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Study of Factors Associated with Neurological Outcome in Traumatic Subarachnoid Hemorrhage
- Clinical Analysis -

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= 국문초록 =

외상성 지주막하 뇌출혈에서 신경학적 예후와 관련된 인자들의 분석
- 임상연구 -

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목 적 : 이 논문의 목적은 외상성 지주막하 출혈 환자의 결과에 영향을 미치는 인자를 규명하여 치료에 도움을 주고자 함이다.

방 법 : 저자들은 2003년 1월부터 2004년 12월까지 최근 2년간 본원에 내원한 전산화단층촬영(computed tomography, CT)에서 외상성 지주막하 출혈 환자로 진단된 90명을 대상으로 후향적으로 분석하였다. 추적관찰 전산화 단층촬영에서의 변화를 Morris-Marshall 분류법에 의하여 규정하였다. 지주막하 출혈량은 modified Fisher 분류법에 의하여 기록하였다. 입원당시 신경학적 상태는 Glasgow Coma Scale (GCS)에 의하여 분석하였고, 수상 후 6개월의 환자상태는 Glasgow Outcome Scale(GOS)에 의하여 분석하였다.

결 과 : 27명(30%)의 환자에게서 좋지 않은 결과를 보였다. 단변량분석에서는 입원 당시의 GCS점수, 입원 당시의 Morris-Marshall 분류, Fisher 분류법, 그리고 전산화 단층촬영에서의 변화가 예후에 영향을 미치는 인자로 판명되었고, 전산화 단층촬영에서의 변화는 입원 당시의 GCS점수, 입원 당시의 Morris-Marshall 분류, Fisher 분류법과 연관이 있는 것으로 판명되었다. 그리고, 다변량분석에서는 독립적으로 결과에 영향을 미치는 인자는 입원 당시의 GCS점수, 복합 뇌좌상(combined contusion), 그리고 전산화 단층촬영에서의 변화이었다. 전산화 단층촬영에서의 변화는 독립적으로 입원 당시의 GCS점수, 복합 뇌좌상(combined contusion)등의 인자와 연관이 있었다.

결 론 : 외상성 지주막하 출혈 환자의 결과를 개선하려면, 뇌좌상의 증식억제와 외상성 지주막하 출혈의 뇌의 효과를 최소화하는데 관심을 집중하여야 한다고 사료된다.

중심 단어 : 외상성 지주막하 뇌출혈 · 뇌 손상 · 결과.

Introduction

Traumatic subarachnoid hemorrhage(tSAH), an increasingly recognized concurrent intracranial diagnosis, demonstrates a distribution of blood that is markedly different from nontraumatic SAH. However, in contrast to spontaneous SAH, not much attention was paid to tSAH until recently. tSAH is caused by bleeding of cortical arteries, veins, and capillaries from brain surface cerebral contusions. Not much information is available regarding the pathology of tSAH, but It is highly probable that multiple mechanisms are involved.

The presence of tSAH had an independent effect on worsening outcomes[16]. The high association described in computed tomography (CT) scans between the presence of contusions and subdural hematomas with the presence of blood in the subarachnoid space might be an additional indicator of the probable source of bleeding in these patients[12,15].

The goal of the current study was to identify the factors, if any, that can predict poor outcomes in a population of tSAH patients. In addition, we evaluated those factors identified from the serial CT scans in the same population that predict lesion progression.

Materials and Methods

We retrospectively studied 90 patients admitted to our hospital in the two-year period from January 1, 2003 to December 31, 2004 with an initial CT diagnosis of tSAH. The exclusion criteria were brain death at admission, severe hypotension caused by extracranial injuries (systolic blood pressure persistently<90mm Hg), patients needing cardiopulmonary resuscitation, and penetrating head injuries not related to road traffic accidents.

The time interval between trauma and the admission CT scan was within 3 hours. All patients underwent a second CT scan within 24 hours after injury. Subsequent CT examinations were scheduled according to clinical and radiologic need. Initial and subsequent CT scans were retrospectively reviewed and classified according to the criteria of Morris-Marshall[22] (Table 1).

The amount of tSAH on the CT scan at admission was determined using a modified Fisher classification[7] in which Grade 2 represents diffuse or thin-layered deposition of blood in the subarachnoid space, without clots and/or vertical layers of blood 1mm or greater in thickness, Grade 3 represents localized clots and/or vertical layers of blood 1mm or greater in thickness, Grade 4 represents diffuse or no subarachnoid blood but the presence of intraventricular clots. No patient was included with a score of Grade 1 (no blood detected), because the patients in the study group all had CT evidence of tSAH. Intracerebral clots, when not associated with intraventricular clots, were excluded from Grade 4 because they were considered to be suspected contusions.

CT change was defined as the presence of a new contusion (a parenchymal lesion on the worst CT scan that was not present on the admission CT scan) or as a lesion that was identified on the first CT scan but had doubled its dimensions in at least one diameter on the worst CT scan.

The Glsagow Coma Scale (GCS) score was analyzed as individual values and was stratified into three categories : 13 to 15 (mild), 9 to 12 (moderate), and less than 9 (severe). A score of 13 (24 patients) was included in the group of mild head injuries[4,9,13] to be consistent with previously published reports and thereby allow comparison.

Outcome was assessed in an outpatient clinic 6 months after injury using the Glasgow Outcome Scale (GOS)[14]. For certain analyses, the outcome was dichotomized as favorable (good recovery and moderate disability) or unfavorable (severe disability, persistent vegetative state, and death).

Frequencies, means, standard deviations, and ranges were used as descriptive statistics. Univariate and stepwise forward multivariate logistic regression analyses were used to identify factors related to unfavorable neurological outcomes or to CT change of the lesions and were also used to control for confounders. The variables included in the multivariate analyses consisted of age, sex, GCS score, Morris-Marshall and Fisher classifications of initial CT findings, combined contusions on the initial CT scan and the CT change. The Morris-Marshall classification on the worst CT scan and any form of CT progression were also taken into account in evaluating the neurological outcome. The entry and removal levels of associated factors were 0.05 and 0.10, respectively. The odds ratios (ORs), together with their 95% confidence intervals (CIs), were also derived. The ORs indicate the estimated risk increase of outcome or lesion progression attributable either to the increase of one category in the predictors or to the increase of age. Statistical analyses were performed on a PC using the SPSS/PC statistical package. Two-tailed p values less than 0.05 were considered statistically significant.

Results

Table 2 presents the tSAH patient characteristics at admission. The mean age of this group was 48.3 years (range, 1−86yr), and 70(78%) of the patients were male, 46(52%) patients had moderate to severe brain injuries and 73(81%) had no contusions at admission.

Each patient underwent an average of 2.7 CT examinations (range, 2−6 scans) during the initial 15 days after injury. The classification was arranged according to Morris-Marshall criteria (Table 1). The 17 patients for whom the first CT scan was not the worst CT scan were evaluated to score the progression of parenchymal damage and the changes in the Marshall classification.

In no case was the worst CT scan caused by the presence of ischemic damage in a vascular area not related to the presence of brain contusions, although in one case a vasospasm was identified clinically by transcranial Doppler on the 7th day after admission (hemispheric index (HI)=3.27). Thereafter the vasospasm was resolved on the 10th day (HI=2.44) and the patient had a good recovery outcome after 6 months.

Fifty-seven patients (63%) had a good recovery, 6 (7%) had a moderate disability, 14(16%) had a severe disability, and 13(14%) died. Therefore, the unfavorable outcomes totaled 27 patients (30%) (Table 2). When relating outcome to the presence of any CT change, 15 (88%) of the 17 patients who demonstrated change on the CT images had an unfavorable outcome as compared with 8(11%) of the 73 patients with no CT change (OR,

Table 1. Morris-marshall classification of traumatic subarachnoid hemorrhage

	Description of CT scan findings
Grade 0	No CT evidence of traumatic (tSAH)
Grade 1	tSAH present only in one location
Grade 2	tSAH present at only one location, but quantity of blood fills that structure or tSAH is at any two sites, filling neither of them
Grade 3	tSAH presents at two sites, one of which is the tentorium filled with blood
Grade 4	tSAH presents at 3 or more sites, any quantity

CT : computed tomographic, tSAH : traumatic subarachnoid hemorrhage

Table 2. Demographic, clinical, and radiological characteristics of the study population (90 patients with traumatic subarachnoid hemorrhage at admission)

Characteristics	Number (%)
Age	
Less than 20	9(10%)
20−50	33(37%)
Above 50	48(53%)
Sex	
Male	70(78%)
Female	20(22%)
GCS score at admission	
Mild (13−15)	44(49%)
Moderate (9−12)	30(33%)
Severe (3−8)	16(18%)
Morris-Marshall classification	
Grade 1	15(17%)
Grade 2	34(38%)
Grade 3	31(34%)
Grade 4	10(11%)
Fisher classification	
Grade 2	35(39%)
Grade 3	25(28%)
Grade 4	30(33%)
Contusion on initial CT scan	
Absent	62(69%)
Present	28(31%)
CT change	
Absent	73(81%)
Present	17(19%)
Outcome	
Good recovery	57(63%)
Moderate disability	6(7%)
Severe disability	14(16%)
Dead	13(14%)

GCS : glasgow coma scale, CT : computed tomographic

Table 3. Univariate analysis of factors associated unfavorable outcome and CT change in traumatic subarachnoid hemorrhage

	Unfavorable outcome	CT Change
Age		
less than 20	3/9 (33%)	2/9 (22%)
20–50	8/33 (24%)	8/33 (24%)
above 50	12/48 (25%)	7/48 (15%)
OR (95% CI)	0.883 (0.438–1.777)	0.692 (0.324–1.480)
P value	0.273	0.657
Sex		
Male	19/70 (27%)	15/70 (21%)
Female	4/20 (20%)	2/20 (10%)
OR : F versus M (95% CI)	0.671 (0.199–2.263)	0.407 (0.085–1.955)
P value	0.480	0.738
GCS score at admission		
Mild : 13-15	2/44 (5%)	4/44 (9%)
Moderate : 9–12	5/30 (17%)	3/30 (10%)
Severe : 3–8	16/16 (100%)	10/16 (63%)
OR (95% CI)	0.036 (0.008–0.154)	0.229 (0.103–0.509)
P value	**<0.001**	**<0.001**
Morris-Marshall classification		
Grade 1	0/15 (0%)	1/15 (7%)
Grade 2	1/34 (3%)	0/34 (0%)
Grade 3	12/31 (39%)	10/31 (32%)
Grade 4	10/10 (100%)	6/10 (60%)
OR (95% CI)	37.654 (5.208–272.263)	5.278 (2.410–18.906)
P value	**<0.001**	**<0.001**
Fisher classification		
Grade 2	1/35 (3%)	1/35 (3%)
Grade 3	2/25 (8%)	2/25 (8%)
Grade 4	20/30 (67%)	14/30 (47%)
OR (95% CI)	12.516 (4.114–38.075)	6.750 (2.410–18.908)
P value	**<0.001**	**<0.001**
Contusion on initial CT scan		
Absent	1/62 (2%)	2/62 (3%)
Present	22/28 (79%)	15/28 (54%)
OR (95% CI)	6.659 (1.440–30.793)	9.391 (1.179–74.828)
P value	0.015	0.034
CT change		
Absent	8/73 (11%)	
Present	15/17 (88%)	
OR (95% CI)	60.937 (11.726–316.686)	
P value	**<0.001**	

CT : computed tomographic, OR : odd ratio, CI : confidence interval, GCS : glasgow coma scale

60.937 ; 95% CI, 11.726–316.686 ; $p<0.001$) (Table 3).

The frequencies of unfavorable outcomes and the change of lesions related to putative predictive factors are reported in Table 3, which presents the percentages, ORs and 95% CIs of poor outcomes and CT change related to clinical or radiological parameters. Prognosis was significantly related to admission GCS score ($p<0.001$), Morris-Marshall CT classification at admission ($p<0.001$), Fisher CT classification ($p<0.001$), and CT change ($p<0.001$). Combined contusion on initial CT scan (OR, 6.659 ; 95% CI ; 0.440–30.793 ; $p=0.015$), age (OR, 0.883 ; 95% CI, 0.438–1.777 ; $p=0.273$) and sex (OR, 0.671 ; 95% CI, 0.199–2.263 ; $p=0.480$) were not related to poor outcome.

In the univariate analysis, significant factors for higher risk of CT change were admission GCS score ($p<0.001$) Morris-Marshall CT classification at admission ($p<0.001$) and Fisher CT classification ($p<0.001$).

Of the 62 patients with no contusions on the admission CT scan, only 2 (3.0%) had CT change on subsequent CT examinations. Conversely, 15 (54%) of 28 patients with contusions on the admission CT scan had CT change on

Table 4. Multivariate and logistic regression analysis of factors associated unfavorable outcome and computed tomographic change in traumatic subarachnoid hemorrhage

	Odds ratio (95% confidence interval)	*P* value
Outcome		
GCS score at admission	2.432 (1.342–13.452)	<0.001
Morris-Marshall classification	2.033 (0.832–17.257)	0.245
Fisher classification	7.932 (3.294–38.873)	0.098
Contusion on initial CT scan	3.621 (0.765–18.242)	0.003
CT change	4.722 (2.042– 9.329)	<0.001
CT change		
GCS score at admission	1.164 (0.325– 4.174)	<0.001
Morris-Marshall classification	3.900 (0.766–19.846)	0.101
Fisher classification	3.062 (0.760–12.333)	0.115
Contusion on initial CT scan	1.445 (0.108–19.580)	0.002

GCS : glasgow coma scale, CT : computed tomographic subsequent CT scans. Age (OR, 0.692 ; 95% CI, 0.324–1.480 ; $p=0.657$) and sex (OR, 0.407 ; 95% CI, 0.085–1.955 ; $p=0.738$) were not related to CT change.

In the multivariate and logistic regression analyses, significant factors for higher risk of poor outcome were GCS score at admission (OR, 2.432 ; 95% CI, 1.342–13.452 ; $p<0.001$), CT change (OR, 4.772 ; 95% CI, 2.042–9.329 ; $p<0.001$) and contusion on initial CT scan (OR, 3.621 ; 95% CI, 0.765–18.242 ; $p=0.003$). The factors predicting CT change were GCS score at admission (OR, 1.164 ; 95% CI, 0.325–13.452 ; $p<0.001$) and contusion on initial CT scan (OR, 1.445 ; 95% CI, 0.108–19.580 ; $p=0.002$) (Table 4).

Discussion

The report from the American Traumatic Coma Data Bank, which is based on the analysis of the initial CT scans of 753 patients with severe head injury, described CT-visible tSAH in 39% of the cases[5]. This study demonstrated that patients with CT-visible tSAH had a two-fold greater risk of dying than those without this finding. The presence of SAH after head injury was shown to be an important predictor of death, irrespective of age and the initial GCS score.

While it is recognized that parenchymal posttraumatic lesions may evolve or progress with time, only recently has it been demonstrated that this phenomenon may involve as many as 50% of patients observed in the first 24 hours[23][27][31]. The presence of tSAH on an admission CT scan was significantly related to the progression of parenchymal damage[25].

In this series, a good outcome was reported in 95.5% of mildly head-injured (GCS score range, 13–15) patients, which is similar to that reported in an unselected (with combined tSAH and non-tSAH patients) series of mildly injured patients[10][26]. Other researchers[29] have reported similar results. Our data do not support the conclusions of a recent report[3] demonstrating poor outcomes in tSAH patients with mild head injuries.

Our data on moderate head injuries (GCS score range, 9–12) showed 5 (16.7%) of 30 patients with a poor outcome, as compared with a published rate in two unselected series ranging from 9 to 12%[6][30]. For combined moderate and severe head injuries, the rate of poor outcomes in the current report was 45.7%, which is far less than the rate of the 85% rate recently published in a multicenter study[24].

The Fisher classification[7] and the more complicated Hijdra classification[13] are controversial and were originally devised for subarachnoid hemorrhage from aneurysms. The Green[11] criteria take into account the amount of blood in the cisterns (with a cutoff at 5mm of thickness) and the presence of a posttraumatic mass lesion. Unfortunately, none of these classifications have been generally adopted. We adopted the Morris-Marshall classification[22], which considers the amount of blood and the number of sites in which tSAH is localized, including the tentorium, and the Fisher classification to asses factors related to tSAH[4][9], with some modifications. In this study, we excluded Grade 1 (positive lumbar puncture with no blood on the CT scan), used Grades 2 and 3 (increasing amount of blood in the cisterns) as originally defined, and modified Grade 4 by including only intraventricular hemorrhage and excluding intraparenchymal clots.

In our study, we identified GCS score[17] at admission and contusion on initial CT scan as the best independently predictive factors for a poor outcome. The absence of increasing age as a prognostic factor of a bad outcome may have been related to the subject selection of our population because tSAH patients are on average older than those in unselected series of brain-injured patients both in our study and in other reports[24]. Therefore, the effect of age on outcomes was weakened.

The presence of combined contusion was confirmed to be positively related to a bad outcome. Our findings confirmed the hypothesis of Demercivi et al[4] that there are two types of traumatic tSAH. Those with tSAH but without associated parenchymal damage have better outcomes, while those with both tSAH and associated parenchymal damage have poorer outcomes.

The two key factors predicting CT change at admission were the presence of contusions and GCS score. The presence of contusions at admission identifies a population at a high risk of CT change (Table 4). Brain contusions occur at the moment of impact, whereas perifocal edema develops some time later[1)18)]. Hemorrhagic contusions often grow larger, whereas brain necrosis is considered to be primary damage that is stable on follow-up examinations[20)]. Recent studies have revealed a significant release of cytotoxic, excitatory amino acids in hemorrhagic contusions[2)], suggesting that neuronal degeneration may be a delayed process occurring on the first to third days after injury. When subarachnoid blood enters the brain through the damaged pia or arachnoid membrane, cytotoxic substances are also released into the extracellular space[21)]. This explains the high predictive value for poor outcomes associated with the amount of subarachnoid blood. The combination of tSAH and brain contusions on an admission CT scan identifies patients at the highest risk of developing brain damage.

A relevant finding of our research was that patients having CT change have significantly worse outcomes than those having no changes, which was in agreement with the reports by Stein et al[28)] and Lobato et al[19)].

The higher frequency of delayed ischemic events was considered for years to be the main cause of the poor outcomes in tSAH patients[20)]. In our study, we found that tSAH is an early indicator of more severe initial brain damage. The anatomic and physiological foundation of tSAH could be related to concurrent brain contusions. Fukuda et al[8)] demonstrated that low-density areas observed on follow-up CT scans of tSAH patients are located at the site of earlier contusions and not, as previously suggested, in vascular territories. When scoring the worst CT scan, there was no case where the worst lesion identified as ischemia was observed in a vascular territory. On the contrary, we found that the amount of tSAH blood and the presence of contusions were strongly related to outcomes and lesion progression.

In this study, we focused on tSAH patients without the benefit of a comparison group. Although our aim was to study a homogeneous patient group, this will have weakened the possibility of generalizing our findings to the overall population of brain-injured patients. Our patients did not undergo systematical study with Doppler ultrasound examinations or xenon computed tomography ; therefore, we were not able to relate our data to arterial blood flow or vasospasm. Furthermore, data were not collected on the coagulation profile of our patients. In a study presented by Stein et al[28)], changes in the mean prothrombin time and mean partial thromboplastin time were related to the development of delayed brain injury

Conclusion

We have demonstrated that poor outcomes among patients with tSAH at admission are related to GCS score, CT change and contusions presence. The GCS score and presence of contusions also predicted significant lesion progression, thus linking CT changes with a prognosis of poor outcomes.

A central finding from our study was the effect of the classification of tSAH classification and associated brain contusions on lesion progression. The presence of changing lesions in areas of cortical tSAH on admission CT scan confirmed the hypothesis of tSAH as an early predictive factor associated with developing brain damage.

It seems that in orther to improve the outcomes in tSAH patients, attention will need to be focused on inhibiting contusion growth and on minimizing the effects of tSAH on the brain.

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