International Journal of Gerontology 14 (2020) 142–145
https://doi.org/10.6890/IJGE.202005_14(2).0011

International Journal of Gerontology

journal homepage: http://www.sgecm.org.tw/ijge/

Original Article

Impact of Immediate Treatment Within Four Days on Prognosis in Severe Traumatic Brain Injury Patients Without Vasospasm

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ARTICLE INFO

Accepted 4 June 2019

Keywords:
computed tomography angiography,
traumatic brain injury,
cerebral perfusion pressure

SUMMARY

Background and objectives: Traumatic brain injury (TBI) is associated with high mortality rate and long-term disability. Application of the Brain Trauma Foundation's "Guidelines for the management of severe traumatic brain injury" would reduce the prevalence of morbidity and mortality. However, the prevalence of some predictors of TBI have not been studied well with respect to the guidelines, for example, vasospasm. This study evaluated the correlation between the prognostic factors and outcome in patients without vasospasm.
Materials and Methods: All patients were treated as per the aforementioned guidelines. Ten patients were prospectively recruited and nine were examined by computed tomography angiography (CTA). The cerebral perfusion pressure (CPP) was measured before and on the fourth postoperative day and was maintained at ≥ 60 mmHg. The results of Glasgow outcome scale (GOS) and Glasgow coma scale (GCS) were collected after four weeks, three months, one year, and two years after admission.
Results: There was no vasospasm noted in any of the assessed patients. Current results showed that the elderly (≥ 65 years) had poor GOS (5/6, 83.3%), whereas the younger group had better GOS (3/3, 100%) ($p < 0.05$). Lower GCS was associated with lower GOS. The subgroup with GCS ≤ 6 ($p < 0.05$) had a lower GOS. We also observed a better outcome when GCS was higher than 9 (≥ 10) (5/5, 100%) on the fourth postoperative day ($p < 0.05$).
Conclusions: The use of CTA to evaluate vasospasm could be a reference while following the guidelines to manage patients with severe TBI. Aggressive treatment within the first four days could help in obtaining better brain resuscitation in severe TBI patients.

1. Introduction

Traumatic brain injury (TBI) could result in a high mortality rate and long-term disability[1] and is considered as one of the major health and socioeconomic problems worldwide. Prospective database analysis can help understand the natural history, definition, assessment, prognosis, and outcome of TBI.[2,3]

Vasospasm is a delayed secondary consequence that can profoundly impact the neurological recovery and functional outcome following TBI. Although vasospasm may result from traumatic subarachnoid hemorrhage (SAH), other mechanisms such as blast-induced neurotrauma have been increasingly recognized as causative factors.[4,5] However, causal inference is problematic due to the complex and multifactorial sequelae of injuries associated with TBI. Zubkov et al.[6] reported an increased incidence of vasospasm, measured using transcranial doppler ultrasonography (TCD), in TBI patients with traumatic epidural and subdural hematomas. Meanwhile, TCD detected cerebral vasospasm by elevated velocity, and the artifact described here is therefore important to recognize.[7,8]

Another study used whole-brain computed tomography angiography (CTA) to detect the changes in microcirculation in patients with SAH. CTA has the advantage of detecting the macroscopically evident vasospasm and can observe the real size of brain vessels. That study's results demonstrated that the mean cerebral blood flow was significantly lower in patients with SAH.[9] However, very few recent studies applied CTA to detect the change in brain vessels in patients with severe brain trauma. On the other hand, cerebral perfusion pressure (CPP) can be easily performed, provides a continuous measurement, and forms part of the management guidelines of the Brain Trauma Foundation (BTF).[10,11] However, the relationship between CPP and change in brain vessels has not been clearly understood. Thus, the purpose of this study was to examine whether CPP > 60 mmHg could reduce the occurrence of vasospasm and find new predictors of severe head injury.

2. Materials and methods

2.1. Patients and methods

This study was approved by the Institutional Review Board of

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Mackay Memorial Hospital (10MMHIS027). From June 2010 to June 2012, we prospectively recruited 10 patients who had severe TBI (Glasgow coma scale [GCS] ≤ 8) and underwent operation, placement of intracerebral pressure (ICP) monitor (Codman, USA), or decompressive surgery with ICP monitor. Demographic data, ICP, CPP, and GCS of the enrolled patients were collected. Patients > 65 years of age were defined as elderly patients. Patients who underwent placement of ICP monitor or decompressive craniotomy with ICP monitor typically underwent the procedure under general anesthesia in the supine position.[12,13] The exclusion criteria of this study included coagulopathy, liver cirrhosis, and end-stage renal disease on hemodialysis. One of the 10 patients withdrew from the study three days after the operation, because the subject's family refused to participate further. The remaining nine patients were regularly treated as per the standards of BTF's "Guidelines for the Management of Severe Traumatic Brain Injury." The CPP of all patients was maintained at ≥ 60 mmHg.

Brain CTA was performed for each patient at two time points (before the operation and four days after operation) to evaluate the presence of vasospasm. Six arterial locations were examined for vasospasm, including the suprasellar internal carotid artery, M1 and M2 segments of the middle cerebral artery, A1 and A2 segments of the anterior cerebral artery, and basilar artery. Moreover, the extent of vasospasm was defined as none, mild (< 30% luminal reduction), moderate (30% to 50% reduction), or severe (> 50% reduction).[14] The baseline of data is the size of the vessels before operation.

The Glasgow outcome scale (GOS) of each patient was also obtained four weeks, three months, one year, and two years after admission. The GOS is a 5-level scale[15] and the scores from 1 to 5 refer to death, vegetative state (patient is unresponsive, but alive; a "vegetable" in lay language), severely disabled (patient is conscious but requires others for daily support due to disability), moderately disabled (patient is independent but disabled), and good recovery (the patient has resumed most normal activities but may have minor residual problems), respectively. In this study, the scores 1, 2, and 3 were deemed as poor outcomes, while the scores 4 and 5 indicated good outcomes.

The data of age, sex, ICP, CPP, GCS, GOS, and presence/absence of vasospasm were collected. The relationship between CPP and vasospasm and that between CPP treatment and GOS after one and two years of operation were further evaluated. Patients ≥ 65 years were defined as the elderly group. We evaluated these data for understanding the prognosis under different indications.

2.2. Statistical analysis

Categorical variables were expressed as number (n/N) or percentage (%) for each item. Comparisons between two groups of patients were analyzed by using Chi-square test or Fisher's exact test. Comparisons within one group for the before and after effects of patients were analyzed using the non-parametric McNemar's test.

All reported *p*-values were based on two-sided tests and were considered statistically significant when $p < 0.05$. The package of the Social Sciences (SPSS) for Windows (version 21.0, Chicago, IL, USA) software was used for statistical analysis.

3. Results

By using CTA for assessment, we found that no patient developed vasospasm in this study. The typical CTA images before and after operation are shown in Figure 1, while detailed data of patients are shown in Table 1. We monitored the brain vessels using CTA and the prognosis with GOS. Two subgroups were formed of patients above and below 65 years of age and GCS on the first and fourth days in order to further explore the correlation between the prognosis and patients' individual factors. Interestingly, we noticed significant differences between the subgroups. The elderly group showed poorer GOS (5/6, 83.3%), whereas better GOS was seen in the younger group (3/3, 100%) ($p = 0.048$). Meanwhile, the p value was > 0.999 in the elderly group (Table 2). With respect to the different GCS scores noted initially (above and below 5 and 6), lower GCS meant lower GOS (p values are 0.048 and 0.012). At the same time, we noticed a better outcome in the patients whose GCS was ≥ 10 (5/5, 100%) on the fourth day after treatment ($p = 0.048$) (Table 3). The GOS at one year and two years after surgery was the same.

4. Discussion

The most important finding of this study was that the GCS on the initial fourth day of severe TBI could be considered as an important predictor of outcomes in patients without vasospasm. Higher GOS was found if the GCS on the initial fourth day was ≥ 10. More aggressive treatment within the first four days, including CPP monitoring, medication to decrease ICP, and decompression operation,

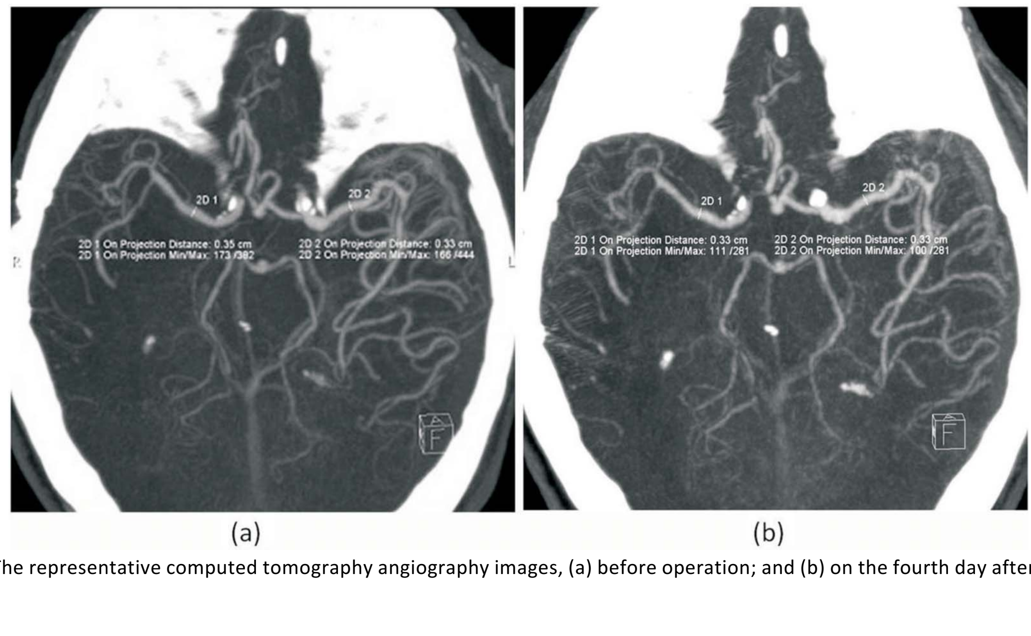

Figure 1. The representative computed tomography angiography images, (a) before operation; and (b) on the fourth day after operation.

Table 1
Demographic data of patients before operation (age, genders) and the calculated scores (GOS, GCS) for different periods.

Subject	Age	Gender	D1GCS	D4GCS	4wGCS	3mGOS	1yGOS	2yGOS	Vasospasm
1	33	F	8	15	15	5	5	5	No
2	83	M	7	10	12	3	4	4	No
3	32	M	6	10	15	4	4	4	No
4	69	F	5	6	6	2	2	2	No
5	84	F	5	5	5	2	2	2	No
6	60	M	8	10	15	4	4	4	No
7	89	M	5	5	4	2	2	2	No
8	43	M	8	10	13	5	5	5	No
9	54	M	8	11	13	5	5	5	No
10*	73	F	5	7	NA	NA	NA	NA	NA

GCS: Glasgow coma scale; GOS: Glasgow outcome scale; D1GCS: GCS of pre-operation, D4GCS: GCS on the fourth day after admission, 4wGCS: GCS after four weeks, 3mGOS: GOS after three months, 1yGOS: GOS after one year, 2yGOS: GOS after two years, *: The tenth patient withdrew from the research on the seventh day.

Table 2
Statistical outcomes between age and Glasgow outcome scale (GOS) with Fisher's exact tests and McNemar's test.

	Fisher's exact tests			McNemar's test		
	GOS = 1,2	GOS = 4,5	*p*-value	GOS = 1,2	GOS = 4,5	*p*-value
Elderly (≥ 65 years)	3 (100%)	1 (16.7%)	0.048	3 (33.3%)	1 (11.1%)	> 0.999
Younger (< 65 years)	0 (0%)	5 (83.3%)		0 (0%)	5 (55.6%)	

Both Fisher's exact tests and McNemar's test revealed the age (above or below 65 years) influences the patient's outcome (GOS).

Table 3
The statistical results between Glasgow coma scale (GCS) and Glasgow outcome scale (GOS).

	Fisher's exact test			McNemar test		
	GOS = 1, 2	GOS = 4, 5	*p*-value	GOS = 1, 2	GOS = 4, 5	*p*-value
D1GCS			0.048			> 0.999
≤ 6	3 (100%)	1 (16.7%)		3 (33.3%)	1 (16.7%)	
> 6	0 (0%)	5 (83.3%)		0 (0%)	5 (83.3%)	
D1GCS			0.012			> 0.999
≤ 5	3 (100%)	0 (0%)		3 (33.3%)	0 (0%)	
> 5	0 (0%)	6 (100%)		0 (0%)	6 (100%)	
D4GCS			0.048			> 0.999
< 10	3 (100%)	1 (16.7%)		3 (33.3%)	1 (16.7%)	
≥ 10	0 (0%)	5 (83.3%)		0 (0%)	5 (83.3%)	

The GCS on the first and fourth day > 5 and 10 influence the GOS. D1GCS: GCS of pre-operation, D4GCS: GCS on the fourth day after admission.

was very critical to brain resuscitation. The results between GCS and GOS were consistent on the initial days. With respect to treatment with different procedures, there was no significant difference between each subgroup.

Vasospasm is a delayed secondary consequence that can profoundly impact the neurological recovery and functional outcome after TBI. However, the condition of brain vessels during TBI treatment was not evaluated sufficiently, if the BTF guidelines were referred. This study thus aimed to monitor the vessel condition of the brain by CTA, which could appropriately detect macroscopically evident vasospasm using CTA,[9] and we wanted to understand what we could do for patients. In the elderly patients and those with lower GCS, there were significantly lower GOS values. Meanwhile, there were strong predictors for GOS in both groups. The elderly and lower GCS with lower GOS were consistent with previous similar studies.[16,17]

In addition to the consideration of contrast medium, the CTA helped to detect a true change in brain vessels.[9] When patients suffered from severe TBI and vasospasm was suspected, the CTA could also provide a quick and actual observation of brain vessels.[9] The current study found that none of the patients' neurological defects worsened after the CTA procedure. It was suggested that the CTA would be beneficial in tracing the vessel conditions and select the appropriate treatment for achieving better outcomes.

Some limitations of the current study should be noted. The number of patients enrolled in this study was limited. The major difficulty in patient recruitment was detailed explanation for study enrollment and obtaining informed consent, which usually took more than 10 minutes. A larger patient demographic data would be more helpful to support our finding. We hope to conduct a multicenter randomized controlled study that can help to understand the initial vessel conditions affecting the clinical outcomes after severe TBI.

5. Conclusions

There was no vasospasm seen on the CTA in all patients with CPP ≥ 60 mmHg. Lower GCS before surgery correlated with lower GOS after surgery. Younger patients (< 65 years old) and those with GCS ≥ 10, four days after surgery, showed a better outcome. Nevertheless, the relationship between GCS and GOS four days after surgery should be analyzed further by analyzing a larger patient cohort in the future. Whether the CPP data of the fourth day after severe brain injury could be indicative of the need of more aggressive treatment for brain resuscitation remains to be determined.

Author contributions

Yu-Jen Chen and Tung-Hu Tsai conceived, designed, and discussed the experiments and supervised all work; Jui-Feng Lin and Cheng-Chia Tsai performed the experiments and data acquisition, analyzed the data, and wrote the paper. All authors have read and approved the final manuscript.

Funding

This study was supported by the MacKay Memorial Hospital (grant number MMH-106-140 MMH-E-107-13 and MMH-E-108-13).

Conflicts of interest

The authors have no conflict of interest to declare.

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