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The Predictors of Survival and Functional Outcome in Patients with Pontine Hemorrhage

Dae Sung Jung, M.D., Byung Chan Jeon, M.D., Ph.D., Yong Sook Park, M.D., Hyung Suk Oh, M.D., Tae Sang Chun, M.D., Ph.D., Nam Kyu Kim, M.D., Ph.D.

Department of Neurosurgery, Kosin University Gospel Hospital College of Medicine, Busan, Korea

Objective : Pontine hemorrhages usually result in a much higher morbidity and mortality than any other intracranial vascular lesion. The purpose of this study was to evaluate survival and the contributing factors for patients with pontine hemorrhage.

Methods : Of the 41 patients who were admitted to our hospital with their first acute pontine hemorrhage from 1997 to 2005, 35 patients were included in this study. Medical records were reviewed to confirm the accuracy of diagnosis and collect demographic, clinical and radiological data. The patients were divided into two groups, survivors and deceased patients; then the survivors were divided again into a group of patients with good results and those with poor results. The location of the hematoma, maximum anteroposterior (AP) diameter, maximum transverse diameter, hematoma volume, ventricular extension, extension into the midbrain, hydrocephalus and initial Glasgow coma scale (GCS) were evaluated.

Results : The two year survival rate was 58.5%. The survival of patients with pontine hemorrhage was affected by initial GCS score and transverse hematoma diameter. Functional outcome of patients who survived was affected by initial GCS, maximum transverse diameter, maximum AP diameter and hematoma volume.

Conclusion : The rate of survival after pontine hemorrhage is associated with the transverse diameter of the hematoma and more importantly the initial GCS. Long-term outcome of survivors is influenced by the initial GCS, transverse diameter, AP diameter and volume. Through the multivariate analysis, initial GCS is the only significant factor on survival. Strictly speaking, initial GCS is not modifiable. However, surgical reduction may be considered to amend theses decisive factors. Additional study for indication, timing and method of surgical management is needed.

KEY WORDS : Pontine hemorrhage · Survival rate · Mortality · Outcome.

Introduction

Primary pontine hemorrhage accounts for approximately 5-10% of intracranial hemorrhages and occurs with a frequency of 2-4 per 100,000 per year[2,4]. Disturbances of consciousness, pupillary abnormalities, ophthalmoparesis, respiratory and motor disturbances are the major presenting symptoms of patients with pontine hemorrhage[9]. The introduction of computed tomography (CT) and magnetic resonance (MR) scans has allowed for discrimination of subtype of brainstem bleeding with a more favorable outcome and guide to surgical intervention[30]. There have been continuous and numerous efforts to improve the outcome of patients with pontine hemorrhage. The development of the procedures of stereotactic surgery and microsurgery has improved the results of pontine hemorrhage outcome[18,19]. Pontine hemorrhage does not have a uniform prognosis; it varies from an early death to long term survival without neurological deficits[30]. Therefore, a study on decisive factors that lead to early death as well as those that lead to a better outcome can be useful for clinical practice.

In this study, we analyzed 35 cases of pontine hemorrhage for evaluation of survival rate, functional outcome of survivors, and factors that contributed to survival and prognosis.

Materials and Methods

Of the 41 patients who were admitted to our hospital with their first acute pontine hemorrhage from 1997 to 2005, 35 patients were included in this study. These patients were all treated conservatively. Medical records and radiological ima-

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• Address for reprints : Byung Chan Jeon, M.D., Ph.D., Department of Neurosurgery, Kosin University Gospel Hospital College of Medicine, 34 Amnam-dong, Seo-gu, Busan 602-702, Korea Tel : +82-51-990-6465, Fax : +82-51-990-3042, E-mail : jbcstar@kosinmed.or.kr

ges were reviewed to confirm the accuracy of the diagnosis and collect demographic, clinical and radiological data. Patients with recurrent pontine hemorrhage and hemorrhages secondary to brain tumors, arteriovenous malformations or other vascular malformations were excluded. The patients with chronic renal failure, use of anticoagulants and end stage malignant disease were excluded as well. The included patients were divided into two groups, survivors and deceased; the survivors were divided again into a group with good outcome and that with poor outcome. The location of the hematoma, maximum AP diameter, maximum transverse diameter, hematoma volume, ventricular extension, extension into midbrain, hydrocephaslus and initial Glasgow Coma Scale (GCS) score were evaluated.

CT scans were performed using the standard method of an orbitomeatal line as a reference line and a 5mm slice. The location of the hematoma was assigned to three groups according to classification proposed by Tanaka : (1) central pontine hemorrhage, (2) baso-tegmentum and (3) tegmentum[33]. The initial GCS was tabulated as a marker of initial clinical severity. Activities of daily living (ADL) were used for the functional result of survivors at the end of the follow-up period. ADL scores of one, two or three were considered as good outcomes; scores of four, five or six were considered poor outcomes.

We analyzed the eight variables listed above with univariate comparison, chi-square test or Fisher's exact test for categorical variables and Mann-Whitney U-test for continuous variables. The parameters proven to be significant on univariate comparison were analyzed again with multivariate regression analysis. Statistical significance was set at $p<0.05$.

Results

The mean age of patients in the study was 57.2 years (range. 31-81 years). Twenty-five patients (71.4%) were men and ten (28.6%) were women. The mean follow up period was 13.9 months. The one year survival rate was 62.7% and the two year survival rate 58.5% (Fig. 1).

Predictors of survival

It has been reported that surgical management was not benefit for the patient with brainstem hemorrhage or small hemorrhage[17,24]. All the patients were treated conservatively. It included supporting of respiratory function, correction of electrolyte imbalance, prevention of secondary infections or pulmonary embolism.

Of the 13 patients who died, 9 died of brainstem insufficiency due to compression of brainstem. Three patients died of pneumonia and 1 patients died of pulmonary embolism.

The mean initial GCS for survivors and patients who died was 9.8±3.69 and 5.7±2.71 respectively. The initial GCS was found to be a statistically significant predictor for survival rate on univariate analysis. The mean maximum transverse diameter of survivors and patients who died was 20.8±10.5mm and 27.0±6.08mm respectively. Maximum transverse diameter was found to be a statistically significant predictor for survival rate with the univariate analysis. The mean maximum AP diameter of survivors and patients who died was 15.9±8.62mm and 22.4±15.77mm respectively. The mean volume of survivors and patients who died was 6.2±6.46ml and 13.4±14.07ml respectively. The hematoma volume showed a marginal significance statistically (p=0.056). The most common location

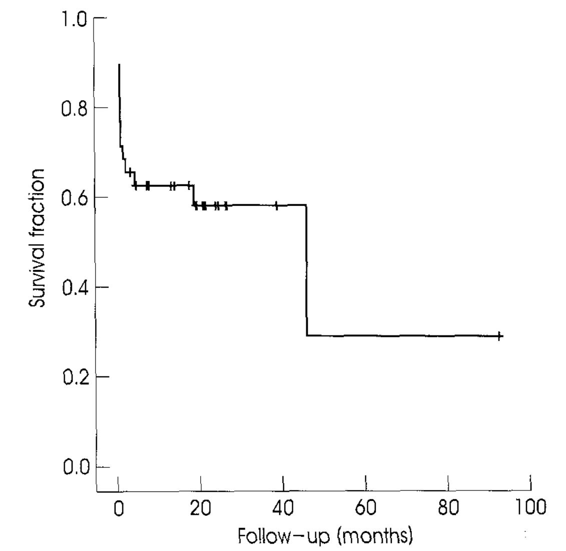

Fig. 1. Cumulative survival curve. One-year survival rate is 62.7% and 2-year survival rate is 58.5%.

Table 1. Clinical and radiological parameters of patients with pontine hemorrhage

Clinical or radiological parameters	Survived (n=22)	Died (n=13)	p value‡
Age (years)	53.5±11.1	63.3±11.4	
Gender (M:F)	17 : 5	8 : 5	
GCS* on admission	9.8± 3.69	5.7± 2.71	0.002
Transverse diameter (mm)	20.8±10.5	27.0± 6.08	0.045
AP† diameter (mm)	15.9± 8.62	22.4±15.77	0.187
Hematoma volume (ml)	6.2± 6.46	13.4±14.07	0.056
	10 tegmental	5 tegmental	0.465
Location of hematoma	5 basotegmental	1 basotegmental	
	7 central	7 central	
Ventricular extension	2 (5.7%)	3 (8.6%)	0.253
Midbrain extension	5 (14.7%)	4 (11.8%)	0.655
Hydrocephalus	3 (9.1%)	5 (15.2%)	0.077

*GCS : Glasgow coma scale, †AP : Anteroposterior, ‡p value : Eight variables were analyzed with univariate analysis. Mann-Whitney U-test was used for GCS on admission, transverse diameter, AP diameter and hematoma volume and chisquare test and Fisher's exact test were used for ventricular extension, midbrain extension and hydrocephalus

Table 2. Significance in multivariate analysis

Clinical or radiological parameters	Significance	Odds ratio	95% confidence interval
Transverse diameter	0.163	0.770	0.115– 5.169
GCS* on admission	0.033	8.671	1.191–63.132

*GCS : Glasgow coma scale

Table 3. Predictors of outcome in patients who survived

Radiological parameters	Good (ADL* 1,2,3) n = 12	Poor (ADL 4,5,6) n = 10	*p* value§
GCS† on admission	12.6±1.77	6.5±2.22	0.004
Transverse diameter (mm)	15.2±8.28	27.6±9.11	0.008
AP‡ diameter (mm)	10.4±4.83	22.5±7.53	0.001
Hematoma volume (ml)	3.1±2.22	9.8±8.01	<0.001
Ventricular extension	0	2	0.195
Midbrain extension	1	4	0.119
Hydrocephalus	1	2	0.553

*ADL : Activities of daily living, †GCS : Glasgow coma scale, ‡AP : Anteroposterior, §*p* value : Seven variables were analyzed with univariate analysis. Mann-Whitney U-test was used for GCS on admission, transverse diameter, AP diameter and hematoma volume and Fisher's exact test was used for ventricular extension, midbrain extension and hydrocephalus

of the hematoma was the tegmentum. Ten of the survivors had the tegmental type. Six of the patients who died had a central or baso-tegmental type. Prognosis was good for patients with the tegmental type, but this was not statistically significant. Ventricular extension was noted in five (14.2%) of the 35 patients. Midbrain extension was noted in nine (25.7%) of the 35 patients, and hydrocephalus was noted in eight (22.9%) of the 35 patients. There were no significant influences of ventricular extension, midbrain extension, or hydrocephalus on survival. The factors related to survival are summarized in Table 1.

Multivariate analysis using the significant factors revealed that initial GCS was the only factor significantly associated with survival (Table 2).

Predictors of good outcome in patients that survived

Of the twenty two patients who survived, a good outcome was noted in 12 patients, and 10 patients had a poor outcome. The 12 patients with a good outcome were able to make a living independently or at least in part. The mean initial GCS for patients with a good or poor outcome was 12.6±1.77 and 6.6±2.22 respectively. The initial GCS was found to be a statistically significant predictor for prognosis of survivors. The mean maximum transverse diameter for good and poor outcome was 15.2±8.28 and 27.6±9.11 respectively. Maximum transverse diameter was found to be a statistically significant predictor. The mean maximum AP diameter for good or poor outcome was 10.4±4.83 and 22.5±7.53 respectively. Maximum AP diameter was found to be a statistically significant predictor. The mean volume of hematoma for good or poor outcome was 3.1±2.22 and 9.8±8.01 respectively.

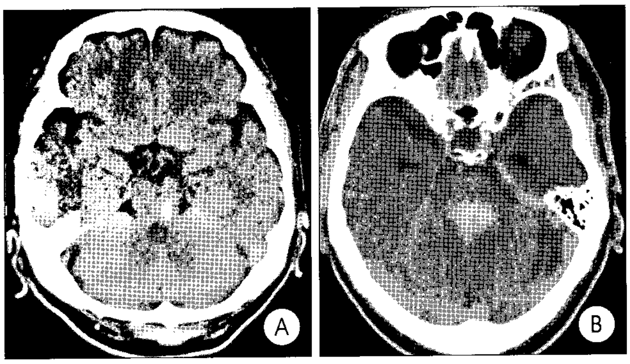

Fig. 2. Computed tomographs showing initial pontine hemorrhage. Illustrative cases, case1 (A) and case 2 (B).

Volume of hematoma was found to be a statistically significant predictor as well. Ventricular extension, midbrain extension and hydrocephalus were not significant predictors for functional outcome in survivors. The factors related with functional outcome are summarized in Table 3.

Illustrative cases (Fig. 2)

Case 1 (good outcome patient who survived)

This 61-year-old man was admitted with acute right hemiparesis, dysarthria and facial palsy.

His initial level of consciousness was drowsy. His pupil was isocoric and reactive to light. GCS on admission was 14. Transverse diameter, AP diameter and hematoma volume on the CT was 5mm, 5mm, 1ml, respectively (Fig. 2A). There was no extension of midbrain and ventricle and hydrocephalus. The hematoma was located in tegmentum. On the 7th day of attack he restored alert consciousness. After a follow-up period of 20 months he made an independent life except dizziness and mild right hemiparesis (motor grade 4+). ADL was 2.

Case 2 (poor outcome patient who survived)

This 54-year-old man was admitted with mental deterioration and weakness of all four extremities. His initial level of consciousness was stupor. His pupil was miotic bilaterally and nonreactive to light. GCS on admission was 7. Transverse diameter, AP diameter and hematoma volume on the CT was 20mm, 20mm, 6ml, respectively (Fig. 2B). There was no hydrocephalus and extension of midbrain but ventricle. The hematoma was located in tegmentum. He survived the acute state under ventilation. After a follow-up period of 13 months, there was no neurologic change. He made a totally dependent life. ADL was 4.

Discussion

Pontine hemorrhage accounts approximately for about 5-10% of intracranial hemorrhages and the incidence of pontine hemorrhage is higher than that of other brain stem hemorrhage of the medulla or midbrain[1,2,8,15,23,28,31].

The etiology of pontine hemorrhage is controversial. Hypertension, microaneurysm, fibrinoid necrosis or lipohyalinosis of the basilar artery have all been reported to give rise to pontine hemorrhage[6]. In general, ruptured vessels are basilar artery branches, paramedian branches or lateral penetrating branches of short circumferential branches. Lesions of pontine hemorrhage are tegmentum pontis, with hemorrhage of a small diameter vessel, and basis pontis, with hemorrhage of a large diameter vessel[6,7,15,16].

Recent studies have reported a survival rate of 40-50%[21,26,34]. In this study, the overall survival rate was 62.9%. The survival rate in this study was not significantly different from that of other studies. In general, the prognosis for patients with pontine hemorrhage is disappointing. However, in this study, the ADL score was one in one patient, and two or three in 11 patients.

Predictors of survival

Wijdicks and Louis reported that the initial level of consciousness is a major factor for predicting outcome; they reported that all 21 patients who died had been comatose, and among the 17 survivors, four had been comatose patients[33]. Choi et al. reported that in 20 cases with a GCS < 12, 17 cases died and with a mortality rate of 85%; in 10 case with a GCS > 13, one patient case died[10]. In this study, seven (53.8%) of 13 patients who died had a GCS < 5, and one (4.5%) of 22 survivors had a GCS < 5. The mean initial GCS of survivors was higher than that of patients who died. The initial GCS was found to be the only statistically significant predictor for survival on multivariate analysis.

It has been reported that the mortality of patients with a transverse diameter longer than 20mm was high[25,34]. In this study, transverse diameter was found to be a statistically significant predictor for mortality on univariate analysis. Broderick reported that all patients with a pontine hemorrhage greater than 5cm^3 of volume died within 30 days[5]. In this study, the hematoma volume had a marginal significance on survival (p=0.056). For the hematoma location, Chung and Kushner reported that the mortality rates of the patients with ventrally located or massive hematoma were significantly higher than the dorsally or unilateral tegmental located lesions[12,21]. Choi reported that among 16 patients, 12 patients had baso-tegmental hemorrhage and they were either in a vegetative state or dead[10]. Among our patients who died : 53.8% had central, 7.7% had baso-tegmental and 38.5% had tegmental localized hemorrhage; in patients who survived, 31.8% had central, 45.5% had tegmental, and 22.7% had baso-tegmental localized hemorrhage and none of them had massive hemorrhages. Massive hemorrhage was higher in patients who died than in survivors but the location of the hemorrhage was not a statistically significant predictor for mortality with univariate analysis. Chung and Park reported that the intraventricular or midbrain extension of pontine hemorrhage was a predictor of poor prognosis[12]. It is known that extrapontine extensions and the volume of hemorrhage are associated with hydrocephalus. In this study, five (14.7%) of the patients who survived had midbrain extension, two (5.7%) patients had intraventricular extension, and three (9.1%) had hydrocephalus; however, among the patients who died, four (11.8%) patients had midbrain extension, three (8.6%) patients had intraventricular extension, and five (15.2%) patients had hydrocephalus. In general, three variables were higher in patients who died than in survivors but these differences were not significant.

Univariate analysis showed that initial GCS and transverse diameter were statistically significant predictors for survival. The initial GCS was found to be the stronger predictor based on significant findings. The initial GCS may reflect the severity of the destruction of critical structures, and the extent of the hematoma involvement. Considering the anatomical arrangement of reticular formation, especially the raphe nuclei and the central nuclei which are required for arousal and consciousness, it is possible to infer that a central or bilateral location of a hematoma is associated with a poor outcome[11]. Bilateral involvement in the cerebral hemisphere is generally more debilitating[29]. Therefore, initial GCS and transverse diameter, rather than AP diameter of the hematoma, are thought to be related to poor outcome and early death. The actual location of the hematoma was not found to be a significant predictor of outcome in this study; these results may be due to small sample size.

Predictors of good outcome in survived patients

In a report by Dziewas[14], a good recovery rate was noted in survivors 25% of 12 survivors; Rabinstein[30], also reported a good recovery in 77% of 36 survivors; Wijdicks[34], also noted a good recovery in 47% of 17 survivors, as did Masiyama[25] in 78% of 14 survivors. In this study, a good recovery was noted in 54.5% of 22 survivors.

Choi et al.[10] reported that among 30 patients, 13 patients who survived had high GCS scores, above 13 points. In this study, the mean initial GCS associated with good outcome was 12.6 ± 1.77. Our findings were consistent with previous reports. Tanabe et al.[32] reported that the prognosis of patients with pontine hemorrhage was related to the transverse diameter; Kuwabara et al.[22] reported that in cases with a transverse diameter above 20mm, the prognosis was poor. In this study, the mean transverse diameter for good outcome patients was 15.2 ± 8.28mm. The mean volume associated with a good outcome was 3.1 ± 2.22. Volume was related to prognosis in survivors.

The initial GCS, transverse diameter, AP diameter and volume were predictors of functional outcome in survivors with pontine hemorrhage. As in survival, these factors are related to the core of the primary hemorrhage and not to the secondary phenomenon such as hydrocephalus or outward involvement such as ventricular hemorrhage or midbrain extension. In addition, the fact that AP diameter of hemorrhage is related with the long term functional outcome suggests that pyramidal tract involvement anteriorly, and cranial nerve nuclei involvement posteriorly are factors important for obtaining neurological independence. Applying these results to the management of pontine hemorrhage, surgical drainage of the hematoma for non-comatose patients may be beneficial in view of the reduction of volume, transverse diameter and AP diameter. Surgical intervention has been a controversial issue. In some reports, craniotomy or stereotactic aspiration for hematoma removal was useful in patients who had mental deterioration or worsening of neurological deficits during conservative treatment[3,20,27]. Hong reported that in cases with low GCS and deterioration of patients over 6-20 days after hospital admission hematoma removal improved prognosis in four patients[19]. To establish the results of surgical management, a controlled comparative study would be needed.

Conclusion

The rate of survival after pontine hemorrhage is associated with the transverse diameter of the hematoma and more importantly the initial GCS. Long-term outcome of survivors is influenced by the initial GCS, transverse diameter, AP diameter and volume. Through the multivariate analysis, initial GCS is the only significant factor on survival. Strictly speaking, initial GCS is not modifiable. However an effort to reduce hematoma volume or hematoma diameter, in other words, surgical reduction may be considered to amend theses decisive factors. Additional study for indication, timing and method of surgical management is needed.

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Commentary

The authors reviewed demographic data of patients with pontine hemorrhage and evaluate the predictors of survival and functional outcome. This study was performed through 35 patients who were treated conservatively during 8 years, and result shows that main predictor of survival after pontine hemorrhage is initial GCS score and predictors of long term functional outcome are initial GCS score, AP and transverse diameter of hematoma and hematoma volume.

As mentioned in paper, pontine hemorrhage usually has high mortality and morbidity. The clinical presentation of pontine hemorrhage is one of rapid onset of disturbance consciousness. Awaked patients may become symptomatic with headache, vomiting, and focal pontine signs such as facial and limb numbness, deafness, diplopia, quadri or paraparesis, and hemiparesis. Treatment depends on the patient's condition (GCS score). Most patients present with acute onset of devastating symptoms and will die. In patients believed to be treatable, there should be immediate attention to respiratory support and control of blood pressure is needed. Ventricular drainage might be used if hydrocephalus is present, but the very presence of hydrocephalus may be marker of fatal hemorrhage. Massive pontine hemorrhages are always fatal, but death may not be instantaneous. Some patients with medium-sized hematoma and most patients with small basal and lateral tegmental hematomas survive with various degrees of residual neurological deficits.

A major role of direct surgery is questionable. On the one hand, hematomas have been followed by CT and have been seen to resorb, occasionally with a good result. On the other hand, several cases, including a few with acute onset, have been thought to have been successfully operated. Stereotactic aspiration has also proved helpful. Other series, however, have suggested that acute surgery does not improve outcome. Collaborative study will probably be needed to define role of direct surgery of patients with pontine hemorrhage.

Sung-Hak Kim, M.D.
Department of Neurosurgery
Ewha Womans University