Effect of decompressive surgery in patients with severe traumatic brain injury and bilateral non-reactive dilated pupils

Ağır travmatik beyin yaralanması ve bilateral reaktif olmayan pupil dilatasyonu bulunan hastalarda dekompresif cerrahinin etkileri

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BACKGROUND
We investigated Glasgow Coma Scale (GCS) scores, intracranial pressure (ICP) and cerebral perfusion pressure (CPP) changes, and long-term clinical outcomes in patients with severe traumatic brain injury (STBI) associated with bilateral non-reactive dilated pupils (BNPD) who underwent decompressive surgery (DS).

METHODS
The study group consisted of 28 patients (11 females, 17 males) with BNPD from among 147 patients who underwent DS due to STBI in our department.

RESULTS
The mean GCS score was 4.96±1.20 at admission and 4 preoperatively. Mean ICP in non-surviving patients after DS was higher (p<0.05). ICP decrease after DS was also higher in surviving patients than in non-surviving patients (p<0.05). The overall mortality rate was 61.02%. A GCS motor score >2 at admission was associated with lower mortality (p<0.05). Four of the surviving patients (14.28%) had a functional outcome (Glasgow Outcome Score: 4 and 5) at one year after hospital discharge.

CONCLUSION
Outcome in patients with BNPD after STBI may not always be fatal or poor. Rapid DS may increase the chance of functional survival, especially in patients with admission GCS score of 6 or 7.

Key Words: Decompressive surgery; traumatic brain injury; non-reactive dilated pupil.

AMACL
Ağır travmatik beyin yaralanması (ATBY) ve bilateral reaktif olmayan pupil dilatasyonu (BRPD) olup, dekompresif cerrahi (DC) uygulanan hastalarda Glasgow koma skala-si (GKS), kafa içi basınç (KİB), serebral perfüzyon basınçı (SPP) değişiklikleri ve uzun dönem klinik sonuçları değerlendirildi.

GEREÇ VE YÖNTEM
Çalışma gurubu, bölümümüzde ATBY nedeniyle DC uygulanan hastalarda BRPD’li hastaların kliniğini incelemek amacıyla, GKS, KIB, SPP değerlerini ve uzun dönemde Klinik sonuçları değerlendirildi.

BULGULAR
Çalışma gurubu, bölümümüzde ATBY nedeniyle DC uygulanan hastalarda BRPD’li hastaların kliniğini incelemek amacıyla, GKS, KIB, SPP değerlerini ve uzun dönemde Klinik sonuçları değerlendirildi.

ŞEKIL
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ANKET
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Anahtar Sözcükler: Dekompresif cerrahisi; travmatik beyin yaralanması; reaktif olmayan dilatato.

Key Words: Decompressive surgery; traumatic brain injury; non-reactive dilated pupil.
Non-reactive fixed and dilated pupils have been well known as the most unwanted and an ill-omened event in neurosurgery. Despite our advances in understanding, monitoring and treating cerebral traumatic pathologies, the outcome for patients with dilated pupils in severe traumatic brain edema remains significantly poor.\[1-5\] However, there are not many reports in the literature that definitively and quantitatively document about the effect of decompressive craniectomy (DC) on intracranial pressure (ICP), cerebral perfusion pressure (CPP) and prognosis in patients with severe head injury (SHI) associated with bilateral non-reactive dilated pupils (BNDP).

In patients with severe traumatic brain edema, uncontrollable ICP ends uncal or central transtentorial herniation showing uni- or bilateral pupil dilation. When the patient develops neurological pons signs with BNDP, irreversible ischemic damage to the brain exists with no chance of recovery. Medical treatment is frequently ineffective in such severe brain trauma.\[6\] When the patient demonstrates compression signs of the upper brainstem in the early period of uncal or central transtentorial herniation due to uncontrollable ICP, despite the modern management protocols (intubation, artificial ventilation, ventricular drainage of cerebrospinal fluid (CSF), and osmotherapy with mannitol), DC has been recommended as a last treatment option.\[7-11\] However, the criteria for the use of DC in such patients with severe traumatic brain injury (STBI) have not been standardized. There are not many reports in the current literature about the necessity of decompressive surgery (DS) in patients with BNDP due to STBI or cerebrovascular accidents (CVA). For these reasons, there is an uncertainty about what should be done when it is confronted early in a patient with SHI associated with herniation syndrome and BNDP, but with spontaneous respiration and motor responses.

In our study, we reviewed 28 consecutive cases during a five-year period to identify the results after DS in patients with SHI associated with BNDP.

**MATERIALS AND METHODS**

**Patient Population**

The study group consisted of 28 patients with BNDP taken from among 147 patients who had undergone DS due to SHI in our department between September 1997 and July 2009. Admission details were taken by the emergency room (ER) for patients brought directly from the scene of the accident or another institution. Data included cause and nature of injury, patient’s age, Glasgow Coma Scale (GCS) score on arrival at the hospital and after resuscitation and preoperatively, pupillary size and pupillary response to light pre- and postoperatively, results of computed tomography (CT) scans, values of ICP and CPP as the difference between mean arterial blood pressure and mean ICP and their response to medical and surgical treatment, and the hospitalization period. Patients with GCS scores of ≤8 on admission and after resuscitation were accepted as SHI. Pupillary size was classified as <4 mm or ≥4 mm, and pupils ≥4 mm were considered dilated, associated with very sluggish or absent light responses. Pupillary improvement was identified as partial or full pupillary constriction of at least 1 mm, toward the normal diameter. Patients with major direct ocular trauma were not initially considered for inclusion in the study, because a major component of early neurological evaluation was based on accurate inspection of both pupils when they were not affected by direct trauma to the eyes and/or the eyelids. Patients with early arterial hypotension (systolic arterial blood pressure of <90 mmHg associated with major extracranial injuries) that was documented in the ER were initially excluded from the study. Any patient fitting the clinical criteria for brain death on admission and patients with open head injury such as gunshot wounds or other penetrating injuries were also excluded.

**Initial Stabilization and Study Protocol**

After admission to the hospital, primary resuscitation and stabilization were performed according to the European Brain Injury Consortium (EBIC) guidelines for SHI.\[12\] Standard management included completion of CT scanning as rapidly as possible at the time of presentation to the ER. CT scans were classified according to the Marshall CT classification system.\[13\] As standardized treatment, sedation, muscle relaxation, normoventilation or sometimes mild hyperventilation, normothermia, normoglycemia, and 30 degree head elevation were provided for all patients. ICP measurement via ventricular catheter was done in all study patients. ICP values were measured and recorded hourly. According to our surgical decompression protocol, DS was performed in the patients who showed neurological deterioration and/or were not responding to standardized treatment methods for decreasing ICP. Also, as a part of our surgical decompression protocol in patients with SHI, DS was immediately performed on patients with BNDP unless brain death, severe arterial hypotension with major extracranial injuries or GCS scores of ≤8 with no obvious CT scan findings were present. In all of the cases having high ICP values, mannitol was given in the form of fractionated bolus, and CSF was drained via the ventricular catheter if necessary. Postoperatively, routine CT scans were taken. No course of barbiturate medication was applied to the patients. The outcome of each living patient was assessed at one year after hospital discharge according to the Glasgow Outcome Scale (GOS).

**Surgery**

The type of surgery was chosen according to neuro-
logical and/or neuroradiological conditions. Unilateral or bilateral large frontotemporoparietal DC combined with duraplasty with temporalis muscle fascia and galea graft were performed. Bilateral DC was performed in all patients with Marshall CT grade 3. Bilateral DC was also performed in patients with Marshall CT grade 4 and unilateral mass lesion when rapidly pulsatile brain swelling was observed after unilateral DC. In order to avoid complications related with sagittal sinus, a bone rim is left on the sinus in bilateral DS operations. A bone flap was inserted under the abdominal fat tissue or preserved in a cold storage at -80°C temperature and replaced 1-4 months after surgery in surviving patients.

Statistical Analysis

All data are presented as the mean ± standard deviation. Comparisons between data groups were computed from the Statistical Package for the Social Sciences (SPSS) 12.0 for Windows. Nonparametric Mann-Whitney U tests were used for independent samples and Wilcoxon signed-rank tests were used for related samples. Statistical significance was defined as a probability value of less than 0.05.

RESULTS

Patient Population

All 28 patients (11 females, 17 males) had BNDP with a GCS motor score of 2 due to STBI in the preoperative period. Cause of injury was traffic accident in all cases. The mean age was 27.60±9.08 years (range: 17-54). The mean GCS score was 4.96±1.20 on admission (after initial resuscitation) and 4.0±0.0 preoperatively. Extracranial injury was found in four cases and all these injuries were in the extremities. All patients were taken for potentially life-saving DS. The mean time span between the accident and surgical decompression was 219±340 minutes. Characteristics at presentation in patients with SHI and the prognosis are shown in Table 1.

Ventricular ICP and CPP Changes

The initial ventricular ICP after the ventricular puncture varied from 25 to 40 mmHg. In the intensive care unit (ICU) after uni- or bilateral DS, ICP values decreased, ranging from -4 to -16 mmHg in all patients. In surviving patients, ICP decreased to 26.54±8.16% of the initial values (p<0.05), whereas in non-surviving patients, ventricular pressures de-

Table 1. Characteristics at presentation in patients with severe head injury associated with bilateral pupillary dilation and the prognosis

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<td>+/-</td>
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<td>Bilateral DC</td>
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</tbody>
</table>

GCS: Glasgow Coma Scale; PR: Post-resuscitation; PrO: Preoperatively; HV: Hyperventilation; ER: Emergency room; CT: Computed tomography; HP: Hospitalization period; GOS: Glasgow Outcome Scale; DC: Decompressive craniectomy; SDH: Subdural hematoma; ICH: Intracerebral hematoma.
creased to 16.05±10.07% of the initial ICP (p<0.05). There was no significant difference for CPP changes initially and after DS between surviving and non-surviving patients (Table 2).

**Table 2.** Comparisons of mean GCS scores, ICP and CPP measurements initially and in ICU after DS and time interval in non-surviving and surviving patients

<table>
<thead>
<tr>
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<th>Non-surviving patients</th>
<th>Surviving patients</th>
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<td>Mean initial GCS score</td>
<td>4.27 ± 0.46</td>
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<tr>
<td>Mean initial ICP (mmHg)</td>
<td>34.05 ± 4.15</td>
<td>27.90 ± 2.60</td>
<td>&lt;0.05</td>
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<td>Mean ICP in ICU (mmHg)</td>
<td>28.66 ± 4.10</td>
<td>20.02 ± 2.25</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mean initial CPP (mmHg)</td>
<td>81.33 ± 11.46</td>
<td>81.6 ± 4.50</td>
<td>NS</td>
</tr>
<tr>
<td>Mean CPP in ICU (mmHg)</td>
<td>74.77 ± 9.59</td>
<td>80.8 ± 4.77</td>
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<tr>
<td>Mean time interval between accident and surgery</td>
<td>153.5 ± 74</td>
<td>320.9 ± 533</td>
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</table>

NS: Not statistically significant; GCS: Glasgow Coma Scale; ICP: Intracranial pressure; CPP: Cerebral perfusion pressure; ICU: Intensive care unit.

**Prognosis**

The overall survival rate was 39.28% (11/28). Seventeen patients (60.71%) died as a result of elevated ICP. These 17 patients had ventricular ICP readings >25 mmHg after DS despite conventional ICP controlling measures such as infusion of hyperosmotic solution, hyperventilation, and CSF drainage. Seven (25%) surviving patients had a poor outcome (GOS score 2 or 3), whereas four (14.28%) surviving patients had a good outcome (GOS score: 4 and 5) (Table 1). In surviving patients, GCS scores at admission were higher than in non-surviving patients (p<0.05). In all surviving patients, the mean hospitalization period was 58 ± 28 days.

**Illustrative Cases**

**Case No. 11** This 54-year-old female patient was admitted to the ER after a motor vehicle accident with a GCS score of 7. In the ER, she suddenly deteriorated and showed decerebrate posturing with BNDP. CT scans showed a left frontoparietal subdural hemorrhage, contusions on the right frontal and left parietal lobes with 10 mm midline shift to right side and diffuse cerebral swelling (Fig. 1a). Left unilateral DC with external ventricular drainage (EVD) was performed urgently and the hematoma was evacuated. Postoperatively, pupils were isocoric and reactive. CT scan obtained one month after the initial procedure demonstrated enlarged ventricles with left frontoparietal subdural hygroma (Fig. 1b). After 42 days of hospitalization, she was discharged with GOS of 3 and the first year GOS was 5.

**Case No. 27** This 17-year-old male patient was

![CT scans](image1.png)

Fig. 1. Brain CT scans of Case no. 11. (a) Initial CT scan demonstrates a left frontoparietal subdural hemorrhage, contusions on the right frontal and left parietal lobes with 10 mm midline shift to right side and diffuse cerebral swelling. (b) CT scan obtained one month after the initial procedure demonstrates enlarged ventricles with left frontoparietal subdural hygroma.
admitted to an external hospital after motor vehicle accident with GCS score of 6. He was referred to our institution because of neurological deterioration. On admission, he was found in decerebrate posturing with BNDP. CT scans showed large contusions on both frontal lobes and a 13 mm midline shift to the left side (Fig. 2a). Urgent bilateral DC with EVD was performed and the hematoma was evacuated. Postoperatively, pupils were isocoric and reactive. The 45th day CT scans showed resorbed contusions and enlarged ventricles (Fig. 2b). At the 46th day of hospitalization, he was discharged with a GOS of 3. The first year GOS was 5 and CT scan obtained at this time was demonstrated in Fig. 2c.

**DISCUSSION**

**Causes of Pupillary Dilation in Patients with Severe Head Injury**

Acute pupillary dilation without major direct ocular trauma in patients with STBI is known as a neurosurgical emergency. Pupil dilation is thought to be the result of uncal herniation causing mechanical compression of the third cranial nerve at the tentorial edge. Continued compression of the medial temporal lobe into the brainstem results in loss of consciousness, decerebrate posturing, and cardiovascular collapse. Also, compromise of brainstem circulation is a major contributing factor to pupillary dilation.[4] This could be the result of either a consequent deformation of the perforating brainstem arteries arising from the basilar artery due to brainstem displacement, or global reduction in whole-brain cerebral blood flow (CBF) that occurred because of raised ICP in the head-injured patient. As a result, the presence of BNDP in patients with SHI may be interpreted as indicative of abnormally high ICP and associated with cerebral hypoperfusion. Additional concern may be raised over ultimately diagnosing clinically significant primary brainstem injury on magnetic resonance imaging (MRI) studies. It would be preferable to diagnose such a potentially grim prognostic feature before undertaking aggressive surgical measures.[7] However, it could be fatal in patients in a coma with severe traumatic brain edema in the short term because the time window for extensive studies such as clinical, radiologic, laboratory investigations, and interventional factors such as elucidation and col lation can require hours and days. Another cause for a patient’s low GCS score or non-reactive pupils may be due to alcohol or drugs (or both) rather than symptoms of brain damage.[14]

**Decompressive Surgery in Patients with Severe Head Injury: Which Patient and When?**

According to the EBIC and the American Brain Injury Consortium (ABIC) guidelines for SHI,[12,15] DS is one therapeutic option for brain edema that does not respond to conventional therapeutic measures such as hyperventilation, osmotherapy with mannitol, ventricular drainage of CSF, and metabolic suppression therapy.[12,16-20] However, specific indications and timing for this intervention have not been standardized as yet. It has been reported that the indications for DS in patients with SHI are the appearance of diffuse unilateral or bilateral brain swelling with correlating clinical deterioration; worsening of GCS score and/or dilation of pupils unresponsive to light; therapy-resistant increase in ICP to ≥30 mmHg and/or a reduction in CPP to <45 mmHg; and initial GCS score of ≥4 and a GCS score of at least 4 on the 1st posttraumatic day.[6,7,9-11] Guerra et al.[6] and Yoo et al.[11] reported that patients with primary fatal brainstem lesions, that is, an initial and persisting GCS score of 3 and/or bilaterally fixed and dilated pupils, did not undergo DS. Additionally, other authors reported that exclusion criteria for DS are patients over 40 years of age with hypertonic extensor
posturing (GCS motor score of 2); bilateral unreactive pupil ≥4 mm in diameter; bilateral intracranial lesions, and life-threatening concomitant medical disease.\textsuperscript{1,9,10} In this study, our patients were the worst subgroup of patients with SHI, associated with bilateral pupillary dilation and extensor motor responses (GCS score: 4); in an unavoidable form and without intervention, the next step would be the progression to brain death. There is no reported definite documentation in the current literature regarding the results of DS for such patients, except case reports including the patients with head injury or CVA.\textsuperscript{21-24} Nevertheless, the question may be raised whether the lack of demonstrable efficacy of DS in our patient study group was due to the small sample size.

Difficulties arise because of timing (early compared with ‘last option’) of the DS, which may well change the pathophysiological responses. It is reported that the right time for DS is determined by clinical follow-up, repeated CT scans, and continuous ICP and CPP monitoring.\textsuperscript{6} It is also suggested that if further evidence is found for the assumed relationships, the B wave will be a new parameter to control brainstem function.\textsuperscript{6} Thus, deterioration in neurological status while the patient is sedated could be detected before pupillary dilation. In our previous study, we compared 40 STBI patients who underwent early bilateral DC as a first-tier treatment with 36 patients in whom surgical treatment was considered as a second step.\textsuperscript{25} In the early bilateral DC group, especially in patients <40 years and with an initial GCS score of ≥6, the favorable outcome rate was significantly higher. However, treatment is not clear in patients who suddenly develop bilateral pupillary dilation in the early posttraumatic period. It is reported that a slowly developing deterioration seems to carry a better prognosis than a rapid one.\textsuperscript{6,26} It is widely accepted that DS should not be postponed so long that irreversible brainstem changes, such as Duret hemorrhages, occur.\textsuperscript{19,27} However, the optimal time at which DS should be performed remains debatable.

**GCS Score, ICP and CPP Changes and Prognosis**

There is also confusion in the current literature regarding prognostic features of patients that have undergone DS. In general, the use of simple clinical data findings to determine outcomes after head injury has been widely employed. Indeed, a number of authors have found that age, GCS score (or motor score), pupillary abnormalities, elevated ICP and the presence of hypotension, shift in CT scans, and abnormal somatosensory evoked potential tracings are regarded as reliable indicators of outcome.\textsuperscript{2,4,14,27,28} The adverse effect of increased age after head injury among the adult population has been verified in numerous series.\textsuperscript{1,29} It has been reported that admission GCS score is closely associated with patient outcome.\textsuperscript{1,14,23,28,30,31} According to the Traumatic Coma Data Bank,\textsuperscript{28} mortality rates progressively decrease with increases in GCS scores; a GCS score of 3 resulted in 78.4% mortality; a score of 4 in 55.9%; 5 in 40.2%; 6 in 21.2%; 7 in 17.6%; and a score of 8 in 11.3% mortality. In another study, Waxman et al.\textsuperscript{5} noted a poor correlation between admission GCS score and outcome, and 10 of 117 patients scoring a GCS of 3 had a good recovery. The current literature has concluded that initial therapy should be aggressive for patients with SHI regardless of the initial neurologic status, because accurate prediction of outcome within six hours of admission is impossible. However, neither of these studies assessed the results of DS with the presence of bilateral pupillary dilation in patients with SHI. Choi et al.\textsuperscript{1} evaluated 21 indicators present at admission to the ER to determine whether any could be correlated with outcome. These authors noted that no patients recording a motor score <4 with no pupillary responses bilaterally had a functional survival. Quigley et al.\textsuperscript{3} reported that the overall functional survival was low (12.5%) in patients with GCS of 3, 4 or 5, and that it was the worst among patients presenting pupillary abnormalities (6.6%). Lieberman et al.\textsuperscript{31} reviewed data from 137 patients with a GCS of 3; 104 had fixed and dilated pupils and 33 did not. The authors concluded that patients with a GCS of 3 as well as fixed and dilated pupils have no reasonable chance of recovery. Similarly, in a retrospective study of Tien et al.\textsuperscript{13} they found that patients with an initial GCS of 3 and bilateral fixed and dilated pupils had a 100% in-hospital mortality rate. Despite the hopeless results of these reports, Chamoun et al.\textsuperscript{33} presented a survival rate of 21.3% and a good outcome rate of 1.5% in this patient group in a recent study. They explained their results as related with young age, initially aggressive treatment and the epidural hematoma (EDH) subgroup, and they emphasized that patients who suffered TBI and presented with a GCS score of 3 should be treated aggressively initially, since a good functional outcome could be obtained in some cases. Cruz et al.\textsuperscript{8} reported that among patients with SHI and BNDP who were treated with ultra-early high-dose mannitol, 43.5% had a favorable outcome at six months. They also reported that patients with abnormal pupillary widening documented at the scene of the injury did not benefit from ultra-early high-dose mannitol treatment, in contrast to those whose bilateral widened pupils were first seen in the ER.\textsuperscript{34} We used mannitol in conventional doses as a way to gain a few minutes of valuable time while patients were transferred to an operating theater for DS.

It is also necessary to ask which is worse, a GCS score 3 or 4? Andrews et al.\textsuperscript{14} reported that a patient with a GCS motor score of 2 and an extension response...
of the limbs may be more severely brain damaged than a patient with a score of 1 because of possible external factors such as alcohol or drugs. Because this score is a constituent part of the GCS, it could explain why a patient with a total score of 3 (the lowest possible score on the scale) may have a better outcome than a patient with a score of 4. In our study, the GCS motor score of ≥2 at admission was associated with lower mortality. All surviving patients with a good outcome were associated with initial GCS scores of 6 and 7. In our previous report, we already proposed that this group of patients were the best candidates for DS.[35]

They also presented with neurological deterioration (GCS score of 4 and BNDP) due to mass effect from a hematoma (subdural hematoma in 4 and intracerebral hematoma in 2 patients). Those patients might have a higher chance of survival and functional recovery than patients whose neurological status is mainly caused by diffuse cerebral swelling. The overall mortality rate in our patients who underwent DS with a GCS score of 4 associated with BNDP in the preoperative period was 61.02%.

Another important issue in SHI is management of CPP.[36-39] CPP is a physiological parameter intimately linked with ICP and mean arterial blood pressure, and it is the greatest determinant of cerebral hemodynamic responses and effects. CPP management directs therapy to the pressure gradient across the brain rather than isolated ICP. However, recent, emphasis has moved again to ICP because episodes of ‘neuro-worsening’ have been shown to be associated with ICP increases and not changes in CPP.[10,38,40] In our patient study group, CPP changes were not found significantly important before and after DS. However, ICP was significantly decreased in surviving patients compared to non-surviving patients.

In conclusion, the accurate prediction of outcome in patients with BNDP after SHI remains elusive, and the outcome may not always be fatal or poor. Rapid DS may increase the chance of functional survival, especially in patients with admission GCS score of 6 or 7 and neurological deterioration due to mass effect from a hematoma. In addition, this study raises high concerns regarding the possibility of saving a patient from death, only for them to survive with severe disability in spite of current methods of reducing ICP.

REFERENCES

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