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지연성 외상성 뇌실질내 출혈 환자의 치료를 결정하는 임상적, 영상학적 예후인자에 대한 평가

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- Abstract -

Assessment of the Clinical and the Radiological Prognostic Factors that Determine the Management of a Delayed, Traumatic, Intraparenchymal Hemorrhage (DTIPH)

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Purpose: Delayed, traumatic, intraparenchymal hemorrhage (DTIPH) is a well-known contributing factor to secondary brain damage that evokes severe brain edema and intracranial hypertension. Once it has occurred, it adversely affects the patient's outcome. The aim of this study was to evaluate the prognosis factors for DTIPH by comparing clinical, radiological and hematologic results between two groups of patients according to whether surgical treatment was given or not.

Methods: The author investigated 26 patients who suffered DTIPH during the recent consecutive five-year period. The 26 patients were divided according to their having undergone either a decompressive craniectomy (n=20) or continuous conservative treatment (n=6). A retrospective investigation was done by reviewing their admission records and radiological findings.

Results: This incidence of DTIPH was 6.6% among the total number of patients admitted with head injuries. The clinical outcome of DTIPH was favorable in 9 of the 26 patients (34.6%) whereas it was unfavorable in 17 patients (65.4%). The patients with coagulopathy had an unexceptionally high rate of mortality. Among the variables, whether the patient had undergone a decompressive craniectomy, the patient's preoperative clinical status, and the degree of midline shift had significant correlations with the ultimate outcome.

Conclusion: In patients with DTIPH, proper evaluation of preoperative clinical grading and radiological findings can hamper deleterious secondary events because it can lead to a swift and proper decompressive craniectomy to reduce the intracranial pressure. Surgical decompression should be carefully selected, paying attention to the patient's accom-

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panying injury and hematology results, especially thrombocytopenia, in order to improve the patient's neurologic outcomes. [J Trauma Inj 2015; 28: 223-231]

Key Words: Delayed, Traumatic, Intraparenchymal hemorrhage (DTIPH) , Decompressive craniectomy, Intracranial pressure (ICP), Head trauma

I. Introduction

As the frequency and type of head injuries have been diversified, pathophysiology and treatment methods for such injuries have also significantly changed. Despite advances in the field of neurosurgery, head injuries are still a major cause of death and disability.(1) The goal of treatment after a head injury is to prevent secondary brain damage early by controlling intracranial pressure. Thus, intracranial pressure monitoring and repeated computed tomography (CT) are important in determining whether conservative or surgical treatment should be administered.(2)

Ban M et al.(3) defined hemorrhage found in the site, which was normal on the first CT scan within 48 hours after the head injury, or near the site where bleeding was first detected as DTIPH.(4) DTIPH is reported to occur in 1 to 8% of patients with severe head injury, and the mortality rate is known to be over 40%. Despite many studies on the mechanisms and treatments of brain injuries, the mortality rate is still high, and though patients survive, serious neurological sequelae remain in many cases.(5,6) The reason the prognosis is poor is that there is no special intracranial primary lesion that causes hemorrhage; an imbalance of intravascular hemostasis and hemolysis (diffuse intravascular coagulopathy) results from the rapture of microvessels by shearing force on the etiopathogenic mechanism, joining of petechia within tissues due to the rupture, or biochemical changes; brainstem compression or cerebrospinal fluid circulation disorders are caused by persistent, severe secondary cerebral edema following the increase of the size of hematoma; and consequently, rapid deterioration in consciousness and serious sequelae occur.(3,7-9)

Recently, positive outcomes have been reported through aggressive treatment, such as early decompressive craniectomy, etc., in severe brain injury patients.(10-14) However, in cases of DTIPH patients, treatment method, timing, and screening of subjects for treatment are still controversial. This study aims to suggest an appropriate treatment plan for patients in the risk group and morbidity group, who might become DTIPH patients, by comparing decompressive craniectomy with conservative treatment in DTIPH patients.

II. Materials and Methods

1. Patients selection

Of 1028 patients who were admitted due to brain injury from January 2000 to October 2005, 794 patients were selected as subjects. A total of 234 patients who experienced chronic or subacute subdural hemorrhage or subdural hygroma more than two weeks after the head injury were excluded. A retrospective research was conducted for 392 patients who have undergone craniotomy because of a head injury. Among them, 20 cases which underwent decompressive craniectomy and six cases that received conservative treatment were investigated.

The authors defined DTIPH as a case of the increase of bleeding or hemorrhage occurring in a new location after a certain period of time after confirming the presence of brain lesions due to injury through the brain CT scan. In terms of size, the hematoma with the largest diameter was examined, and a follow-up examination was performed when clinical symptoms were exacerbated, or within 12 hours after the first examination.

2. Methods

Medical records and radiological findings were retrospectively researched, targeting 20 patients

who have undergone decompressive craniectomy and 6 patients who have undergone conservative treatment. Clinically, factors such as age, gender, cause of injury, initial hematologic findings, accompanying damage, and neurological examination were investigated. In terms of radiological findings, presence of hematoma on the initial CT, degree of midline movement, and findings from the follow-up CT were examined. In most cases, secondary hematoma exists as more than one diffuse hematoma, if present, or in the form of small cerebral contusion around the large hematoma, thus the size of hematoma itself or location, etc., were excluded from radiological findings.

The initial level of consciousness was assessed using the Glasgow Coma Scale (GCS),(2,4,5,15,16) and classified by score into severe consciousness disorder (GCS<8), moderate consciousness disorder (GCS: 8-11), and mild consciousness disorder (GCS>12). Neurologic prognosis was assessed by using the Glasgow Outcome Scale (GOS),(15-17) and classified into favorable prognosis when GOS was 4-5 points and poor prognosis when GOS was 3 points or less.

For the statistical analysis, using SPSS 12.0 (Chicago, IL, USA), Fisher's exact test and independent samples T-test were performed, and p values less than 0.05 were considered statistically significant.

3. Indications of Surgical and Non-surgical Treatments.

Among the cases in which brain tissue herniation or the midline was pushed to the opposite side as surrounding brain tissues were severely pressured by hematoma due to DTIPH, and cerebral edema occurred, the cases requiring decompressive craniectomy were as follows: the midline was pushed more than 10 mm to the opposite side on the follow-up brain CT scan; the cerebrospinal fluid structure of basal or sylvian cistern was not observed; at the same time the state of the patient's consciousness showed a decrease in GCS due to brain damage after the neurological examination; the state of the patient's consciousness rapidly declined because of the rise of intracranial pressure; and mydriasis was caused in the bilateral or unilateral pupil, or the pupillary reflex gradually disappeared.

On the other hand, conservative treatment was conducted in the following cases: diffuse multiple cerebral contusions with a diameter less than 2 cm were scattered in both cerebral hemispheres; unilateral craniotomy or local surgery was not effective; movement of the midline was not noticeable; DTIPH was present at the site where the decrease in the patient's GCS could not be explained; and local intracranial hemorrhage other than DTIPH (acute subdural hematoma, acute epidural hematoma) was significant in relation to the state of the patient's consciousness.

III. Results

1. Frequency of Occurrence and Causes

During the research period, among the total number of patients included in the study, 26 patients had DTIPH, and the incidence rate was 6.6%. In terms of age, patients aged 20~29 years whose physical activity was vigorous accounted for 26.9%, which was the largest, and 19 patients were males (73.1%), which was greater than the number of female patients. With regard to the type of accident,

Table 1. Summary of patient's characteristics. (n=26)*

Clinical features	No. of patients (%)
Sex	
Male	18 (69.2)
Female	8 (30.8)
Age	
<10	0 (0)
10-19	4 (15.4)
20-29	7 (26.9)
30-39	6 (23.1)
40-49	2 (7.7)
50-59	4 (15.4)
60<	3 (11.5)
Type of injury	
TA	14 (53.8)
Pedestrian TA	8 (30.8)
In Car TA	6 (23)
Motor Cycle TA	6 (23)
Fall down	4 (15.4)
Assault	2 (7.7)

* TA: traffic accident

Table 2. Sequential changes of neurologic worsening and radiologic worsening*.

Neurologic change	No. of patients (%)	
	Initial GCS	Worsening GCS
15	0 (0)	0 (0)
13-14	10 (38.5)	0 (0)
8-12	14 (53.8)	8 (30.7)
3-7	2 (7.7)	18 (69.3)
Time to radiologic worsening		
<6 hours	13 (50)	
6-12 hours	7 (27)	
12-24 hours	3 (11.5)	
24-72 hours	3 (11.5)	

* Neurologic worsening is defined as decrease in Glasgow coma scale (GCS), and the time to radiologic worsening is determined when noticing delayed traumatic intraparenchymal hemorrhage (DTIPH) on serial computed tomographic scan.

pedestrian traffic accident appeared to be the cause in 8 cases (30.8%); driver or passenger traffic accident in 6 cases (23%); motorcycle accident in 6 cases (23%), fall in 4 cases (15.4%); and head injury by beating in 2 cases (7.7%) (Table 1).

2. Change in Clinical Findings and DTIPH Detection Time

In the GCS that was initially conducted at the emergency room, 10 patients (38.5%) had 13~14 points, 14 patients (53.8%) 8~12 points, and 2 patients (7.7%) 3~7 points. In general, most patients had more than 8 points in the initial GCS. However, in the GCS performed after the confirmation of DTIPH on the CT conducted due to the findings showing lowered consciousness or a decline in the neurological examination, 8 patients (30.7%) had 8~12 points, while 18 patients (69.3%) had 7 points or less. The GCS after the detection of DTIPH was below 8 points in all patients (Table 2).

In terms of the time spent from identifying the findings showing lowered consciousness or a decline in the neurological examination until the confirmation of DTIPH, 13 persons were diagnosed within 6 hours (50%); 7 persons between 6 and 12 hours (27%); 3 persons between 12 and 24 hours; while the other 3 persons were diagnosed between 24 and 72 hours. The increase of bleeding within 6 hours was the most common symptom, which was present in 50% of the cases.

Table 3. Computed tomographic findings with relevant to the midline shift.

Degree of midline shift (mm)	
Initial midline shift	6.09 ± 4.5
Follow-up midline shift	13.45 ± 3.01
Difference of midline shift	$+6.18 \pm 2.54$

3. Degree of cerebral midline Movement (on initial and follow-up CT)

The mean degree of brain midline movement on the CT initially scanned at the emergency room was 6.09 mm with the minimum of 2 mm and the maximum of 11.3 mm. The mean degree of brain midline movement on the CT scan upon determining whether or not surgery should be done after confirming DTIPH was 13.45 mm with the minimum of 9 mm and the maximum of 16 mm. The differences in the degree of brain midline movement at the initial stage and before surgery due to exacerbation were at the minimum of 4 mm, at the maximum of 9 mm, and a mean of 6.18 mm (Table 3).

4. Abnormal Findings on Hematology Tests

On the hematology tests initially performed at the emergency room, 9 patients had thrombocytopenia (platelet<100.000 mm^3). On coagulation tests, 8 patients had prothrombin time (PT) increased for more than 4 seconds, 4 patients had bleeding time (BT) increased for more than 4 minutes, and 4

patients had coagulation time (CT) increased for more than 7 minutes (Table 4).

Among patients with thrombocytopenia, 4 patients with a history of liver cirrhosis had coagulopathy showing abnormal findings in all three tests, prothrombin time (PT), bleeding time (BT), and coagulation time (CT), and died after decompressive craniectomy.

5. Prognosis of Patients

Among 26 patients, 11 patients died, and the mortality rate was 42.4%. Four patients (15.4%) were in the vegetative state, 2 patients (7.6%) had severe disability, and 7 patients (27%) had moderate disability (27%). When mild and moderate disabilities were defined as favorable prognosis and below severe disability as poor prognosis, 9 patients (34.6%) had favorable prognosis, and 17 patients (65.4%) had poor prognosis (Table 5).

6. Correlation between clinical and radiologic findings and prognosis

In the favorable prognosis group, 6 patients (23%) were males, and 3 patients (11.5%) were females. In the poor prognosis group, 13 patients (50%) were males, and 4 patients (15.5%) were females. There was no statistically significant correlation between gender and prognosis (p=0.40).

With regard to the association between age and prognosis, the mean age was 33 years in the favorable prognosis group and 43 years in the poor prognosis group. Although the mean age of the poor prognosis group was older than that of the favorable prognosis group, the difference was not statistically significant (p=0.40).

Table 4. Abnormal hematologic findings on admission*.

Hematologic findings	No. of patients (%)
Thrombocytopenia (<130.000)	9 (34.7)
PT (>4 sec)	8 (30.7)
BT (>4 min)	4 (15.3)
CT (>7 min)	4 (15.3)

* PT: prothrombin time, BT: bleeding time, CT: coagulation time

With regard to the association with the time spent until the confirmation of DTIPH, in the favorable prognosis group, 4 persons (15.5%) were diagnosed within 6 hours, 3 persons between 6 and 12 hours (11.5%), one person between 12 and 24 hours, and one person between 24 and 72 hours. In the poor prognosis group, 9 persons were diagnosed within 6 hours (34.5%), 4 persons between 6 and 12 hours (15.5%), 2 persons between 12 and 24 hours, and 2 persons between 24 and 72 hours. There was no statistically significant association between the duration of DTIPH confirmation and prognosis (p=0.215).

Among patients who have underwent decompressive craniectomy, 9 patients (34.5%) were included in the favorable prognosis group and 11 patients (42.5%) in the poor prognosis group. Among patients who did not undergo surgery, no one had favorable prognosis, and all 6 patients had poor prognosis. Relatively favorable prognosis appeared in patients who have undergone decompressive craniectomy, which was statistically significant (p=0.002).

With regard to GCS score before performing decompressive craniectomy for DTIPH, the mean score was 8.4 points in the favorable prognosis and 6.3 points in the poor prognosis group. Patients with high GCS scores showed favorable prognosis, which was statistically significant (p=0.003).The mean degree of brain midline movement was 12.95 mm before surgery in the favorable prognosis group, and 14.49 mm in the poor prognosis group, which was statistically significant (p=0.034). With regard to coagulopathy, 7 out of 9 patients with thrombocytopenia died, and 10 out of 17 patients with normal platelet counts died. Patients with thrombocytopenia

Table 5. Outcome of DTIPH according to the Glasgow outcome score (GOS)*.

Glasgow outcome scale	No. of patients (%)
Good recovery (GR)	2 (7.6)
Moderate disability (MD)	7 (27)
Severe disability (SD)	2 (7.6)
Vegetative (V)	4 (15.4)
Death (D)	11 (42.4)
Total	26 (100.0)

* DTIPH: delayed taumatic intraparenchymal hemorrhage
Overall outcome is dichotomized into favorable (GR, MD; 34.6%) and unfavorable (SD, V, D; 65.4%) outcome.

before surgery revealed a significantly higher mortality rate (p=0.005).There were 23 cases with accompanying damage. Among them fractures in long bones were most common, followed by hemothorax, pneumothorax, liver injury, etc. The association between accompanying damage and prognosis was not statistically significant (p=0.116) (Table 6).

IV. Discussion

Head injury is known as the most common cause for death and severe disability in young people. For this reason, many initial treatments and methodologies with scientific basis have been proposed recently.(15,16) In patients with severe head injury (patients with GCS of 3-8), there is a high risk of secondary brain injury elements, such as low blood pressure, hypoxia, or cerebral edema.(6) The risk is even higher in DTIPH patients, and the elements are known as common causes for exacerbation of secondary neurologic findings after the head injury.

Fukamachi et al.(18) classified intraparenchymal hemorrhage occurring after the head injury into four types. The first type is a hematoma already seen on the initial CT; the second type is a case involving small or medium-sized hematomas that are gradually increasing in size; the third type is a hematoma developing in the location that was not seen on the initial CT; and the fourth type is a case in which the location where the density increased just like dots (salt and pepper, flecked high density change) on the initial CT scan progresses to hemorrhagic contusion. In this study, type 2 and type 4, based on the classification of Fukamachi et al.(18) appeared in 11 cases (42.3%) and 8 cases (31%), respectively, among DTIPH patients.

The clinical feature of DTIPH was as follows: relatively good consciousness at the initial stage before rapidly worsening, and after worsening, there was no improvement in general. In most cases, decompressive craniectomy was performed immediately after the CT. Intraparenchymal hemorrhage, where lesions that are not present right after the head injury develop after a certain period of time, is reported to occur within 4 hours to 4 days after the injury in general. In this study, intraparenchymal hemorrhage developed within a minimum of 4 hours to a maximum of 72 hours. As a pathogenesis mechanism, first, there is an increase of permeability of endothelium,(19) due to the loss of blood flow and automatic control mechanism, and next, extravasation in the site of cerebral contusion can be argued2). In particular, delayed hemorrhage in the cerebellum region has been reported to occur always in the site of the cerebral contusion,(17,19) delayed hemorrhage also occurred in one case 6 hours after

Table 6. Correlations of outcome with clinical and radiological feature. (n=26)

Variables		Outcome		p value
		Favorable	Unfavorable	
Sex	Male	6 (23%)	13 (50%)	0.40
	Female	3 (11.5%)	4 (15.5%)	
Age		33.40±15.23	43.49±19.21	0.116
Duration	<6 hours	4 (15.5%)	9 (34.5%)	
	6-12 hours	3 (11.5%)	4 (15.5%)	0.215
	12-24 hours	1 (3.8%)	2 (7.6%)	
	24-72 hours	1 (3.8%)	2 (7.6%)	
Operation	(+)	9 (34.5%)	11 (42.5%)	0.002
	(-)	0 (0%)	6 (23%)	
Worsening GCS		8.40±1.95	6.34±1.54	0.003
Midline shift		12.95±1.87	14.49±2.43	0.034
Thrombocytopenia	(+)	2 (7.6%)	7 (27.1%)	0.005
	(-)	7 (27.1%)	10 (38.2%)	
Combined injury	(-)	2 (7.6%)	1 (3.8%)	0.166
	(+)	7 (27.1%)	16 (61.5%)	

injury at the cerebellum contusion site. Or it is associated with diffuse intravascular coagulation fibrinolysis and vascular wall damage due to pH change caused by cell damage.(13) In case damaged blood vessels are pressured by hematoma in the upper or lower intracranial space other than intraparenchymal hematoma (tamponade), DTIPH may occur after its surgical removal.(20)

In hematology tests, thrombocytopenia is commonly diagnosed among DTIPH patients, and in a report, thrombocytopenia was argued as a factor in increasing hemorrhagic contusion and was a strong prognosis factor.(21) These abnormalities in coagulation factors are closely associated with increased intake of anticoagulants, such as aspirin and warfarin, due to the recent increase in cardiovascular and cerebrovascular diseases, and patients who took such medicines increased the mortality rate four times compared to patients who did not take the medicines.(22) In this study, two patients who had a history of cerebral infarction and were taking aspirin and anticoagulants died after surgery. Of nine patients who had thrombocytopenia, seven died, revealing that thrombocytopenia itself has an adverse effect on the prognosis regardless of whether or not surgery is administered.

In general, old age is known as statistically significantly associated with prognosis because age may affect sclerosis and weakening of blood vessel, etc.; hypertension, diabetes, and amyloidosis are common among the elderly; and cerebral hemorrhage is more commonly expressed among the elderly.(23)

Moreover, gender is also associated with prognosis. The reason that males have a higher incidence seems to be associated with differences in the amount and extent of physical activity through which males might be exposed to head injury.(13) Among females, it has been reported that the neuroprotective effects of estrogen and progesterone are associated with lowering the frequency of delayed intracranial hemorrhage. Estrogen is known to decrease cell membrane destruction and fat oxidation, reduce platelet aggregation and apoptosis, and increase cerebral blood flow. Progesterone is known to be associated with cell membrane stability, inhibition of glutamate receptor, and enhancement of gamma amino butyric acid (GABA).(24)

After head injury, severe cerebral edema may be caused by vasogenic edema, cytotoxic edema, cerebral vasocongestion.(2. If conservative treatment fails to treat accelerated intracranial pressure, hypothemia, hyperventilation, barbiturate coma therapy, decompressive craniectomy, etc., can be conducted. Among these, decompressive craniectomy is the fastest way to decrease the intracranial pressure, and it presents the lowest number of complications.(12,14) For patients with DTIPH, it is impossible to close the brain itself, which is already swelling using endocranium and skull only, by locally removing hematoma in most cases. Therefore, when surgery is considered, decompressive craniectomy is not an option but a requirement. For this reason, surgery was limited to decompressive craniectomy, not simple hematoma removal, in this study. In particular, based on animal experiments and clinical data reported recently, decompressive craniectomy can lower accelerated intracranial pressure by expanding the limited space and removing the skull, and improve the patient's prognosis by regulating cerebral blood pressure and the amount of cerebral blood flow to appropriate levels.(10,11) Moreover, when the brain tissue whose autonomous control function for blood flow after hematoma removal is lost, hemorrhage is not arrested, which may result in a secondary problem if the brain tissue is removed with hematoma. Therefore, decompressive craniectomy can be the most reasonable option.

Generally, clinical studies reporting that decompressive craniectomy, performed mainly in patients with cerebral infarction, rapidly lowered intracranial pressure and surgery outcomes were good. However, most patients with cerebral infarction who have undergone decompressive craniectomy had neurologic states of GCS 10~12 points, and when compared to the patients of this study with less than 8 points on average upon decompressive craniectomy, the neurologic state can be deemed as the major reason that the neurologic outcomes were not good.(25). Additionally, unlike cerebral infarction, head injury causes irreversible damages in the over-

all brain tissue, including brainstem, thus there is an argument that decompressive craniectomy is not effective. On the contrary, several studies argue that decompressive craniectomy is effective not only in treating head injury but also in severe cerebral edema caused by other brain diseases.(10-12) However, patients should be carefully screened, considering treatment effects and complications following the treatment.

The prognosis of surgical treatment, including decompressive craniectomy, is clearly different from that of conservative treatment, but what type of treatment should be given to which patient group prospectively is still controversial. Specifically, when the head injury patient's status is exacerbated over time, if there is no DTIPH that can explain the symptoms seen on the follow-up CT, or if cerebral edema is seen, including brainstem, due to scattered diffuse cerebral contusion, it is doubtful whether or not unilateral decompressive craniectomy may improve symptoms or prevent secondary brain damage. With these diffuse cerebral edema findings, whether or not extensive bilateral decompressive craniectomy would be effective must be investigated by prospective multicenter studies, targeting larger patient population, and follow-up tests are required by cerebral blood flow measurement, including the brainstem area, transcranial doppler ultrasound, etc.

V. Conclusion

Among 26 patients who developed DTIPH due to head injury, the outcomes of 20 patients who have undergone decompressive craniectomy and those of 6 patients who have undergone conservative treatment based on neurologic symptoms and brain CT findings were investigated. As a result, the mortality rate was over 40%, and the prognosis was poorer when thrombocytopenia or coagulopathy is present. The patients who had high GCS scores before surgery or patients whose degree of brain midline movement was small showed favorable prognosis. Therefore, in determining prognosis after surgery, GCS score before surgery and brain midline movement assessment will be helpful. Furthermore, three DTIPH patients who did not undergo decompressive craniectomy revealed poor prognosis. Compared to this outcome, decompressive craniectomy is considered an effective treatment method in lowering accelerated intracranial pressure. Surgical treatment should be carefully selected, paying attention to the patient's accompanying damage and hematology test results, especially thrombocytopenia, in order to improve the patient's neurologic outcomes. Moreover, if neurologic deficit is found within 6 hours after injury in treatment outcomes, an appropriate and rapid treatment must be chosen through immediate CT.

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