT scan was suggested possible prognostic factor in sample t-test, but it was found no significance in the logistic regression test of prognostic factors. Brain CT scan is most useful tool for diagnosis of SAH and determining severity. Fischer grade is used for measuring amount of SAH by CT scan. Low density lesion on initial CT scan is poor prognostic factor in HHG V patients. However, there are some different opinions. For example, O'Sullivan et al reported that intracerebral hematoma, intraventricular hemorrhage and hydrocephalus are associated with worse prognosis[16]. And

Shimoda et al insisted that irreversible periventricular brain damage is already complete immediately after packed IVH occurs[17]. Despite these different opinions, it can be stated that low density lesion on initial CT scan may mean severe brain damage that is caused by initial hemorrhage. Initial low density may be reversible lesion but it is hard to be recovered before sufficient CBF recovery. As stated previously, aggressive management for sufficient CBF recovery before aneurysm occlusion increases the risk of rebleeding, and without aggressive management, low density lesion may be not improved. Hutchinson et al suggested that initial bleeding, aneurismal rebleeding and delayed ischemia are major cause of death following SAH[11]. The brain MR scanning will be helpful, if patient can be tolerable during the scanning time.

Other factors are not statistically significant in our study. Aneurysm in posterior circulation tended to have worse outcome. But the number of patients with aneurysm in posterior circulation is small in our study, so it does not truly represent grade V patients. On the other hand, Kremer et al reported that better treatment outcome was found in patients with aneurysms in the posterior circulation than in the anterior circulation[18]. Therefore, more studies are needed to define the relation of location of aneurysm and the outcome of SAH. Vasospasm and ischemia did not affect outcome. Delayed ischemia is well known complication of SAH, but its role in poor grade patients was not major. This can be supported by Ungersbock et al, who reported that severe disability was mainly attributed to primary brain damage, while vasospasm played a minor role[19].

Apart from clinical factors used in our study, some other factors were suggested as predictable values. Alberti et al insisted the admission plasma glucose level to be an independent prognosticator of outcome[20]. Mocco et al reported that hyperglycemia on admission after poor grade aneurismal SAH increased the likelihood of poor outcome, and was a potentially modifiable risk factor[21, 22]. Yoshimoto et al insisted that bilaterally unreactive pupils on admission were a powerful predictor of death and motor response was a less powerful predictor than pupillary reactivity[23]. Ungersbock reported that improvement may only be achieved by early referral of SAH patients to neurosurgical centres. Sarrafzadeh et al studied about microdialysis for extracellular glucose, lactate, lactate/pyruvate (L/P) ratio, glutamate, and glycerol and suggested that the L/P ratio was the best metabolic independent prognostic marker of 12-month outcome of SAH[24].

Several methods were applied to poor grade patients for predict outcome. Claassen et al used continuous electroencephalogram (cEEG) monitoring[25]. They insisted that cEEG monitoring provided independent prognostic information in patients with poor grade SAH, even after controlling for clinical and radiological findings and unfavorable findings include periodic epileptiform discharges, electrographic status epilepticus, and the absence of sleep architecture. Ritz et al evaluated the prognostic value of somatosensory evoked potentials in poor grade patients[26]. They insisted that SSEP are superior to clinical grading scales in determining prognosis in poor-grade patients.

We discussed prognostic factors before surgery, but there are many studies about different treatment modalities and surgical procedures in relation to outcome of SAH. Early surgical aneurysm obliteration is necessary, because rebleeding is dismal and more frequent in poor grade patients[13]. Versari et al insisted that early surgery achieved favorable outcome in 73% of poor grade patients[27]. Suzuki et al suggested that early endovascular therapy was successful in decreasing repeated aneurysm rupture and in enabling aggressive medical management during the acute phase of SAH[28]. And there was no good outcome without surgical treatment. Lee et al reported that rebleeding is the only preventable cause of unfavorable outcome, urgent management is necessary to prevent rebleeding[29]. Shin et al also reported that one-stage embolization can prevent ultra-early rebleeding followed by aggressive resuscitation[30]. Oda et al stated that early aneurysm surgery and postoperative dehydration therapy were effective in the treatment of patients with severe SAH but reversible primary brain damage[31]. Nowak et al reported that poor grade aneurysm patients can achieve better outcome with active treatment based on immediate ventriculostomy and optimal hemodynamic parameters after hematoma evacuation and early occlusion of the aneurysm[32].

While Ross et al stated that early GDC aneurismal occlusion has had a minimal impact on overall outcome[33], Inamasu on the other hand reported that endovascular treatment improved HHG V patients' survival rate but not their favorable outcome rate in comparison with conservative treatment[34].

Gasser et al suggested that long-term hypothermia was effective to manage poor grade patients[35]. Bailes et al insisted that poor grade aneurysm patients usually presented with intracranial hypertension, even those without an intracranial clot and ventriculomegaly, and immediate ventriculostomy had to be performed[36]. Petruk et al insisted that nimodipine treatment in poor grade patients with SAH resulted in an increase in the number of good outcomes and a reduction in the incidence of delayed neurological deterioration due to vasospasm[37]. Alberti et al suggested that hypertonic saline safely and effectively augmented CBF in patients with poor grade SAH and significantly improves cerebral oxygenation[20].

Despite of many studies on poor grade SAH patients, there are no defined prognostic factors and treatment modalities. Therefore more studies which include minute factors such as metabolites or genes should be conducted.

V. CONCLUSION

In poor clinical grade patient on arrival, active management should be performed in younger patients or the patients with improvement of clinical grade.

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ABSTRACT(IN KOREAN)

헌트-헤스 5 등급 뇌지주막하출혈 환자의 예후인자

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유 남 규

서론 : 이 연구는 뇌동맥류에 의한 뇌지주막하출혈의 헌트-헤스 5등급 환자에서의 예후 인자를 확인하기 위해 계획되었다.
재료 및 방법 : 1996년3월부터 2007년6월까지의 기간동안 헌트-헤스 5 등급인 81명의 환자를 선택하였다. 임상경과는 적합화된 글래스고우회복등급을 사용하였다. 가능한 예후인자들을 분석하였고 이분 로지스틱 회귀분석을 시행하였다.
결과 : 남자는 32명 여자는 49명이었고 연령의 중간값은 55.5세였다. 뇌전산단층촬영의 피셔등급은 3등급이 23명, 4등급이 58명이었다. 24명은 병원도착전에 재출혈이 확인되었다. 전대뇌동맥의 뇌동맥류가 25명, 내경동맥의 동맥류는 21명, 중간대뇌동맥의 뇌동맥류는 25명, 척추-기저동맥의 동맥류는 10명이었다. 헌트-헤스 등급의 향상은 41명의 환자에서 확인되었다. 5등급에서 4등급으로는 37명이었고 3등급으로는 2명, 2등급으로는 2명이었다. 미세현미경 수술은 51명에서 시행되었고 혈관내수술은 30명에서 시행되었다. 3일 이내의 조기 수술은 46명에서 시행되었고 4~7일사이는 24명, 그 이후는 11명이었다. 임상경과는 우수함 21명, 양호 14명, 불량 25명, 사망 21명이었다. 통계학적인 분석결과 좋은 회복의 예후인자는 수술전 헌트-헤스 등급의 향상과 어린 나이였다. 좋지 못한 회복은 초기 출혈의 뇌손상, 치료와 관련된 합병증 그리고 동맥류의 재출혈 때문일 것이다.
결론 : 초기의 임상 양상이 좋지 않더라도 젊은 환자와 헌트-헤스 등급의 호전이 있다면 더욱 적극적인 치료가 필요하다.

핵심되는 말 : 지주막하출혈, 헌트-헤스 5등급, 예후인자