CLINICAL ARTICLE
Korean J Neurotrauma 2013;9:114-119

pISSN 2234-8999 / eISSN 2288-2243
http://dx.doi.org/10.13004/kjnt.2013.9.2.114

Risk Factors for Reoperation after Traumatic Intracranial Hemorrhage

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Objective: Progression after operation in traumatic brain injury (TBI) is often correlated with morbidity and poor outcome. We have investigated to characterize the natural course of traumatic intracranial hemorrhage and to identify the risk factors for postoperative progression in TBI.

Methods: 36 patients requiring reoperation due to hemorrhagic progression following surgery for traumatic intracranial hemorrhage were identified in a retrospective review of 335 patients treated at our hospital between 2001 and 2010. We reviewed the age, sex, Glasgow Coma Scale, the amount of hemorrhage, the type of hemorrhage, rebleeding site, coagulation profiles, and so on. Univariate statistics were used to examine the relationship between the risk factors and reoperation.

Results: Acute subdural hematoma was the most common initial lesion requiring reoperation. Most patients had a reoperation within 24−48 hours after operation. Peri-lesional edema (p=0.002), and initial volume of hematoma (p=0.013) were the possible factors of hemorrhagic progression requiring reoperation. But preoperative coagulopathy was not risk factor of hemorrhagic progression requiring reoperation.

Conclusion: Peri-lesional edema and initial volume of hematoma were the statistical significant factors requiring reoperation. Close observation with prompt management is needed to improve the outcome even in patient without coagulopathy.

(Korean J Neurotrauma 2013;9:114-119)

KEY WORDS: Traumatic brain injury · Rebleeding · Progression · Risk factor · Reoperation.

Introduction

Delayed enlargement of traumatic contusions and hematomas is the most common cause of clinical deterioration and death in patients in traumatic brain injury (TBI).[2,14] Therefore, early identification and treatment is most important to improve neurological outcome. Though repeated computerized tomography (CT) scans and intracranial pressure (ICP) monitoring and serial neurological examinations are used for early identification, it is also important to identify the predictable risk factors above all.

The goals of this study were to identify the risk factors for postoperative progression, and to compare the results with other previous reviews, and to prepare for neurological deterioration effectively.

Received: August 18, 2013 / **Revised:** October 9, 2013
Accepted: October 9, 2013
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Materials and Methods

Patient population and data

A retrospective review of 335 patients who experienced operation after TBI between 2001 and 2010 was performed. Of total 335 patients, we excluded 33 patients having operation due to simple or compound comminuted depressed fractures which were not combined with hematoma showing mass effect or requiring immediate evacuation. We also excluded the case which had been operated in other institute and transferred out to our hospital followed by secondary operation, due to the unavailability of initial data. In addition, we excluded the patients of initial Glasgow Coma Scale (GCS) below 4 or having multiple systemic trauma, due to the difficulty in evaluation of progression and the lack of viability.

Among 302 patients except for those cases, 36 patients required reoperation due to hemorrhagic progression fol-

lowed by surgery for acute traumatic lesion. All patients were evaluated with an initial CT scan and were followed by serial neurological examinations and repeated CT scans were also obtained immediately after the occurrence of neurological deterioration in all patients.

We investigated the data of patients including sex and age, the mechanism of injury, and initial GCS. The mechanism of injury was divided to seven groups of fall down, slip down, roll down, in-car accident, pedestrian accident, motorcycle accident, and other causes including penetrating injuries. We evaluated the initial GCS of patients, and divided them into three groups of severe (5−8), moderate (9−12), and mild (13−15).

By analyzing CT images, we classified the type of initial hemorrhage and divided them by the main lesion led to the operation to three as epidural hematoma (EDH), subdural hematoma (SDH), intracerebral hemorrhage (ICH). Hemorrhagic contusion was included in the group of ICH. We measured the size of the hemorrhage by using ABC/2 method,[7] the maximum length (A) in cm was multiplied by the maximum width (B) in cm and the maximum depth (C) in cm. The depth (C) was determined by multiplying the number of slices on which hematoma was visible by the slice thickness of CT scan, and the final product was divided by 2.[7] We also identified the presence of skull fracture, perilesional edema, and sulcal effacement. We recognized perilesional edema seen as an abnormal area of low attenuation or abnormal signal intensity confined to white matter around the lesion, and sulcal effacement was defined as loss of definition of the sulcus due to edema.

We defined the progression of hemorrhage as an evident increase in the appearance of lesion size, and the case requiring operation for management. To characterize the progression of hemorrhage, we investigated the location and the type of hemorrhage compared to the initial preoperative CT findings. If the patients had CT scan more than two times before deterioration, we chose the CT scan taken just before the reoperation. We also divided the progression of hematoma into the three types of EDH, SDH, and ICH. In the case of having multiple lesions, we only recognized the main lesion as the main cause of progression requiring additional operation. In addition, we checked the interval time between the primary and second operation after deterioration.

All patients were evaluated their coagulation status including prothrombin time (PT), activated partial thromboplastin time (aPTT), and platelet (PLT) count when admitted and after operation. Coagulopathy is limited as often broadly defined as a prolongation of the PT, an elevation of the aPTT, or a decrease in the PLT count.[6] Laboratory data were collected to assess the pre and post operatively coagulation status of the patients. Normal coagulation values were defined as 1.2% or less International Normalized Ratio (INR) for PT, 41.7 sec or less for aPTT, and $130\times10^3/\mu L$ to $450\times10^3/\mu L$ for PLT count.

Statistical analysis

Data were analyzed using SPSS version 17.0 (SPSS Inc., Chicago, IL). The categorical variables were analyzed using chi-square test. The continuous variables were assessed using the Student's *t*-test. A *p*-value of <0.05 was considered to be statistically significant.

Results

Patient demographics

In this retrospective review, among 302 patients treated after TBI, the number of patients who experienced the hemorrhagic progression after first operation was 36.

The summary of the demographics of the whole patients are listed in Table 1. The age distribution was ranged from nine to 86 years old and the mean age was 55.2 years. The mechanism of injury was largely divided to groups of fall down (9.6%), slip down (35.8%), roll down (16.6%), in-car accident (14.9%), pedestrian accident (12.6%) and motorcycle accident (9.9%), and other causes including penetrating injuries (0.7%). The most common cause of TBI was slip down as 108 patients (35.8%). The initial GCS of 302 patients divided into 3 groups composed of severe (26.5%), moderate (55.3%), and mild (18.2%). The most common traumatic lesions were subdural hematoma (54.6%, n=165). 46.4% (n=140) showed the presence of skull fracture and 41.4% (n=125) showed peri-lesional edema. Sulcal effacement was combined with hematoma in 76.2% of patients.

Progression of hemorrhage

The overall rate of reoperation due to hematoma progression was 11.9% (n=36)(Table 1). The progression group contained 23 males and 13 females ranged from eight to 84 years and the mean age of them was 57.0 years. The slip down group was most common cause of requiring reoperation after TBI as 12 (33.3%). Among 36 patients, it is noticeable that the proportion of mild GCS group was quite high as 30.6% (n=11). The number of moderate GCS group was highest of all as 16 (44.4%), and the severe GCS group was 9 (25%). The mean GCS of progression group was 10.6. The most common lesion requiring reoperation was SDH accounting for 58.3% (n=21). EDH and ICH account for 22.2%

TABLE 1. Demographics and statistical analysis of total 302 patients having decompressive craniectomy and hematoma removal operation after traumatic brain injury and 36 patients with postoperative hemorrhagic progression

Patient demographics	Progression group (n, %)	Non-progression group (n, %)	Total (n, %)	*p*-value
No. of patients	36	266	302	
Mean age (years)	57.0	55.9	55.2	0.306**
Sex				0.125*
Male	23 (63.9)	222 (83.5)	245 (81.1)	
Female	13 (36.1)	44 (16.5)	57 (18.9)	
Mechanism of injury				0.819*
Fall down	4 (11.1)	25 (9.4)	29 (9.6)	
Slip down	12 (33.3)	96 (36.1)	108 (35.8)	
Roll down	7 (19.5)	43 (16.2)	50 (16.6)	
In-car accident	6 (16.7)	39 (14.7)	45 (14.9)	
Pedestrian accident	4 (11.1)	34 (12.8)	38 (12.6)	
Motorcycle accident	3 (8.3)	27 (10.2)	30 (9.9)	
Etc.	0 (0)	2 (0.8)	2 (0.7)	
GCS				0.984*
Severe (5−8)	9 (25)	71 (26.7)	80 (26.5)	
Moderate (9−12)	16 (44.4)	151 (56.8)	167 (55.3)	
Mild (13−15)	11 (30.6)	44 (16.5)	55 (18.2)	
Radiographic findings				
SDH	21 (58.3)	144 (54.1)	165 (54.6)	0.394*
EDH	8 (22.2)	78 (29.3)	86 (28.5)	0.416*
ICH	7 (19.5)	44 (16.5)	51 (16.9)	0.275*
Skull fracture	14 (38.9)	126 (47.4)	140 (46.4)	0.258*
Peri-lesional edema	25 (69.4)	100 (37.6)	125 (41.4)	0.002*
Sulcal effacement	26 (72.2)	204 (76.7)	230 (76.2)	0.784*
Preoperative coagulopathy	11 (30.6)	71 (26.7)	82 (27.1)	0.342*

*statistical significance was evaluated by chi-square test, **student's *t*-test. Etc.: other causes including penetrating injury, GCS: Glasgow Coma Scale, SDH: subdural hematoma, EDH: epidural hematoma, ICH: intracerebral hemorrhage

(n=8) and 19.5% (n=7), respectively. Combined skull fracture was presented in 38.9% (n=14) and the presence of peri-lesional edema was 69.4% (n=25) and sulcal effacement was 72.2% (n=26). The mean initial volume of non progression group was 49.2 cm^3 and in 206 (77.4%) patients the volume was above 30 cm^3 (Table 2). In progression group, the group above 30 cm^3 was more (86.1%, n=31) than the group below 30 cm^3 (13.9%, n=5) and the mean volume of hematoma was 52.6 cm^3.

The most common progressive hemorrhagic lesions were subdural hematoma (n=21, 58.4%), especially, enlarged SDH in the initial site was 47.2% (n=17)(Table 3). 77.8% (n=28) occurred in the adjacent site comparing with initial lesion, but the case occurred in the other site was as many as 22.2% (n=8).

The interval between the primary and second operation after deterioration was ranged from one hour to even two months, and 61.1% (n=22) was occurred within 48 hours, and 22.2% (n=8) within two to seven days. Six cases (16.7%) deteriorated after seven days from initial operation.

Univariate statistical analysis was carried out to identify factors associated with hemorrhagic progression. This showed statistically significant correlation between hemorrhagic progression and peri-lesional edema (p=0.002)(Table 1), and initial volume of hematoma (p=0.013)(Table 2). It demonstrated that patient's age, sex, the mechanism of injury, initial GCS, the type of hemorrhage, the presence of skull fracture, sulcal effacement, and initial coagulation status were not statistically significant factors (p>0.05)(Table 1).

Coagulation profiles

We reviewed the data of 302 patients to assess the patients' coagulation status including PT, aPTT, and PLT count. We recognized the initial coagulation profiles as the preoperative coagulation status, and the coagulation profiles done immediately after the first operation as the postoperative ones. We evaluated the occurrence of hemorrhagic progression according to existence of coagulopathy. Of total 302 patients, overall 27.1% (n=82) showed abnormal coagulation status preoperatively at least in one of the parameters (PT,

aPTT, and PLT). Among 57 patients initially showing abnormal PT, only four patients showed evidence of progression, and seven patients of 38 patients initially showing abnormal aPTT showed evidence of progression. Among 23 patients having abnormalities in PLT count initially, 5 patients showed hemorrhagic progression.

The mean pre and postoperative PT, aPTT, and PLT count were compared between the progression and non-progression group (Table 4). The mean preoperative PT of non-progression group was 1.15±0.45 (INR)[mean±standard deviation (SD)], whereas that of progression group was 0.98 ±0.08 (INR)(mean±SD)(p=0.296). The mean preoperative aPTT of non-progression group was 32.31±7.51 (sec)(mean ±SD), whereas that of progression group was 30.29±7.21 (sec)(mean±SD)(p=0.415). The preoperative PLT count was 248.92±86.43 ($\times 10^3/\mu L$)(mean±SD) for non-progression group, whereas that of progression group was 223.00± 69.26 ($\times 10^3/\mu L$)(mean±SD)(p=0.375). In the same manner, as for postoperative coagulation status, there was no statistically difference in pre and postoperative PT, aPTT, and PLT count between the two groups (p=0.469, 0.560, 0.279, respectively). Therefore, this analysis suggests that there was no significant difference in coagulation status between the progression and non-progression group in both pre and postoperative time.

TABLE 2. The initial volume of the hematoma on CT scan of patients after TBI

Volume (cm^3)	Non-progression group (n=266)(%)	Progression group (n=36)(%)	p-value*
<30	60 (22.6%)	5 (13.9%)	
≥30	206 (77.4%)	31 (86.1%)	
Mean volume	49.2	52.6	0.013

*student's t-test. The volume was calculated using the following formula: (ABC)/2 (cm^3), A: maximum diameter (cm), B: the diameter at 90° to the maximum diameter (cm), C: the total number of 10 mm axial slices, CT: computed tomography, TBI: traumatic brain injury

TABLE 3. Comparison of the lesions requiring reoperation with the initial location of hemorrhage on the CT scan

Location	Types of hemorrhage	n=36 (%)	Total (%)
Initial site	EDH	6 (16.7)	28 (77.8)
	SDH	17 (47.2)	
	ICH	5 (13.9)	
Other site	EDH	2 (5.5)	8 (22.2)
	SDH	4 (11.2)	
	ICH	2 (5.5)	

EDH: epidural hematoma, SDH: subdural hematoma, ICH: intracerebral hemorrhage, CT: computed tomography

Discussion

The incidence of progression of intracranial hemorrhage after acute head trauma is as reported as up to 23−48%,[16] and this study shows the overall rate of 11.9% of reoperation due to hemorrhagic progression. There are many previous reviews about the relationships between the progression of hemorrhage and several risk factors. Chang et al.[2] quantified lesion size and further characterized the natural course of traumatic intracerebral hemorrhage (tICH).[12] Initial volume of hematoma was found to be a strong predictor of progression, with larger hematomas tending to increase in size, and for each cm^3 of initial volume, the odds of growth increased by 11%.[2,12] There is evidence that the amount of hemorrhage has significant effect on progression. Reportedly, the outcome of patients with traumatic subarachnoid hemorrhage at admission is related to the amount of blood and these patients also have a significant risk of CT progression.[4] The previous results of the first multicenter, prospective study about progression of tICH also confirmed that larger initial lesions tend to have substantially greater hematoma increase, with a greater likelihood of clinical impact.[12] Our results show that the mean volume of initial hematoma of the non-progression group was 49.2 cm^3, while the mean volume of the progression group was 52.6 cm^3 and

TABLE 4. Comparison of the pre and postoperative coagulation profiles of 302 patients after TBI

Variables	Non-progression group (mean±SD)	Progression group (mean±SD)	p-value*
PT (INR)			
Preoperative	1.15±0.45	0.98±0.08	0.296
Postoperative	2.17±4.19	1.30±0.12	0.469
aPTT (sec)			
Preoperative	32.31±7.51	30.29±7.21	0.415
Postoperative	59.45±81.33	33.66±5.57	0.560
PLT count ($\times 10^3/\mu L$)			
Preoperative	248.92±86.43	223.00±69.26	0.375
Postoperative	169.37±71.38	140.88±58.32	0.279

*p-value was analyzed between non-progression and progression groups. PT: prothrombin time, INR: International Normalized Ratio, aPTT: activated partial thromboplastin time, PLT: platelet, SD: standard deviation, TBI: traumatic brain injury

there was statistically significant difference between the two groups. But there are some limitations in measurement of hemorrhage. It was difficult to compare precisely because we only targeted main lesion causing operation and passed over other minor lesions, thus it might resulted in biased outcome. In addition, the comparison was done among different type of hemorrhage, thus we cannot completely exclude the biased error.

Carhuapoma et al.[1] suggest a dose-effect interaction between volume and intensity of response that brain tissue exhibits in blood-mediated edema. Our results could be understood in the similar context. Univariate analysis showed statistically significant correlation between hemorrhagic progression and initial volume of hematoma (p=0.013) and peri-lesional edema (p=0.002).

Peri-lesional edema on the initial CT scan was strongly predictive course, thereby leading to surgical management. In this study, among patients who experienced hemorrhagic progression after operation, 69.4% presented peri-lesional edema on initial CT scan. Analysis showed statistically significant correlation between hemorrhagic progression and peri-lesional edema (p=0.002). Brain edema increases progressively in the first 24 hours and remains elevated for 4 to 5 days, and then begin to resolve.[10] There are several theories on the mechanism of the edema formation. According to the study supporting the concept of the role of the coagulation cascade in brain edema formation, the coagulation cascade and thrombin specifically play a key role.[9] There is a suggestion that thrombin produced by clotted blood, causes changes in brain water and ion contents consistent with edema from an intracranial hemorrhage.[11] Others propose that factors released from activated platelets at the site of hemorrhage, may interact with thrombin to increase vascular permeability and contribute to the development of edema.[15] Brain edema is nearly maximal by 24 hours[19] and most of the growth seems to occur within the first 48 hours of surgery. In that the rate of high GCS group was quite high in patients requiring reoperation, patients in good mental status initially also need to be monitored carefully especially within the first 48 hours after trauma.

The exact mechanisms of coagulopathy in TBI have not been fully understood. According to Cohen et al.[5] TBI accompanied hypoperfusion lead to coagulation derangements, associated with the activation of the protein C pathway. Cohen et al.[5] found thrombocytopenia at admission to be a strong predictor of progression of hemorrhagic injuries. But the reliability in predicting hemorrhagic progression of three parameters (PT, aPTT, and PLT count) used to define coagulopathy in this study is still controversial.[3] From the outcomes of previous studies, we found that coagulation abnormalities were a risk factor for hemorrhage expansion.[13,17,18] According to Carole and colleagues, INR was significantly higher in the group that demonstrated progression (INR of 1.4) compared with the other group (INR of 1.2).[18] While, Engström et al.[6] found no differences in when analyzing PT and aPTT at any time between non-progression and progression groups.[8] Engström et al.[6] also found no statistical difference in initial PLT count between the two groups, but in analysis on PLT count after 24 hour after injury, there was a statistical difference between the two groups, and the mean PLT count was $166\times10^3/\mu L$ for non-progression group, and $106\times10^3/\mu L$ for progression group (p=0.004).[6] In our study, the overall incidence of coagulopathy was 27.1% and univariate analysis showed that initial coagulation status was not the strongest predictors of hemorrhagic progression, too. But abnormalities in initial aPTT occurred in 5.9% of patients and 19.4% in postoperative aPTT. Abnormalities in initial PLT count occurred in 7.1% of patients but the rate was increased in postoperative time as 29.8%. The relationship between coagulopathy and reoperation is still controversial, but this suggests that patients with TBI have a more affected coagulation system. It is suggested that TBI has some impact on coagulation system in the process of injury and recovery even in patients without previous coagulopathy, although there might be some influences from loss of blood or transfusion during surgery or extended operation time for larger hematoma. Prospective studies are required to confirm this correlation in patients with TBI.

Limitations

There are several potential limitations in this study. As remarked above, because we only targeted the main lesion causing operation, there might be an error in measuring the volume of hematoma and thereby it causes the measurement error. In addition, we could not describe the patients' history of use of drugs or alcohol, systemic disease in detail due to the missing data in a retrospective review, and it may influence on the biased results.

As regards ICP monitoring, we could not get the data of ICP monitoring because it was not applied to all patients including the patients in good neurologic status initially. It is also due to old missing data and the difficulties in comparing the risk between the monitoring group and others.

We recognize that these are analysis based on a retrospective, possibly biased review. A prospective study in which CT scans and laboratory data obtained at specified intervals is required to measure and evaluate the correlated factors

on hemorrhagic progression after TBI.

Conclusion

On the basis of our data, peri-lesional edema and initial volume of hematoma were the statistical significant factors requiring reoperation. Patients with TBI seem to have more affected coagulation system, even if they didn't have coagulopathy initially. Close observation and prompt correction of coagulation abnormalities can prevent patient requiring reoperation from progression and deterioration, especially in patients who are at risk of delayed or recurrent lesions.

■ The authors have no financial conflicts of interest.

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