Original Article

eISSN2465-891X The Nerve.2016.2(2):59-65
https://doi.org/10.21129/nerve.2016.2.2.59
www.thenerve.net

Risk-benefit Analysis of Barbiturate Coma Therapy in Patients Who Received Decompressive Craniectomy for Malignant Cerebral Infarction

Myung Sung Joo, Sang Woo Song, Dong Sun Park, Young Il Chun, Young-Cho Koh

Department of Neurosurgery, Konkuk University College of Medicine, Seoul, Korea

Objective: In our study, we analyzed the risks and benefits of barbiturate coma therapy (BCT) in patients who received decompressive craniectomy for malignant cerebral infarction (MCI) in the past 11 years. Additionally, we evaluated the factors affecting the functional outcomes in these patients.

Methods: A retrospective analysis was performed for all patients who underwent decompressive craniectomy for MCI between August 2005 and May 2016. Based on the routine use of BCT, patients were divided into two groups: BCT group with immediate use of BCT after decompressive craniectomy and control group without use of BCT.

Results: There was no significant difference in one-month mortality between the BCT and non-BCT groups (p=0.477). One-year survival rates were 65.7% and 58.4%, and 2-year survival rates were 56.3% and 54.2% in the BCT and control groups, respectively. Glasgow Outcome Scale scores of the two groups showed a significant difference in favour of control group at 1 month after the surgery (p=0.034), but not at 6 months after surgery (p=0.494). Adverse events and complications occurred more frequently in the BCT group than in the control group.

Conclusion: Based on our results, we concluded that BCT for patients with MCI does not always result in a positive outcome. We oppose the use of BCT as a routine conventional treatment. However, it may be considered as an adjunct measure when maximum conventional treatment fails.

Key Words: Barbiturates · Decompressive craniectomy · Cerebral infarction · Glasgow outcome scale

INTRODUCTION

Malignant cerebral infarction (MCI) accounts for 10% to 15% of all acute ischemic stroke cases, and the mortality rate is approximately 80%[2,8,17]. MCI usually denotes a large middle cerebral artery (MCA) infarction, with or without involvement of the ipsilateral anterior and posterior territories of the cerebral artery[20]. MCI presents with acute brain swelling in the first 48 hr after stroke, resulting in elevated intracranial pressure (ICP) or brain herniation. The majority of patients with MCI are threatened by secondary complications such as brain edema, intracranial hypertension, midline shifting, and failure of intracranial circulation. Most complications are related to early death due to subsequent brain herniation and increased ICP[23].

Corresponding author: **Sang Woo Song**
Department of Neurosurgery, Konkuk University Medical Center, Konkuk University College of Medicine, 120 Neungdong-ro, Gwangjin-gu, Seoul 05029, Korea
Tel: +82-2-2030-7357, Fax: +82-2-2030-7359
E-mail: 20120168@kuh.ac.kr

Treatment methods including head elevation, hyperosmolar agents, hypothermia, and hyperventilation have so far been ineffective for MCI, with reported mortality rates as high as 80%[6]. Due to the limitations of medical treatment, decompressive craniectomy has been proposed for patients with MCI. Several previously reported studies have shown its efficacy in decreasing mortality rates from 80% to 30%[1,21]. This surgical treatment can prevent secondary tissue damage by making compensatory space to accommodate the swollen brain[22]. Along with surgical treatment, barbiturate coma therapy (BCT) was also recommended to control increased ICP that was refractory to surgical and maximum conservative treatment. BCT for the treatment of increased ICP has been studied since the 1970s with varying outcomes[13,19,22]. Barbiturates change the cerebral vascular tone and decrease metabolic demand from the brain, thus decreasing the ICP.

In patients with severe traumatic brain injury and malignant infarction, decompressive craniectomy and BCT are currently being used as second-tier means for the control of increased ICP. The current study attempts to determine whether the routine use of BCT after decompressive craniectomy could be beneficial in patients with MCI.

MATERIALS AND METHODS

1. Patient Selection

A retrospective analysis was performed including all consecutive patients who underwent decompressive craniectomy for MCI since the new opening of our institution. In total, 42 patients with MCI were treated with decompressive craniectomy in our institution from August 2005 to May 2016. The inclusion criteria were infarction involving >50% of unilateral MCA territory with or without extension to other adjacent territories evaluated using computed tomography (CT) and/or magnetic resonance imaging (MRI) along with the acute onset of corresponding clinical symptoms and signs[8]. Patients with hemorrhagic transformation or infarctions, bilateral infarctions, and any concomitant severe medical disease or terminal illness contraindicating surgery were excluded. Immediate BCT after craniectomy was routinely initiated in our center from 2012 onwards, thereby dichotomizing our study sample based on the time span. Among the 42 patients, 4 patients who were sedated with propofol and/or midazolam instead of barbiturate were excluded, and the final study cohort comprised 38 patients. Following craniectomy, 12 patients were immediately treated with BCT and were categorized as the "BCT group", whereas 26 received conservative therapy apart from sedation and were categorized as the control or the "non-BCT group." The baseline characteristics of the BCT and control groups were compared and are shown in Table 1.

2. Operative Methods

Large ipsilateral craniectomy and large duroplasty were performed on all 38 patients for relief of mass effect. The surgery involved a large reverse question-mark scalp flap, large frontotemporoparietal craniectomy of at least 15 cm in the largest diameter. We achieved adequate subtemporal skull decompression to prevent uncal herniation and ensured that the medial margin of craniotomy was at least 2 cm lateral from the midline to avoid injury to the superior sagittal sinus and to prevent excessive bleeding near the sinus. Large dura incision and spacious duraplasty was performed using synthetic dura, and subdural-type ICP-monitoring catheter (Spiegelberg GmBH & Co. KG, Hamburg, Germany) was placed on the temporal cortex just before the closure of the dura. The surgical bone flap was stored in freezer at -60°C until cranioplasty.

3. BCT Protocol

For patients in the BCT group, BCT was initiated by intravenously (IV) administering a dose of 5 mg/kg pentobarbital for 10 min, followed by a maintenance dose at rate of 5 mg/kg/h IV for 24 hr and reduced to 2.5 mg/kg/h. If the ICP increased above 20 mmHg during BCT, a bolus of 5 mg/kg pentobarbital was injected IV. The patient's neurological state was re-checked to evaluate if full coma was reached. We have been followed up the brain CT and re-evaluated as to whether surgical decompression is necessary. If the ICP was stable for more than 2 days, pentobarbital dosage was gradually reduced at a rate of 1 mg/kg/h/d, and then tapered out. No neuromuscular blockers were used.

4. Outcome Evaluation

We used Glasgow Outcome Scale (GOS) score to evaluate the clinical and functional recovery of patients. The functional outcomes at 1 and 6 months after surgery were divided into good outcome (GOS=3, 4, 5) and poor outcome (GOS=1, 2) groups, respectively. The following variables were analyzed for correlation with outcome: age (<67 years old vs. ≥67 years old), sex, laterality of infarction, midline shifting (<10 mm vs. ≥10 mm), infarction range (MCA vs. MCA+others), administration of BCT, initial GCS score (≤12 vs. >12), pupillary

Table 1. Baseline patient's characteristic of barbiturate coma therapy and control groups

Characteristic	BCT group (n=12)	Control group (n=26)	Total (n=38)	p-value*
Mean age (years)	65.0±12.0	64.9±1.9	64.79±1.61	0.931
Sex ratio (M:F)	7:5	13:13	20:18	0.734
Mean initial GCS	12.7±1.4	11.9±2.1	12.05±0.33	0.155
Mean preoperative GCS	9.5±1.7	8.8±1.8	9.08±0.29	0.244
Midline shifting >10 mm	7/12	10/26	17/38	0.307
Hemorrhagic transformation	2/12	6/26	8/38	1.000

Fisher's exact test was used to compare proportions of the categorical variables and Mann-Whitney U test was used to compare continuous variables.
*$p \leq 0.05$ was considered statistically significant. BCT: barbiturate coma therapy; M: male; F: female; GCS: Glasgow Coma Scale.

change, time interval between onset of infarction and surgery <24 hr vs. ≥24 hr), and existence of hypertension, diabetes mellitus, and/or atrial fibrillation.

Additionally, we compared the clinical outcomes of the BCT group and the control group. GOS scores and mortality rate at 1 and 6 months after surgery were analyzed to determine significant differences in outcome between the two groups. Differences in the frequency of medical complications between the two groups were also compared.

In addition, we analyzed the trend of ICP change over time. ICP monitoring was introduced in our institute since 2007, and ICP monitoring was performed for 10 patients in the BCT

Table 2. Association between patients clinical characteristics and outcomes (Glasgow Outcome Scale 6 months)

Characteristic	Good outcomes (n=19)	Poor outcomes (n=19)	p-value*
Age (years)	61.33±8.80	65.44±10.13	0.516
<67	10 (55.6%)	8 (44.4%)	
≥67	9 (45.0%)	11 (55.0%)	
Sex			
Male	12 (60.0%)	8 (40.0%)	0.194
Female	7 (38.9%)	11 (61.1%)	
Laterality			0.189
Right	9 (40.9%)	13 (59.1%)	
Left	10 (62.5%)	6 (37.5%)	
Midline shifting			0.744
<10 mm	10 (47.6%)	11 (52.4%)	
≥10 mm	9 (52.9%)	8 (47.1%)	
Infarction range			<0.001*
Within middle cerebral artery	18 (72.0%)	7 (28.0%)	
Beyond middle cerebral artery	1 (7.7%)	12 (92.3%)	
Barbiturate coma therapy			0.485
Yes	5 (41.7%)	7 (58.3%)	
No	14 (53.8%)	12 (46.2%)	
Hypertension			0.744
Yes	10 (47.6%)	11 (52.4%)	
No	9 (52.9%)	8 (47.1%)	
Diabetes mellitus			0.283
Yes	4 (36.4%)	7 (63.6%)	
No	15 (55.6%)	12 (44.4%)	
Atrial fibrillation			0.511
Yes	7 (43.8%)	9 (56.3%)	
No	12 (54.5%)	10 (45.5%)	
Initial GCS score	12.74±1.79	11.37±2.08	0.097
≤12	5 (33.3%)	10 (66.7%)	
>12	14 (60.9%)	9 (39.1%)	
Change of pupillary response			0.050*
Yes	7 (35.0%)	13 (65.0%)	
No	12 (66.7%)	6 (33.3%)	
Time to operation (hr)	52.68±28.91	49.74±50.38	0.163
<24 hr	4 (33.3%)	8 (66.7%)	
≥24 hr	15 (57.7%)	11 (42.3%)	

Fisher's exact test was used to compare proportions of the categorical variables and Mann-Whitney U test was used to compare continuous variables.

*p≤0.05 was considered statistically significant. GOS: Glasgow Outcome Scale; GCS: Glasgow Coma Scale; hr: hours.

group and 20 in the control group depending on this point of time. We obtained the ICP level every 6 hr up to 7 days after surgery and evaluated the effectiveness of BCT in decreasing ICP.

5. Statistical Analysis

We compared the differences between BCT group and control group using chi-square test, t-test, or Mann-Whitney U test. The Kaplan-Meier curve analysis was used to estimate mean survival time and to check curves for overall survival in both groups. Moreover, Bonferroni's method was used to assess the trend of ICP change between the BCT and the control groups. A p-value less than 0.05 was considered significant. Logistic regression analysis was used to evaluate the likelihood of a better GOS score at 6 months post-surgery. Univariate analyses were used to determine the effects of age (<67 years old vs. ≥67 years old), sex, laterality, midline shifting (<10 mm vs. ≥10 mm), infarction range (MCA vs. MCA+ others), BCT, hypertension, diabetes mellitus, atrial fibrillation, initial GCS (≤12 vs. >12), pupillary change, and time to operation (<24 hr vs. ≥24 hr) on GOS at 6 months post-surgery. Variables that were found to be associated with better GOS score were subjected to multivariate analyses. Statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA).

RESULTS

1. Overall Outcome

The mean and median follow-up periods were 28.1 months and 11.9 months (range, 0.2-107.7 months), respectively. Seven patients died within a month after decompressive craniectomy, 25 patients (65.8%) died during follow-up, and 10 patients (26.3%) were alive during data collection. Four patients were lost to follow-up. The overall survival rate at 6 months, 1 year and 2 years were 70.4±0.8%, 61.4±0.8%, and 54.8±0.9%, respectively.

The correlations between preoperative clinical and radiological variables and degree of recovery were represented by GOS scores at 6 months after surgery. Among the 38 patients included in this study, 20 were male and 18 were female (male-female ratio, 1.11:1). The mean and median age was 64.79±1.61 years (range, 45-85 years) and 67 years; median initial Glasgow Coma Scale (GCS) score, 12.05±0.33 (range, 6-15); median preoperative GCS score, 9.08±0.29 (range, 5-13) (Table 1); and mean interval from onset of infarction to decompressive craniectomy, 51.2±6.6 hr. In 25 patients, only the MCA territory was affected, whereas in the remaining 13, the anterior cerebral artery and/or the posterior cerebral artery territories were also involved at the time of surgery. Non-dominant hemisphere was involved in 22 patients (57.8%), while dominant hemisphere involvement was seen in 16 patients (42.2%). The clinical and radiological characteristics of the patients are summarized in Table 2. Univariate analysis revealed that the volume of the infarcted brain and pupillary change at the time of surgery were associated with a poor outcome ($p<0.001$ and $p<0.050$, respectively). The three factors with $p<0.1$ were re-analyzed using multiple logistic regression models, and infarction volume was identified as an independent predictor of outcome. Patients with infarcted brain within the MCA territory showed better GOS scores at 6 months post-surgery than those with brain infarctions beyond the MCA territory ($p=0.002$, adjusted odds ratio [OR]=0.032; 95% confidence interval [CI]=0.004-0.298).

2. Risk-Benefit of BCT

There was no significant difference in 1-month mortality between the patients with MCI treated with BCT and those treated without BCT ($p=0.477$). One-year survival rates were 65.7% and 58.4%, and 2-year survival rates were 56.3% and 54.2% in the BCT and control groups, respectively. There was no significant difference between the two groups (Fig. 1).

GOS scores at 1 month post-surgery in the BCT group were significantly worse than in control group ($p=0.034$). However, GOS scores at 6-month follow-up showed no significant difference between the two groups ($p=0.494$; Table 3).

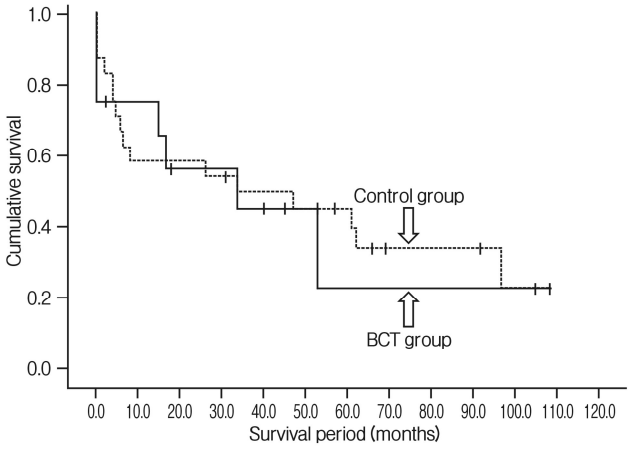

Fig. 1. Kaplan-Meier curve shows cumulative survival rate after operation between BCT and control groups. Statistical analysis was performed with Kaplan-Meier curve analysis ($p=0.808$). *$p\leq0.05$ was considered statistically significant. BCT: barbiturate coma therapy.

Table 3. The comparision of Glasgow Outcome Scale score at 1 month, 6 months after operation between barbiturate coma therapy and control groups

GOS score	BCT group (n=12)	Control group (n=26)	p-value*
GOS 1 month score	1.75±0.75	2.38±0.85	0.034*
GOS 6 month score	2.25±0.96	2.50±1.06	0.494

Statistical analysis was performed with Mann-Whitney U test.
*$p \leq 0.05$ was considered statistically significant. GOS: Glasgow Outcome Scale; BCT: barbiturate coma therapy

Table 4. The comparision of complication between barbiturate coma therapy and control groups

Complications	BCT group (%) (n=12)	Control group (%) (n=26)	p-value*
Lung problem	12 (100%)	15 (57.7%)	0.010*
Hepatic problem	10 (83.3%)	6 (23.1%)	0.006*
Renal problem	8 (66.7%)	6 (23.1%)	0.006*
Cardiology problem	8 (66.7%)	17 (65.4%)	0.096

Statistical analysis was performed with Fisher's exact test
*$p \leq 0.05$ was considered statistically significant. BCT: barbiturate coma therapy.

There were various complications in both groups, including pulmonary (pneumonia, pulmonary edema), hepatic (aspartate transaminase/alanine transaminase elevation), renal (azotemia, electrolyte imbalances, diabetes insipidus), and cardiac complications (cardiac marker elevation, tachycardia, atrial fibrillation, hypotension, B-type natriuretic peptide elevation) within 1 month post-surgery (Table 4). The pulmonary comorbidity was found in all patients administered with BCT and 15 patients (57.7%) in the control group. This difference was significant (p=0.01). Additionally, hepatic comorbidity was dominant in the BCT group (83.3%) than in the control group (23.1%; p=0.006). Renal comorbidity was also more frequent in the BCT group (66.7%) than in the control group (23.1%; p=0.006). However, the incidence of cardiac comorbidity was similar in the two groups.

The changes in ICP for 7 days post-surgery are illustrated in Fig. 2. There was no difference in the ICP between the two groups for the first 24 hr. After 24 hr, ICP seemed to be controlled better in the BCT group than in the control group; however, this finding was not significant (p=0.261). During ICP monitoring, we defined patients who underwent reoperation for ICP control or expired due to uncontrolled increase in ICP as "failure of ICP control." There was no significant difference between the BCT group and the control groups regarding "failure of ICP control"; two patients (20%) in the BCT group showed "failure of ICP control," compared to 4 (20%) in the control group.

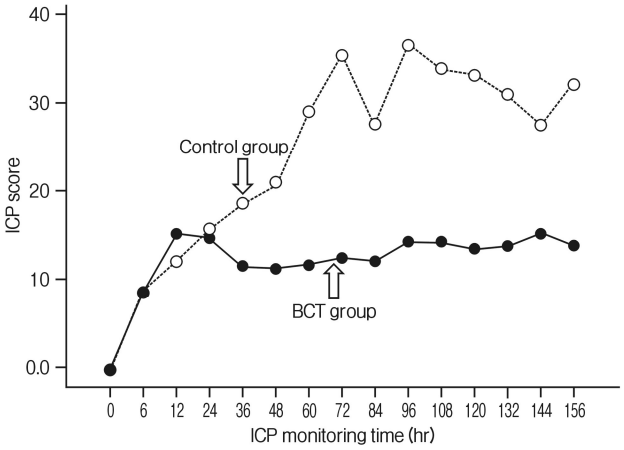

Fig. 2. The comparision of ICP score trend between BCT and control groups for 156 hr. Statistical analysis was performed with Bonferroni's method (p=0.261).
*$p \leq 0.05$ was considered statistically significant, ICP: intracranial pressure; BCT: barbiturate coma therapy.

DISCUSSION

The treatment of patients with MCI remains a challenge. Moreover, a more substantial comparison of the risks with the merits of the combination of BCT and decompressive craniectomy in patients with MCI has yet to be made[14,24]. High-dose barbiturate is known to decrease ICP. It is known for many years that barbiturates play an important role in the management of ICP[3,7]. The mechanism of action of barbiturate in patients with ICP is thought to be derived from rerouting blood to ischemic brain areas by vasoconstriction in normal brain areas and decreasing metabolic demand[10,11]. Barbiturate may show protective effects in other mechanisms such as stabilizing lysosomal membrane, modifying amino acids and release of neurotransmitters, reduction of calcium concentration within the cells, delaying cerebrospinal fluid production, reforming of fatty acid metabolism, clearance of free radicals, and seizure suppression[3,4,24].

The associations between the clinical outcome and level of ICP have been well documented in previously studies. According to Lee et al.[11], the patients whose ICPs were adequately controlled by pentobarbital, had 5 times greater chances of survival. Eisenberg et al.[7] reported the results of a 5-center randomized controlled trial of high-dose barbiturate therapy for uncontrollable ICP in patients with poor GCS score, and showed that the patients in the pentobarbital group had improved outcome.

In previous studies, ICP control was better achieved in the BCT group. However, in our study, there were no significant differences in GOS and overall survival between the two

groups at 6 months post-surgery. Although after 24 hr, ICP seemed to be controlled better in the BCT group than in the control group; however, this finding was not significant (p=0.261). This can be explained by the stronger effect of decompressive craniectomy than that of BCT in the management of increased ICP. Moreover, our study was a small sample size and the GOS scores were significantly worse in the BCT group than in the control group at 1 month post-surgery. This may be due to frequent medical complications in the BCT group, which could delay patients' functional recovery. Widely known complications of BCT include cardiac dysfunction including hypotension, electrolyte imbalance, pulmonary comorbidities, hepatic dysfunction, renal dysfunction, and infection[10,14,18,24]. In this study, medical complications such as pneumonia, aspartate transaminase/alanine transaminase elevation, hypernatremia, and diabetes insipidus were more frequently seen in the BCT group than in the control group. It has been reported by many other studies that more than 70% of the patients who underwent BCT showed widely known complications such as hypotension, respiratory distress, electrolyte imbalance, and liver failure[18,24]. Similarly, electrolyte imbalance and respiratory complications occurred in majority of the patients in the BCT group in our study.

Generally accepted prognostic factors of MCI are age, timing of surgery, dominance of the infarcted hemisphere, and the extent of infarcted territory[9,10,12,16]. In our study, dominance of the infarcted hemisphere showed no significant difference. This may be because of the low number of samples and, instead of the dominant hemisphere, the area of infarction might have contributed significantly to the prognosis. Age, however, was discarded as a prognostic factor in our study due to statistical insignificance (p=0.516). This may be because of the low number of samples, which made it difficult to run a statistical test. The cut-off age was set to 67 years base on the median age. In addition, advantages of early surgery (<24 hr) also failed to prove significant. This may be because, of the 12 patients who underwent early surgery, 6 had larger infarction beyond MCA territories, which could have affected the outcome. Only the extent of infarction affected the outcome in our study, which concurred with numerous other studies accepting it as a prognostic factor[5,15].

This study has important limitations which could influence the reliability of our results. First, this study was conducted retrospectively; therefore, it is subject to selection bias. Application of BCT was decided by each surgeon's preference or operative findings or postoperative CT findings rather than by randomization. Nevertheless, the patients had similar baseline clinical characteristics (Table 1) and similar ICP within 24 hr (Fig. 2) between the BCT and control groups, which may have reduced selection bias. The small sample size is another major limitation of our study. To overcome this limitation, we analyzed all patients treated since the new opening of our institute and minimized the exclusion criteria. Only 4 patients were excluded from our study because they received intended sedative treatment using midazolam or propofol. Hence, the heterogeneity of study population was inevitable. For example, hemorrhagic transformation or coagulopathies were not considered in this study. We suggest including as many patients as possible to reduce the selection bias in the study of the utility of BCT in the management of MCI.

CONCLUSION

In summary, the present study demonstrates that the use of BCT following decompressive craniectomy in the management of MCI is associated with high frequency of medical complications, which could delay functional recovery and adequate rehabilitation, even though it could provide a favorable effect to ICP control in previous studies. Therefore, we suggest that BCT should not be used as a routine protocol following decompressive craniectomy. Instead, it should be used as an adjunctive or selective measure when maximum conventional treatments fail. Future studies are required to ascertain when BCT could be beneficial in patients with malignant MCA infarction.

REFERENCES

1. Aarabi B, Hesdorffer DC, Ahn ES, Aresco C, Scalea TM, Eisenberg HM: Outcome following decompressive craniectomy for malignant swelling due to severe head injury. J Neurosurg 104: 469-479, 2006
2. Berrouschot J, Sterker M, Bettin S, Köster J, Schneider D: Mortality of space-occupying ('malignant') middle cerebral artery infarction under conservative intensive care. Intensive Care Med 24:620-623, 1998
3. Branston NM, Hope DT, Symon L: Barbiturates in focal ischemia of primate cortex: effects on blood flow distribution, evoked potential and extracellular potassium. Stroke 10:647-653, 1979
4. Cai Z, McCaslin PP: Acute, chronic and differential effects of several anesthetic barbiturates on glutamate receptor activation in neuronal culture. Brain Res 611:181-186, 1993
5. Chen CC, Cho DY, Tsai SC: Outcome of and prognostic factors for decompressive hemicraniectomy in malignant middle cerebral artery infarction. J Clin Neurosci 14:317-321, 2007
6. Cheung A, Telaghani CK, Wang J, Yang Q, Mosher TJ, Reichwein RK, et al.: Neurological recovery after decompressive craniectomy for massive ischemic stroke. Neurocrit Care 3:216-223, 2005
7. Eisenberg HM, Frankowski RF, Contant CF, Marshall LF, Walker MD: High-dose barbiturate control of elevated intracra-

nial pressure in patients with severe head injury. J Neurosurg 69:15-23, 1988
8. Hacke W, Schwab S, Horn M, Spranger M, De Georgia M, von Kummer R: 'Malignant' middle cerebral artery territory infarction: clinical course and prognostic signs. Arch Neurol 53:309-315, 1996
9. Hao Z, Chang X, Zhou H, Lin S, Liu M: A cohort study of decompressive craniectomy for malignant middle cerebral artery infarction: A real-world experience in clinical practice. Medicine (Baltimore) 94:e1039, 2015
10. Kim YI, Park SW, Nam TK, Park YS, Min BK, Hwang SN: The effect of barbiturate coma therapy for the patients with severe intracranial hypertension: a 10-year experience. J Korean Neurosurg Soc 44:141-145, 2008
11. Lee MW, Deppe SA, Sipperly ME, Barrette RR, Thompson DR: The efficacy of barbiturate coma in the management of uncontrolled intracranial hypertension following neurosurgical trauma. J Neurotrauma 11:325-331, 1994
12. Lin TK, Chen SM, Huang YC, Chen PY, Chen MC, Tsai HC, et al.: The outcome predictors of malignant large infarction and the functional outcome of survivors following decompressive craniectomy. World Neurosurg 93:133-138, 2016
13. Marshall LF, Smith RW, Shapiro HM: The outcome with aggressive treatment in severe head injuries. Part II: acute and chronic barbiturate administration in the management of head injury. J Neurosurg 50:26-30, 1979
14. Nordby HK, Nesbakken R: The effect of high dose barbiturate decompression after severe head injury. A controlled clinical trial. Acta Neurochir (Wien) 72:157-166, 1984
15. Raffiq MA, Haspani MS, Kandasamy R, Abdullah JM: Decompressive craniectomy for malignant middle cerebral artery infarction: Impact on mortality and functional outcome. Surg Neurol Int 5:102, 2014
16. Rahmanian A, Seifzadeh B, Razmkon A, Petramfar P, Kivelev J, Alibai EA, et al.: Outcome of decompressive craniectomy in comparison to nonsurgical treatment in patients with malignant MCA infarction. Springerplus 3:115, 2014
17. Ropper AH, Shafran B: Brain edema after stroke. Clinical syndrome and intracranial pressure. Arch Neurol 41:26-29, 1984
18. Schalén W, Messeter K, Nordström CH: Complications and side effects during thiopentone therapy in patients with severe head injuries. Acta Anaesthesiol Scand 36:369-377, 1992
19. Schwartz ML, Tator CH, Rowed DW, Reid SR, Meguro K, Andrews DF: The University of Toronto head injury treatment study: a prospective, randomized comparison of pentobarbital and mannitol. Can J Neurol Sci 11:434-440, 1984
20. Simard JM, Sahuquillo J, Sheth KN, Kahle KT, Walcott BP: Managing malignant cerebral infarction. Curr Treat Options Neurol 13:217-229, 2011
21. Spagnuolo E, Costa G, Calvo A, Johnston E, Tarigo A: Descompressive craniectomy in head injury. Intractable I.C.P.. Neurocirugia (Astur) 15:36-42, 2004
22. Subramaniam S, Hill MD: Decompressive hemicraniectomy for malignant middle cerebral artery infarction: an update. Neurologist 15:178-184, 2009
23. Uhl E, Kreth FW, Elias B, Goldammer A, Hempelmann RG, Liefner M, et al.: Outcome and prognostic factors of hemicraniectomy for space occupying cerebral infarction. J Neurol Neurosurg Psychiatry 75:270-274, 2004
24. Ward JD, Becker DP, Miller JD, Choi SC, Marmarou A, Wood C, et al.: Failure of prophylactic barbiturate coma in the treatment of severe head injury. J Neurosurg 62:383-388, 1985