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Prognostic value of traumatic brainstem injury in early computed tomography in paediatric population

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ABSTRACT

Introduction: In India, children aged <16 years constitute 35% of the total population and contribute to 20–30% of all head injuries. Prognostication of severe TBI in children based on early imaging and biomarkers has been universally challenging. The Marshall, Rotterdam, Stockholm, and Helsinki CT scores were developed to use acute head CT images to predict mortality at 6 months. Notably, none include criteria related to traumatic brainstem injury (BSI). The objective of this study was to compare the long-term outcome of pediatric patients with BSI identified on CT, along with an effort to classify BSI based on lesion volume, lesion location, presence of subarachnoid hemorrhage (SAH) and intraventricular hemorrhage (IVH) and how, the presence of these subset of injuries affect the outcome.

Methods: A retrospective analysis of pediatric patients presenting with TBI was undertaken from 2019 to 2023. CT scans were reviewed for brainstem lesions and, when present, characterised by location, size, and type (traumatic axonal injury (TAI), contusion, and duret haemorrhage). Clinical, demographic, and outcome data were then compared with the type of lesion, position of lesion, lesion volume, presence/absence of SAH and IVH.

Results: We found that lesion volume of more than 1 cm^3 is associated with a poorer GOSE score ($p< 0.001$). Similarly, lesions spanning both anterior and posterior quadrant are associated with poor outcome (GOSE: 3.4 +_ STD 2.9). We also found significant correlation with presence of SAH and IVH related to a poorer outcome ($p < 0.001$).

Conclusion: Early evidence from the current study suggests that certain TBI patients with BSI can have positive outcomes. BSI can further be classified into TAI, duret and brainstem contusions, each with variable outcome. Brainstem lesions with volume of >1 ml have been found to have a poorer outcome. Similarly, lesions spanning both quadrants tend to have a worse prognosis. Although there was no significant difference in outcome when compared with BSI – cases. These findings suggest of patients with brainstem injuries may exist with divergent recovery potential after TBI.

Keywords
traumatic brainstem injury, paediatric population

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INTRODUCTION

Trauma remains one of the most common causes of death in all age groups, but this is especially true in the pediatric population. Traumatic injuries are the leading cause of death and a major cause

of disability among children. [1,2] Greater than 45% of deaths in children aged 1–14 years in the United States are secondary to trauma. [3] However, predicting, in the early phase, the long-term neurologic outcome in head injury children is still a challenge. In the 1990s, Sharples et al. [4] found that with adequate management, prompt and accurate assessment, and early initiation of critical care is of crucial importance and has been shown to decrease mortality by almost 30%. Secondary brain lesions from systemic origin contribute to worsening of primary brain lesion. Hypoxia and hypotension are major sources of secondary brain lesions that worsen outcome. The deleterious influence of uncontrolled secondary brain insults of systemic origin must also be considered when trying to define predictive factors of outcome. [5]

For TBI triage, nonenhanced computed tomography (CT) is still an essential technique when used in conjunction with the neurological assessment. CT scans can be performed quickly and are very sensitive for injuries that need urgent care or neurosurgical intervention. [6] CT provides sufficient sensitivity to identify fractures, contusions, mass effects, and acute, potentially fatal cerebral hemorrhages. For these reasons, nonenhanced head CT is a class I recommendation for patients with moderate to severe TBI. [7] Acute head CT images were used to generate the Marshall, Rotterdam, Stockholm, and Helsinki CT scores, which were designed to predict outcome at six months [8]. Although these classification systems have become increasingly valuable in their contribution to predicting outcome, they remain imperfect and notably, none include criteria related to traumatic brainstem injury (BSI).

The paucity of existing studies utilizing traumatic brain stem injury (BSI) on computed tomography (CT) as an outcome predictor could be attributed to CT's lower sensitivity in identifying these lesions in contrast to magnetic resonance imaging (MRI) [9, 10]. Even after adjusting for other clinical, demographic, and imaging variables, a number of studies show that adding brainstem lesions to models improves prognosis accuracy [11, 12]. Previously thought to herald a catastrophic neurologic prognosis, research has shown that individuals with brainstem TAI have outperformed expectations in terms of their outcomes [13, 14]. Despite ubiquitous use of CT imaging in the acute TBI, ongoing efforts to refine prognostic tools based on head CT and increasing evidence that traumatic BSI on MRI is associated with more variable outcomes than previously assumed, minimal data are available that relate acute traumatic BSI on CT to long-term functional outcome. Moreover, no study has been done yet to analyze the impact of BSI in pediatric population and how the presentation of these cases and the lesion determine the outcome. Hence the need of the hour was to undertake a study solely dedicated to pediatric head injury, to assess the long-term outcome with BSI identified on CT brain and devise a classification to prognosticate such cases. Along with it we wanted to compare the outcome with that of patients with similar TBI injury but without BSI in an effort to identify subsets of patients with divergent probabilities of functional recovery.

Material and methods

A retrospective study was performed on pediatric patients, less than 16 years of age who presented to Trauma Centre, King George's Medical University, Lucknow, India, with intracranial injuries between January 2019 to December 2023. Patients were included if there was any evidence of cranial injury on the basis of imaging findings warranting admission in trauma centre. Pateints with polytrauma was excluded from the study. Data collected and recorded included the patient's age, gender, mechanism of injury, systolic blood pressure, and arterial blood oxygenation levels. In addition, Glasgow Coma Scale (GCS) score, injury description, and in hospital mortality were recorded. The type of neurological injury was determined based on the results of initial CT scans. Hypotension was defined as a blood pressure that for >5 min was below the 5th percentile for age. Hypoxia was defined as PaO2 less than 80 mm Hg at ABG on presentation to emergency department.

874 cases of pediatric head injury were identified, of which 354 were excluded because they underwent operative intervention. 520 cases were managed conservatively. Of the 520 patients, 19 were identified to have brainstem lesions (BSI+). From the remaining 501 patients with TBI, we matched each patient with BSI+ by age, sex, and admission Glasgow Coma Scale (GCS) score to patients with TBI without brainstem lesions (BSI−). Nineteen of the patients with BSI+ were matched exactly on all three factors, staying within the same severity range (moderate or

severe). Matching on admission GCS score was done to ensure comparable levels of brain injury severity in consideration of long-term outcome as the fairest possible way to investigate any unique contribution of brainstem lesions. In total, 38 pediatric patients with TBI, 19 with BSI+ and 19 with BSI−, were used for the analysis in this study. The primary outcome of interest was observed GOSE score. Favorable GOSE scores were defined as 5 to 8, and unfavorable scores were 1 to 3 (lower severe disability).

CT IMAGING

The earliest head CT of interpretable quality from within 48 hours of recorded injury was selected for detailed qualitative and quantitative analysis. CT scans with brainstem lesions were again further characterized. All pathoanatomic TBI lesions were demarcated, measured, and recorded. A suspected lesion was only recorded and used for analysis if it (1) appeared qualitatively to represent hemorrhage over other hyperdense elements, such as bone in the skull base, artifact, etc.; (2) had at least three contiguous pixels with Hounsfield unit measurements equal to or greater than the measured average Hounsfield units parallel to the tuberculum sellae-occipital protuberance line.

BSI+ lesions were analyzed by volume, location and lesion subtype (TAI, contusion, or Duret) (Figure 1).

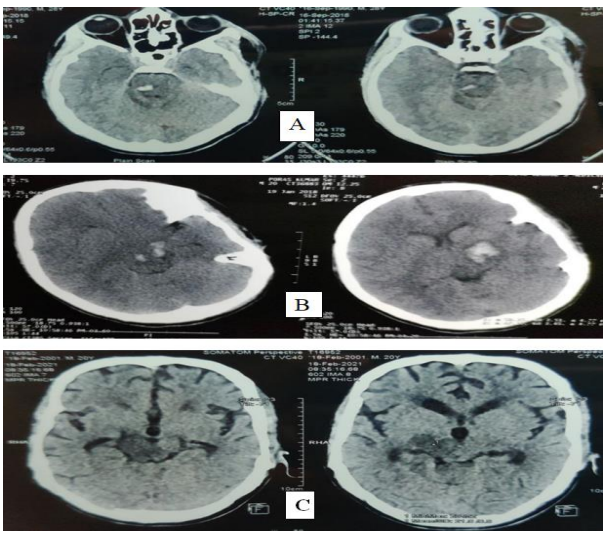

Figure 1. Subsets of BSI+ cohort. **A**. Small, isolated hemorrhagic lesions without associated mass effect or edema most consistent with traumatic axonal injury (TAI). **B**. Larger petechial hemorrhagic lesion with associated edema consistent with brainstem contusion. **C**. Dusky intervening nonhemorrhagic parenchyma consistent with Duret hemorrhage.

Separation of lesions into location by specific brainstem structures was not possible because of bony artifact and low tissue resolution. To improve statistical confidence, location delimitation was limited to anterior and posterior. Lesions were classified as anterior if the majority of the measured volume was situated anterior to a lateral line drawn perpendicular to the anterior–posterior midpoint of involved brainstem structures on relevant axial CT cuts. Patients with BSI+ were then divided into groups based on those with only one or more posterior, those with only one or more anterior, and those with at least one brainstem lesion in both the anterior and posterior halves of the brainstem. (Figure 2)

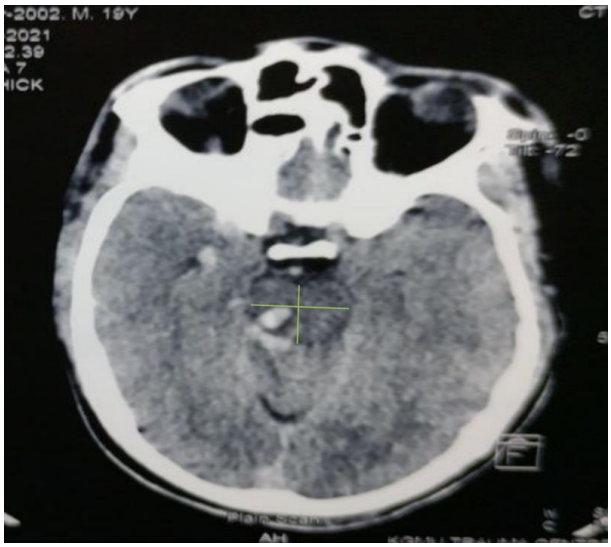

Figure 2. Axial head computed tomography (CT) slice demonstrating right pontine traumatic brainstem injury. The green line drawn perpendicular to each other divide the brainstem into 4 quadrants, where we consider anterior, posterior or lesion spanning both the anterior and posterior.

The association between lesion volume and outcome was analyzed by grouping BSI+ lesions above and below a cutoff point of 1 ml (1 cm3), whereas lesion type was consider as either TAI, duret and contusion. For lesion volume, this cutoff appeared to best segment lesions resulting from microscopic versus macroscopic mechanisms (i.e., isolated TAI versus arterial injury, venous stasis hemorrhage, etc.). Larger, diffuse hemorrhage lesion

of at least 1 ml in size were compared with those with all lesions less than 1 ml with regard to GOSE scores.

Statistical analysis

The distribution of patients with BSI+ and BSI− within subgroups of variables was analyzed using Fisher's exact and Mann–Whitney U-tests, as appropriate. The difference between long-term GOSE scores among groups in variables of interest was analyzed using Mann–Whitney and Spearman correlation, as appropriate. Similarly, bivariate differences in long-term GOSE scores among different subtypes of BSI+ were analyzed using Mann– Whitney and Spearman correlation, as appropriate. Significance tests in all bivariate analysis were conducted without assumptions about underlying distributions. Given the small sample size, multivariate regression analysis was conducted with exact logistic regression and was limited to no more than three parameters.

Results

Nineteen patients with BSI+ and 19 patients with BSI− were evaluated. The mean age for all patients was 11.05 years (standard deviation 3.17). Of 38 total patients, 31 patients evaluated were men (81.6%) and 7 were women (18.4%).

Table 1. Comparison of the distribution of patients with and without BSI

		Groups						
		Bsi +		Bsi -		Total		P value
		N	%	N	%	N	%	
Age	5-10 years	5	26.3%	7	36.8%	12	31.5%	.485
	11-15 years	14	73.7%	12	63.2%	26	68.4%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Sex	Male	16	84.2%	15	78.9%	31	81.6%	0.675
	Female	3	15.8%	4	21.1%	7	18.4%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Loc	Present	19	100.0%	19	100.0%	38	100.0%	1.000
	Absent	0	.0%	0	.0%	0	.0%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Seizure	Present	3	15.8%	3	15.8%	6	15.8%	1.000
	Absent	16	84.2%	16	84.2%	32	84.2%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Ent bleed	Present	2	10.5%	2	10.5%	4	10.5%	1.000
	Absent	17	89.5%	17	89.5%	34	89.5%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Vomiting	Present	1	5.3%	1	5.3%	2	5.3%	1.000
	Absent	18	94.7%	18	94.7%	36	94.7%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Type of head injury	Moderate	5	26.3%	7	36.8%	12	31.6%	0.485
	Severe	14	73.7%	12	63.2%	26	68.4%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Hypoxia	Present	12	63.2%	16	84.2 %	28	73..6%	0.14
	Absent	7	36.8%	3	15.8%	10	26.3%	
	Total	19	100.0%	19	100.0%	38	100.0%	

Hypotension	Present	5	26.3%	5	26.3%	10	26.3%	1.000
	Absent	14	73.7%	14	73.7%	28	73.7%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Hemoglobin	< 9 gm/dl	6	31.6%	4	21.1%	10	26.3%	0.461
	> 9 gm/dl	13	68.4%	15	78.9%	28	73.7%	
	Total	19	100.0%	19	100.0%	38	100.0%	
Hematocrit	<21	3	15.8%	5	15.8%	8	15.8%	0.426
	>21	16	84.2%	14	73.7%	30	78.9%	
	Total	19	100.0%	19	100.0%	38	100.0%	

Statistical comparison by Fisher's exact/ Mann–Whitney U-tests as appropriate.

Table 2. Outcome analysis between the two groups

	Group						
	Bsi positive		Bsi negative		Total		P value
	Mean	Sd	Mean	Sd	Mean	Sd	
Length of stay	7.00	3.40	5.53	2.01	6.26	2.85	0.271
Gcs score	5.89	2.21	6.84	2.01	6.37	2.14	0.166
Gos e	4.37	2.99	5.21	2.30	4.79	2.66	0.674

Table 3. Outcome analysis in BSI positive group based on mean GOSE

		GOS E		
		Mean	Standard deviation	P-value
Lesion type	Brainstem contusion	5.6	2.5	0.214
	Duret	4.0	4.2	
	Tai	2.7	2.9	
Hypoxia	Absent	5.3	3.0	0.125
	Present	3.8	3.0	
Hypotension	Absent	4.8	3.0	0.2596
	Present	3.2	3.0	
Hemoglobin	< 9 gm/dl	3.8	3.1	0.354
	> 9 gm/dl	4.6	3.0	
Hemocrit%	< 21	3.0	3.5	0.958
	>21	1.0		
Impact site	Infratentorial	4.3	2.9	0.325
	Supratentorial	4.6	3.4	
Skull fracture	Absent	4.3	3.0	0.256
	Present	6.0		
Lesion volume (cm 3)	< 1	5.4	2.8	0.001
	> 1	3.0	2.8	
Location of lesion	Anterior	7.0	0.0	0.01
	Both	3.4	2.9	
	Posterior	4.4	3.3	
Traumatic sah	Absent	5.4	2.8	0.007
	Present	3.6	3.0	
Traumatic ivh	Absent	5.1	2.8	0.001
	Present	2.2	2.7	

Table 4. Predicting favorable outcome after TBI in patients with brainstem lesions using exact logistic regression

Univariate Analysis							
		Gos E Score				**Or (95% Ci)**	**P Value**
		Favourable (5-8)		Unfavourable (1-4)			
		N	%	N	%		
Lesion Type	Brainstem Contusion	8	72.7%	2	25.0%	Ref	
	Duret	1	9.1%	1	12.5%	4.00 (0.17-95.76)	0.392
	Tai	2	18.2%	5	62.5%	10.00 (1.05-95.46)	**0.045**
Hypoxia	Present	6	54.5%	6	75.0%	Ref	
	Absent	5	45.5%	2	25.0%	0.40 (0.06-2.93)	0.367
Hypotension	Present	2	18.2%	3	37.5%	2.70 (0.33-21.98)	0.353
	Absent	9	81.8%	5	62.5%	Ref	
Hemoglobin	< 9 Gm/Dl	3	27.3%	3	37.5%	1.60 (0.23-11.27)	0.637
	> 9 Gm/Dl	8	72.7%	5	62.5%	Ref	
Hemocrit%	<21	1	9.1%	2	25.0%	3.33 (0.25-45.11)	0.365
	>21	10	90.9%	6	75.0%	Ref	
Impact Site	Infratentorial	7	63.6%	5	62.5%	Ref	
	Supratentorial	4	36.4%	3	37.5%	1.05 (0.16-6.92)	0.960
Lesion Volume (Cm 3)	<1 Cm^3	8	72.7%	3	37.5%	Ref	
	>1 Cm^3	3	27.3%	5	62.5%	4.44 (0.63-31.29)	0.134
Traumatic Sah	Present	5	45.5%	6	75.0%	3.60 (0.49-26.40)	0.208
	Absent	6	54.5%	2	25.0%	Ref	
Traumatic Ivh	Present	1	9.1%	4	50.0%	0.100 (0.008-1.193)	0.069
	Absent	10	90.9%	4	50.0%	Ref	
Multivariate Analysis							
		Gos E Score				Or (95% Ci	P Value
		Favourable (5-8)		Unfavourable (1-4)			
		N	%	N	%		
Lesion Type	Brainstem Contusion	8	72.7%	2	25.0%	21.33 (2.94 – 154.56)	0.0025
	Bsi Negative	3	15.5%	16	84.5%	Ref	
	Duret	1	9.1%	1	12.5%	5.33 (0.25 – 110.80)	0.279
	Bsi Negative	3	15.5%	16	84.5%	Ref	
	Tai	2	18.2%	5	62.5%	2.133 (0.27 – 16.6)	0.469
	Bsi Negative	3	15.5%	16	84.5%	Ref	

There was no significant difference in age, sex, presenting symptoms, severity of head injury, hypotension, hypoxia, hemoglobin and hematocrit among the two groups with p ranging from 0-14 to 1.00.

Outcome, as evidenced by GOSE score, did not identify a significant difference between BSI+ and BSI− groups, although there was a trend toward the BSI+ group having less favorable outcome (BSI+ mean GOSE score 4.37, BSI− mean GOSE score 5.21, p = 0.64).

This was also the case with length of stay (LOS) wherein there was no significant difference but the BSI + cases had a mean stay of 7 days in comparison to 5.53 days of the BSI – group (p=0.271).

Subgroup analysis of BSI + cases

To examine this further, we next completed subgroup analysis of the BSI+ group. In the group we tried to analyse the different factors resulting in any significant difference in outcome within the same group (Table 3). To begin with the lesion type did not affect the outcome, although TAI tend to have a poorer outcome with mean GOSE of 2.7. by lesion size, lesion location, and lesion type. Assessment of patients with BSI+ by lesion volume above or below 1 cm3 revealed significant differences in outcome. Assessment of presenting symptoms, hypotension, hypoxia, hemoglobin and hematocrit did not reveal any significant factor for outcome, although the presence of hypoxia, hypotension, hemoglobin less than 9 gm/dl and hematocrit of <21 is associated with a poorer outcome. Infratentorial impact and presence of skull fracture is again associated with poorer outcome but of not statistically significant.

Eight cases had lesions more than 1 cm3 achieving mean GOSE scores of 3, whereas 11 patients with brainstem lesions lesser than 1 cm3 made it 5.4 (p = 0.001), signifying that a lesion size of more than 1 cm3 is associated with poorer outcome. Assessment of patient outcome by brainstem lesion location did identify significant difference in outcome among those subgroups, with lesion extending both sides associated with a poorer outcome (mean GOSE 3.4), followed by posterior (mean GOSE 4.4) and then anterior (mean GOSE 7, p = 0.01). Presence of SAH and IVH is associated with poorer outcome, evident by a mean GOSE score of 3.6 and 2.2, respectively (p=0.001).

Exact logistic regression analysis was then used to evaluate the predictive ability of brainstem injury characteristics in an exploratory fashion compared to other clinical parameters. First, univariate exact logistic regression was employed to test the predictive ability of BSI volume, and BSI type. Subgroup of BSI + specifically TAI (OR 10, CI 1.05-95.46, p = 0.045), and BSI volume greater than 1 cm3 (OR 4.4, CI 0.6- 31.2, p = 0.13) is associated with an unfavourable outcome. Given these univariate findings, we last explored whether multivariate modeling of the significant univariate elements would strengthen the overall prediction of favorable outcome and whether there would be a unique contribution of brainstem lesions. Multivariate modeling of brainstem lesion type and volume identified a significant and unique contribution of brainstem lesion type, brainstem contusion to less favorable outcome (OR 21.33, CI 2.94 – 154.56, p = 0.002).

Discussion

This study provides evidence that pediatric patients with brainstem lesions evident on acute head CT done within 48 hours of injury, have the potential for favorable outcome and do not differ significantly when compared directly with patient with TBI with similar injury severity that do not have brainstem lesions. Outcome, as evidenced by mean GOSE score, did not identify a significant difference between BSI+ and BSI− groups, although there was a trend toward the BSI+ group having less favorable outcome (BSI+ mean GOSE score 4.37, BSI− mean GOSE score 5.21, p = 0.64). This was also the case with length of stay (LOS) wherein there was no significant difference but the BSI + cases had a mean stay of 7 days in comparison to 5.53 days of the BSI – group. Although no specific previous study has been conducted, solely to find out the significance of BSI in pediatric age group, but similar results was gained by John R. Williams et al, [15] who showed no significant difference in 6-month GOSE scores in patients with BSI+ (mean 2.7) compared with patients with similar but only cerebrum injuries (mean 3.9). In a study conducted by C Wedekind, et al [16] concluded that brainstem involvement in survivors of severe traumatic brain injury conveys a negative impact on long-term outcome. Similarly another study found that poor prognosis is more common in those with brainstem injury. The study concluded that understanding the anatomy and extent of brainstem injury, as well as its relationship to supratentorial abnormalities, and early use of MRI brain, would help assist in prognosticating and counseling of families. [17]

A lower GOSE profile was observed in our BSI+ cohort with lesions above a volume threshold of 1 ml. BSI volume greater than 1 ml was associated with a mean GOSE score of 3.0, implying most patients in that group did not survive. Conversely, patients with hemorrhage volume less than 1 ml had a significantly better mean outcome score of 5.4 (p = 0.001), and a reasonable chance of gaining functional independence. The lesion type did not affect the outcome significantly, although TAI tend to have a poorer outcome with mean GOSE of 2.7. In

univariate analysis TAI was found to significantly predict less favorable outcome (OR 10, CI 1.05-95.46, p = 0.045). Assessment of patient outcome by brainstem lesion location did identify significant difference in outcome among those subgroups, with lesion extending both sides associated with a poorer outcome (mean GOSE 3.4), followed by posterior (mean GOSE 4.4) and then anterior (mean GOSE 7, p = 0.01). Presence of SAH and IVH is associated with poorer outcome, evident by a mean GOSE score of 3.6 and 2.2, respectively (p=0.001). Another study conducted by A Hilario, et al showed 66% of BSI cases in their study had poor outcome. He also found that bilateral involvement was strongly associated with poor outcome (P < .05). Posterior location showed the best discriminatory capability in terms of outcome (OR 6.8, P < .05) and disability (OR 4.8, P < .01). [18]

In our study pediatric patients with brainstem injury have a reasonable chance for functional recovery, and for this reason, traumatic BSI should not be interpreted as a categorical entity from a mechanistic, pathologic, or prognostic standpoint. Multiple studies indicate added precision in prognostication when brainstem lesions are included in models, even when controlling for other clinical, demographic and imaging factors [15]. Although MRI acquisition in the early stages of post-TBI care is often not feasible in our setup, a study designed to compare early CT with early MRI in patients with traumatic BSI would allow more insight into the best characterization of BSI subtype and other TBI lesions outside the brainstem that may be contributing to observed long-term outcomes.

This study's findings should be balanced by its limitations, which include a small sample size, restricting statistical analysis and confidence, lack of further patient follow-up. Another drawback is not using dedicated volumetric analysis of lesions in our study. Furthermore, the data were analyzed in a retrospective and unblinded fashion, and as such, we acknowledge that the findings of this study may be heavily influenced by confirmation bias. Further prospective study of BSI lesions on early head CT in their relation to additional imaging, clinical parameters, and long-term outcome is needed before they can be incorporated into widely used prognostic models.

Conclusion

Early evidence from the current study suggests that certain TBI patients with BSI can have positive outcomes. It appears that early head CT can identify two different groups of patients with acute traumatic brain stem injury (BSI): a group with larger lesions consistent with duret hemorrhage or contusion with a lower chance of functional independence recovery, and a group with smaller lesions consistent with TAI. Brainstem lesions with volume of more than 1 ml have been found to have a poorer outcome. Similarly, lesions in brainstem spanning both anterior and posterior tend to have a worse prognosis. Although there was no significant difference in outcome when compared with BSI – cases, we conclude that the data support the notion that newer CT imaging classification systems must include these subsets of injury pattern, which may augment traditional clinical measures and provide a better individualized care to the patients and bring in limelight that patients with TBI, especially brainstem injuries stand a higher chance of favorable outcome.

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