



Original Article

Brainstem Diffuse Axonal Injury and Consciousness

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ABSTRACT

Background: Severe traumatic brain injuries (TBI), commonly due to motor vehicle accidents may cause death and long-term disability especially when the acceleration-deceleration force on the brain is massive. This may cause shearing of the axonal connections within the cerebral cortex and brainstem in a process referred to as diffuse axonal injury (DAI). Extensive DAI has been postulated to be a poor prognostic indicator for neurological recovery. In our institution, several patients with Grade 3 DAI were observed to recover and achieve neurological outcomes greater than expected given the presence of brainstem injury.

Methods: MRI studies from 100 patients admitted to a large tertiary trauma center for TBI were retrospectively analyzed by two fellowship-trained neuroradiologists. The size of DAI lesions, location of injury within the brainstem, and the number of discrete DAI lesions were measured and recorded. Glasgow Coma Scale (GCS) on arrival and at discharge was noted, as well as the presence of other neurological injuries.

Results: Of 20 patients initially noted to have DAI with lesions of the brainstem, eight of them were discharged with Glasgow Coma Scale (GCS) of 14–15. The 12 patients discharged with reduced consciousness (average GC 7.1) demonstrated a greater number of larger lesions, with a predilection for the dorsal pons.

Conclusion: These results suggest that large, numerous pontine lesions may indicate worse neurological outcomes in patients with these findings.

Keywords: Traumatic brain injury, Diffuse axonal injury, Magnetic resonance imaging, Ascending reticular activating system, Consciousness

INTRODUCTION

TBI is responsible for approximately 2 million Emergency Department visits per year and over 250,000 hospital admissions in the United States civilian population. While most patients with mild TBI tend toward clinic follow-up after the initial assessment, those with moderate and severe TBI are routinely admitted to intensive care units (ICU) with average lengths of stay between 9 and 17 days. The costs for immediate hospitalization are approximately 11.5 billion dollars with the overall lifetime needs of survivors estimated at greater than 64 billion dollars.^[1] DAI was found in 56% of patients with moderate TBI and 90% of patients with severe TBI.^[2] DAI is caused by profound acceleration-deceleration injury such as that seen in motor vehicle accidents, falls, and assault. Primary axotomy (transection of axons) at the time of injury may contribute to pathology. A greater contributor is stretch injury without primary axotomy, which disrupts axonal cytoskeletal elements. This impairs axonal transport mechanisms, disrupting

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neuronal homeostasis and leading to secondary axotomy. Stretch-induced depolarization may cause glutamate toxicity and subsequent sodium/calcium channelopathy, altering the electrochemical gradient and leading to mitochondrial damage. Cellular energy starvation, oxidative stress, and neuroinflammation proceed in a cascade potentially leading to devastating neurological injury peaking 1–2 days after the initial TBI.^[3] Treatment options for severe TBI are currently lacking, but therapeutic hypothermia may reduce the secondary damage incurred by reducing the metabolic rate, and thus, the intracranial energy demand.^[4]

Head computed tomography (CT) is routinely performed for patients with moderate and severe TBI in the emergency department; however, this can only identify hemorrhagic lesions, present in 10% of cases of DAI. The presence of hemorrhagic lesions on initial CT imaging was found to be associated with a favorable neurological outcome and improved overall survival compared to patients with DAI and no microhemorrhages seen on CT. This is contradictory to past studies which correlated hemorrhagic lesions with poor neurological outcome.^[5] Magnetic resonance imaging (MRI) is more sensitive than CT and can detect DAI in the absence of microhemorrhages; however, it is frequently not feasible to perform MRI on unstable trauma patients. Pragmatically, MRI may be delayed until the patient fails to regain consciousness after their acute trauma-related medical problems have been stabilized. This may delay recognition of DAI for several days after the initial insult, during which time the damaging secondary effects of the axonal stretch injury may have run their course. MRI yields better resolution in assessing DAI with different sequences, including diffusion-weighted imaging (DWI) [Figure 1a], gradient-recalled echo (GRE) [Figure 1b], and susceptibility-weighted imaging (SWI) [Figure 2b and c].^[6] DAI severity has been demonstrated to correlate with outcome in comatose patients, and thus are used to aid in clinical prognostication.^[7]

DAI is conventionally graded according to location, with Grade 1 (lesions to the subcortical lobar white matter or cerebellum only), Grade 2 (lesions in the corpus callosum, w/or w/o lesions in the lobar white matter), and Grade 3 (traumatic lesions in the brainstem in areas typical of DAI (dorsolateral quadrant of the upper brainstem, superior cerebellar peduncles) with or without lesions in the lobar white matter or corpus callosum, Figure 2a). The Adams classification was originally developed in the landmark 1989 histopathological study and subsequently applied to clinical practice when MRI came into widespread use.^[8] The use of this scoring system for prognostication was validated by a meta-analysis which demonstrated an increased risk of poor neurological outcome, as well as increased mortality for patients with Grade 3 DAI.^[9] Grade 3 DAI patients were shown to take an average of 2 months to regain

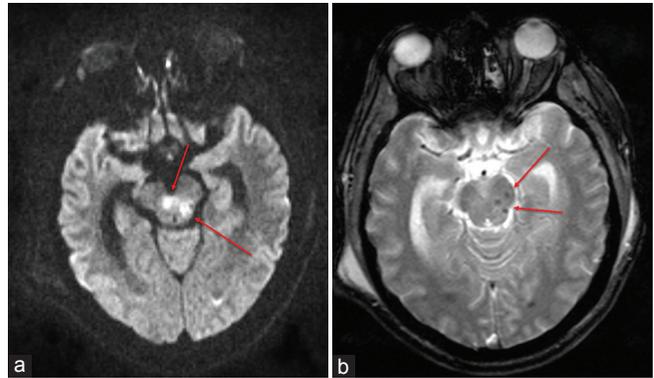


Figure 1: 53-year-old male with no significant medical history presenting with polytrauma after being a pedestrian struck by a motor vehicle. Initially diagnosed by CT with multiple cervical spine fractures, subarachnoid hemorrhage, splenic laceration, and multiple hemorrhagic contusions. Underwent cervical spine fixation and splenic artery embolization. After stabilization, brain MRI was performed 8 days post-injury revealing Grade 3 DAI. (a) Axial DWI at the level of the superior midbrain demonstrating Grade 3 DAI (red arrows). (b) Axial T2*GRE at the level of the midbrain demonstrating Grade 3 DAI (red arrows).

consciousness in contrast to 2 weeks for Grade 2 and several days for Grade 1. These patients are initially very vulnerable, however, some Grade 3 patients have been observed to make good long-term recovery.^[10] Another recent meta-analysis determined that although the likelihood of unfavorable neurologic outcome increased three-fold with each successive grade of DAI, 37% of patients with Grade 3 DAI achieved a favorable neurologic outcome.^[11] Neuroradiologists at a 695 bed academic hospital and level one trauma center noted repeated instances of Grade 3 DAI patients regaining consciousness before hospital discharge. Therefore, this study was performed to further elucidate the prognostic value of brainstem lesions, specifically on consciousness at hospital discharge.

MATERIALS AND METHODS

An MPower search was performed at our institution for patients from 2014–2018 with keyword searches of “traumatic brain injury,” “TBI,” “diffuse axonal injury,” “DAI,” and “shear injury” based on radiological criteria. One hundred patients were found. On review of these patients, 50 were found to have DAI. Imaging studies were reviewed by two fellowship-trained neuroradiologists with certificates of additional qualification (CAQ). One neuroradiologist had 10 years of post-training experience in neuroradiology. The other had 9 years of post-training experience. Each neuroradiologist reviewed the scans independently and assigned each patient a DAI grade. Patients who did not have trauma, Grade 3 DAI, or did not undergo brain MRI were excluded from the study. The difference between the

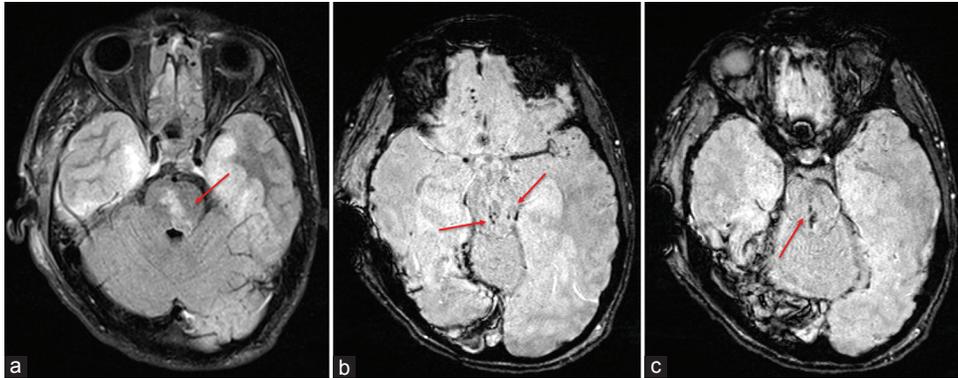


Figure 2: 18-year-old male with no significant medical history presented with traumatic brain injury from high-speed motor vehicle collision diagnosed initially by CT with diffuse extra-axial hemorrhage, subarachnoid hemorrhage causing right to left midline shift, subfalcine, and uncal herniation. Right frontoparietal craniectomy performed to evacuate hematoma and place ventricular catheter. MRI performed 6 days post-trauma after patient stabilization, Grade 3 DAI diagnosed at that time. (a) Axial FLAIR at the level of the pons demonstrating extensive Grade 3 DAI (red arrows). (b) Axial SWI at the level of the midbrain demonstrating several hemorrhagic lesions in the central midbrain (red arrows). (c) Axial SWI at the level of the pons demonstrating several hemorrhagic lesions in the central pons (red arrows).

date of admission and the date the MRI was performed was calculated and recorded. No patients were excluded based on the number of days post-injury that the MRI was performed. Lesions were determined to be secondary to DAI based on the clinical setting of injury, i.e., history of head trauma. The medical record was reviewed for signs or symptoms related to infarct or vascular injury. No patients were noted to have a clinical suspicion of the infarct. One potential confounder is patients who may have had injury secondary to increases in intracranial pressure; however, all patients had DAI in the subcortical white matter and corpus callosum in addition to brainstem injuries, excepting for one patient who had isolated Grade 3 DAI, and other intracranial traumatic injuries. Discrepancies were reviewed after independent analysis and were resolved by consensus. For patients with Grade 3 DAI, the size and location of the brainstem lesions were measured. The total number of lesions was recorded. GCS scores were documented for patients as noted by rescue personnel in the field, at the time of admission and at the time of discharge. The number of days spent in the hospital was recorded. The Ranchos Los Amigos level of cognitive functioning scale (RLAS) at discharge was also recorded.^[12]

Lesion location was designated by location in the midbrain, pons, and medulla. Lesion location within the midbrain and pons were further subdivided as ventral or dorsal. Ventral versus dorsal location was assigned according to the system devised by Izzy *et al.*, with the boundary demarcated by the dorsal border of the inferior olives for the medulla, the medial lemniscus for the pons, the posterior aspect of the decussation of the superior cerebellar peduncles for the caudal midbrain, and the posterior aspect of the red nuclei for the rostral midbrain.^[13] Patients were scanned a 1.5 T Siemens Avanto. FLAIR/T2/DWI/ADC/GRE was obtained for all patients, and SWI sequences were obtained when available. Standard

T1 sequences with and without gadolinium were acquired. Slice thickness was 4 mm with a 1 mm skip, and FOV was 23 cm for all sequences. Parameters for axial DWI/ADC were TE: 102 ms, TR: 5400, with a 190 × 190 matrices. Parameters for axial T2 were TE: 90–130 ms, TR 3000–6000 ms, nex = 2, ETL: 11, flip angle: 150 with a 512 × 512 matrices. Parameters for FLAIR were TE: 90–130 ms, TR: 8000–9000 ms with inversion time of 2440 ms, nex=1, variable bandwidth with a 512–416 matrices. Parameters for GRE were TE: 20–35 ms, TR: 800–1300 ms, flip angle: 20 with a 512–416 matrices. Parameters for SWI were TE: 40–50 ms, TR: 40–50 ms, flip angle: 15 with a 320 × 260 matrices. Parameters for sagittal/axial T1 were TE min 8.7 ms, TR: 400–800 ms with a 320 × 260 matrices. The fluid-attenuated inversion recovery (FLAIR), DWI, or T2 abnormalities were measured in the largest axial dimension (anterior-posterior or transverse). The size of a hemosiderin lesion was measured on GRE or SWI imaging in the same fashion. In lesions, where both FLAIR/DWI abnormality and hemorrhage were present, the FLAIR/DWI abnormality was used. Total lesion burden per patient was calculated by summing the total size of all lesions in a subgroup, then dividing by the number of affected patients in that subgroup. This process was repeated to calculate total pontine lesion burden. The average lesion size was calculated by summing the total size of all lesions in each subgroup, then dividing by the total number of lesions in that subgroup. Due to the retrospective nature of the study, consent was not required as determined by IRB, which approved this study. No patient identifying information is included in this research article.

RESULTS

Average patient age was 35 years, with 13 males and 7 females. All patients were discharged to inpatient rehabilitation

facilities, except for two who died during their hospital admission. Of 20 patients determined to have Grade 3 DAI, 8 of them regained consciousness and were discharged with a GCS of 14–15 [Table 1]. Average RLAS for these patients was 5.5. Conscious patients had an average of one brainstem lesions with an average size of 4.6 mm. Two of these patients had lesions located in the dorsal pons, three in the ventral midbrain, and three in the dorsal midbrain. The lesions in the dorsal pons for these patients were small (1 mm) and hemorrhagic. The two patients in this group with non-hemorrhagic lesions (9 mm and 3 mm) had these lesions located in the ventral midbrain.

The remaining 12 patients were discharged with an average GCS of 7.1, and an average RLAS of 2.1. These patients had had an average of 2.6 brainstem lesions, with one patient having many diffuse hemorrhagic lesions. Of the 10 patients with measurable lesions, the average total affected area was 13.8 mm. Eight of these patients had involvement of both the pons and midbrain. Three of those eight had involvement of both the ventral and dorsal pons and midbrain. Eight of the patients with reduced consciousness had lesions located in the dorsal pons. Average pontine lesion burden was 8.8 mm for patients with reduced consciousness at discharge and pontine involvement in contrast to 1 mm for those that fully regained consciousness. Length of stay was similar between

the two subgroups of patients.

Trends were observed between prognostic factors such as number of brainstem lesions, total lesion burden, lesion burden in the pons, patient age, and outcome measures such as GCS and RLAS at discharge [Table 2]. A statistically significant correlation was demonstrated between pontine lesion burden and GCS at discharge (Spearman correlation coefficient = -0.51 , $P = 0.023$). The correlation was stronger between pontine lesion burden and RLAS at discharge (Spearman correlation coefficient = -0.59 , $P = 0.006$). These associations were also observed a total number of brainstem lesions and GCS/RLAS at discharge (Spearman correlation coefficients were $-0.60/-0.62$, and P -values were $0.005/0.003$, respectively). Age and total lesion burden did not achieve statistical significance as prognostic factors.

DISCUSSION

In this retrospective analysis of patients with Grade 3 DAI, a correlation was demonstrated between discharge GCS/cognitive function and the number of brainstem lesions and pontine lesion burden. Patients with a larger area of injury in the pons tended to display reduced consciousness at hospital discharge [Figure 3a-d]. A total number of lesions and pontine lesion burden correlated most strongly

Table 1: Comparison of MRI findings of DAI for patients who recovered consciousness fully and those with decreased consciousness at hospital discharge.

	Fully conscious at discharge	Decreased level of consciousness at discharge
Average GCS in field	4.6	5.3
Average GCS on admission	6.6	5.2
Average GCS on discharge	14.8	7.1
Average RLAS at discharge	5.5	2.1
Average length of admission	28.1 days	27.6 days
Average number of brainstem lesions	1 lesion	2.6 lesions
Average total size of brainstem lesions	4.6 mm	13.8 mm
Presence of dorsal pontine lesion (s)	2/8	8/12
Average size of pontine lesion burden for patients with pontine involvement	1 mm	8.8 mm

Table 2: Correlation between prognostic variables and GCS/RLAS at discharge was determined by calculating the Spearman correlation coefficient.

Prognostic Variable	Correlation Coefficient, P -value for GCS at discharge	Correlation Coefficient, P -value for RLAS at discharge
Pontine lesion burden	-0.51 , 0.023	-0.59 , 0.006
Total brainstem lesion burden	-0.39 , 0.089	-0.39 , 0.087
Number of brainstem lesions	-0.60 , 0.005	-0.62 , 0.003
Patient age	-0.42 , 0.066	-0.22 , 0.345

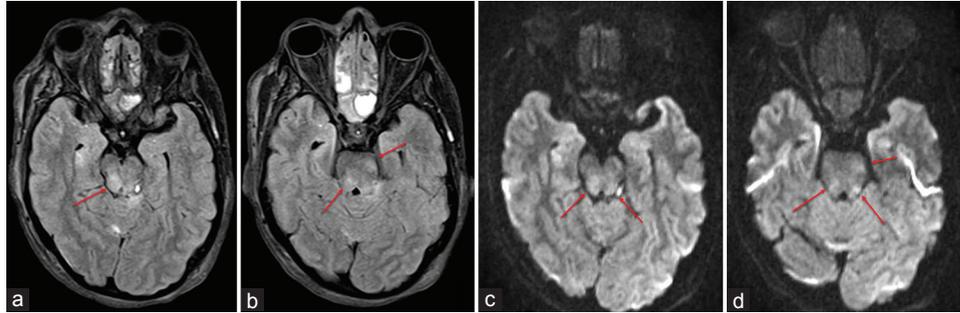


Figure 3: 31-year-old female with no significant medical history presented with polytrauma from high-speed motor vehicle collision initially diagnosed by CT with intraventricular hemorrhage, intraparenchymal hemorrhage, and bilateral pneumothoraces. Intracranial pressure monitor, endotracheal tube, and bilateral chest tubes placed and MRI performed 14 days post-trauma. Grade 3 DAI diagnosed by MRI at that time after patient stabilization. (a) Axial FLAIR at the level of the midbrain demonstrating Grade 3 DAI extensively involving the pontomesencephalic junction (red arrows). (b) Axial FLAIR at the level of the pons demonstrating Grade 3 DAI extensively involving the pontomesencephalic junction (red arrows). (c) Axial DWI at the level of the midbrain demonstrating Grade 3 DAI extensively involving the pontomesencephalic junction (red arrows). (d) Axial DWI at the level of the pons demonstrating Grade 3 DAI extensively involving the pontomesencephalic junction (red arrows).

with reduced GCS/RLAS at discharge. Patients that had minimal or no pontine involvement by DAI were generally able to regain consciousness before hospital discharge [Supplemental Table 1]. In contrast, patients with large DAI lesions involving the pons tended to remain unconscious at hospital discharge [Supplemental Table 2]. It has been demonstrated that severe TBI carries a worse prognosis and elevated health-care costs.^[14] Identifying patients who are at increased risk for the poor neurological outcome may allow for changes in management, which may result in socioeconomic benefits.^[15,16] Clinical decision-making may be enhanced with increased sensitivity and specificity of imaging studies such as SWI for DAI with small hemorrhagic foci.^[17] SWI was utilized to document an association between total DAI lesion burden and white matter atrophy at 1 year in patients with moderate to severe DAI, although these patients were able to improve their cognitive functioning with rehabilitation.^[18] As imaging techniques continue to be refined and the data they generate are analyzed with regard to prognosis, MRI may play a larger role in the clinical management of comatose patients with severe TBI and DAI. The blanket description of Grade 3 for brainstem DAI lesions was of concern in this study as several patients initially assessed as Grade 3 DAI regained consciousness with GCS of 15 before hospital discharge. It is possible that Grade 3 lesions may warrant further inspection with regard to the extent of the injury and neuroanatomical location before prognostication.

The ascending reticular activating system (ARAS) contains structures vital to consciousness and travels through the pontomesencephalic tegmentum. Brainstem strokes associated with coma were shown to be clustered around this region of the rostral pons which contains the raphe nuclei, locus coeruleus, and other nuclei associated with the

ARAS.^[19] Precise neuroanatomical localization of the ARAS is difficult with current imaging modalities; however, DTI was used to reconstruct the ARAS originating from the pontine reticular formation and coursing through the mesencephalic tegmentum to the thalamus.^[20] Indeed, the location of DAI lesions was shown to be an independent predictor of poor prognosis when deep lesions are identified in the region of the substantia nigra and mesencephalic tegmentum on SWI. SWI was shown to detect these lesions with higher sensitivity compared to GRE. These observations led to the proposal of an extended grading system for DAI, with an additional Grade 4 assigned for lesions involving the substantia nigra and/or mesencephalic tegmentum.^[21] Microhemorrhages affecting the dorsal region of the brainstem, specifically the nuclei associated with the ARAS were found to correlate with a neurological disability at 1 year.^[13] The findings from these studies reinforce the notion that MRI reports of Grade 3 DAI may vary widely in regard to a number of lesions, total affected area, and location. These details may be relevant to prognosis in addition to the traditional Grades 1–3 classification scheme and may be pertinent to communicate between the neuroradiologist and the treating physician.

Recently, attempts have been made to correlate specific locations of injury to prognosis including brainstem involvement,^[9] mesencephalic tegmental involvement,^[21] and corpus callosal involvement.^[11] Poor prognosis was correlated with bilateral brainstem lesions as well as dorsal brainstem lesions.^[22] There are many limitations in this field of research, including the high prevalence of confounding factors including comorbid traumatic injuries, hospital course, time to diagnosis, and initiation of therapeutic hypothermia among many others. These limitations decrease the quality of evidence by introducing bias, and there is a need to expand the current literature before

a definitive conclusion can be drawn. Although TBI is common, severe TBI resulting in Grade 3 DAI is incurred due to severe trauma, and patients may not survive until an MRI can be performed. For comatose patients that do survive the initial trauma and are medically stabilized, accurate prognostication is vital. In this study, patients with numerous, large volume brainstem lesions, especially those affecting the dorsal pons were less likely to recover consciousness. This may indicate the involvement of structures vital to achieving consciousness such as those found in the ARAS which courses through the dorsal pons. In contrast, several patients initially determined on MRI to have Grade 3 DAI with small, solitary brainstem lesions went on to fully recover consciousness before hospital discharge. These patients incurred fewer, smaller lesions located more anteriorly, sparing the dorsal pons and possibly, ARAS structures responsible for maintaining consciousness. Eleven patients with Grade 2 DAI, or lesions in the corpus callosum, but no brainstem lesions, were discharged with an average GCS of 13.6 after an average length of stay of 39 days, further supporting the hypothesis that lesions in the dorsal brainstem where the ARAS is located may mediate impairment of recovery of consciousness in DAI.

Limitations to this study include loss of follow-up when patients were transferred to long-term rehabilitation facilities. Due to the retrospective nature of the study, the patient's clinical courses were unable to be followed long term. Even those patients who were unconscious at discharge may have recovered consciousness after undergoing prolonged rehabilitation. The small sample size obtained for this rare injury is a further limitation of this study. A confounding factor may be coincident traumatic intracranial injuries, which were sustained by the majority of the patients, which may affect consciousness at discharge. Two patients in the decreased consciousness at discharge group had injuries causing cerebral midline shift; one was surgically evacuated. Another patient with decreased consciousness had breast cancer metastatic to the brain at the time of injury. Numerous patients in both groups had additional intracranial injuries, most commonly subarachnoid hemorrhage, intraparenchymal hemorrhage, intraventricular hemorrhage, subdural hematoma, and cerebral contusion. Only two patients had isolated DAI as the presenting intracranial injury. In addition, prolonged time from injury to MRI in this study may diminish the imaging characteristics observed. Average days elapsed from admission to MRI was 7.5 days, however, if five outliers who received delayed MRIs at 12, 13, 14, 18, and 37 days post-admission are excluded, the average time from admission to MRI was 3.5 days. Finally, levels of serum biomarkers for TBI were not analyzed for these patients. It has recently been demonstrated that blood biomarkers may be able to help

predict unfavorable outcomes for patients who have suffered a TBI. Candidate biomarkers that may predict poor outcome after severe TBI include several markers of inflammation, coagulation, brain structural proteins, and maintenance of homeostasis.^[23] The function of these proteins identified to have “good” performance for identifying poor outcome after severe TBI further supports the hypothesis that axonal shear injury disrupts neuronal homeostasis and cellular transport necessary to repair the damage done by the initial insult. The resultant cascade may lead to secondary axotomy with catastrophic damage and poor outcome. Analyzing the levels of serum biomarkers in conjunction with the radionomics of TBI may enhance understanding and allow more accurate prognostication for patients with Grade 3 DAI.

CONCLUSION

Patients with severe TBI may remain comatose for extended periods of time, especially in the presence of Grade 3 DAI. Prognostic information in these situations is valuable to clinicians and family members, in terms of the possibility of recovery of consciousness and the potential for meaningful recovery. This study shows decreased neurological recovery when patients have numerous, large lesions located in the deep structures of the pons and midbrain. It may be pertinent to consider the number, size, and location of brainstem DAI lesions before accepting the prognostic implications of Grade 3 DAI.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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SUPPLEMENTARY

Supplemental Table 1: Patients conscious at discharge.

Time from injury to MRI	Age and sex	Discharge GCS	Discharge RLAS	Days admitted	Sequence measured	Brainstem location	Number of brainstem lesions	Size of brainstem lesions	Dorsal or ventral pons	Dorsal or ventral midbrain	Additional intracranial injuries
3 days	21F	15	6	30	T2 GRE	1 pons	1	pons (1 mm)	Dorsal	n/a	Subarachnoid hemorrhage
2 days	23M	15	4	30	T2 GRE	1 pons	1	pons (1 mm)	Dorsal	n/a	n/a
1 day	49M	15	5	11	FLAIR	1 midbrain	1	mb (9 mm)	n/a	Ventral	Intraparenchymal hemorrhage, subdural hematoma, cerebral contusion
2 days	30M	15	6	30	FLAIR	1 midbrain	1	mb (3 mm)	n/a	Ventral	Intraparenchymal hemorrhage, subdural hematoma
37 days	27M	15	7	30	T2 GRE	1 midbrain	1	mb (5 mm)	n/a	Dorsal	Diffuse subarachnoid hemorrhage, multifocal intraparenchymal hemorrhages, small subdural hemorrhage
13 days	28F	14	5	40	DWI	1 midbrain	1	mb (3 mm)	n/a	Dorsal	Intraparenchymal hemorrhage, intraventricular hemorrhage, subarachnoid hemorrhage, subdural hemorrhage
18 days	56M	14	6	40	T2 GRE	1 midbrain	1	mb (8 mm)	n/a	Ventral	Subarachnoid hemorrhage with right frontal hemorrhagic contusion
2 days	16M	15	5	14	FLAIR	1 midbrain	1	mb (7 mm)	n/a	Dorsal	Hemorrhagic cortical contusion within the left frontal lobe

Supplemental Table 2: Patients with decreased level of consciousness at discharge.

Time from injury to MRI	Age and sex	Discharge GCS	Discharge RLAS	Days admitted	Sequence measured on	Brainstem location	Number of brainstem lesions	Size of brainstem lesions	Dorsal or ventral pons	Dorsal or ventral midbrain	Additional intracranial injuries
6 days	54M	3	0	14	FLAIR	1 midbrain	1	1mm	n/a	Dorsal	Large subdural hematoma with craniectomy
14 days	31F	5	1	26	T2 GRE	1 midbrain/5 pons	4	mb (2 mm), pons (9 mm, 4 mm, 7 mm)	Both	Both	Intraventricular hemorrhage, intraparenchymal hematoma, subarachnoid hematoma
0 days	60M	3	0	7	DWI	1 pons/midbrain	2	mb (3mm), pons (2mm)	Dorsal	Dorsal	Subarachnoid hemorrhage, intraventricular hemorrhage, cerebral contusion
2 days	63M	6	3	60	FLAIR	pons/midbrain/medulla	3	mb (5 mm), pons (4 mm), med (3 mm)	Dorsal	Ventral	Subarachnoid hemorrhage
8 days	54M	4	1	13	T2 GRE	1 pons/midbrain	3	mb (5 mm, 6 mm), pons (9 mm)	Dorsal	Dorsal	Hemorrhagic contusions, intraventricular hemorrhage
1 day	25M	7	3	23	T2 GRE	1 midbrain	1	mb (7 mm)	n/a	Dorsal	Frontal hemorrhagic contusions, intraparenchymal hemorrhage, intraparenchymal hemorrhage, subarachnoid hemorrhage
7 days	17F	7	2	30	DWI	1 midbrain	3	mb (6 mm), pons (4 mm, 4 mm)	Dorsal	Ventral	Subdural hematoma, multifocal intraparenchymal hemorrhages, intraventricular hemorrhage, subarachnoid hemorrhage
7 days	18M	9	2	60	FLAIR	1 pons/midbrain	4	mb (12 mm, 14 mm), pons (16 mm, 3 mm)	Both	Both	Intracerebral hemorrhage, cerebral contusion, midline shift

(Contd...)

Supplemental Table 2: (Continued).

Time from injury to MRI	Age and sex	Discharge GCS	Discharge RLAS	Days admitted	Sequence measured on	Brainstem location	Number of brainstem lesions	Size of brainstem lesions	Dorsal or ventral pons	Dorsal or ventral midbrain	Additional intracranial injuries
4 days	52F	10	3	30	FLAIR	2 pons	2	pons (3 mm, 1 mm)	Ventral	n/a	Intraparenchymal hematoma, subarachnoid hematoma, intraventricular hemorrhage
12 days	18F	10	2	23	T2 GRE	1 pons/midbrain	2	mb (6 mm), pons (3 mm)	Dorsal	Dorsal	Subarachnoid hemorrhage, intraventricular hemorrhage
4 days	19M	10	4	23	T2 GRE	1 pons	many	1 mm or less	Both	Both	n/a
6 days	47F	11	4	22	FLAIR	midbrain	1	7 mm	n/a	Dorsal	Extra axial hemorrhage seen near the sella, scattered subarachnoid hemorrhages, extensive facial fractures