

Original Article

Outcome of traumatic diffuse axonal injury in correlation to Marshal, Rotterdam and Adams grading systems

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Abstract: Background: Traumatic brain injury is one of the leading causes of diffuse axonal injury (DAI) that is associated with significant morbidity and mortality. This study was designed to determine the characteristics and outcome of traumatic DAI in correlation to Marshal, Rotterdam and Adams grading scores. Method: Data for this retrospective and cross-sectional study were collected from 33 DAI patients whose ages ranged from 15 to 60 years from 2017-2020. Data regarding gender, age, cause of trauma, associated brain findings, Marshal CT score, Rotterdam CT score, Adams MRI Grade, and outcome were collected and analyzed. Results: Out of 33 DAI patients, 21 (64%) were discharged to their home, 6 (18%) transferred to a peripheral hospital, and 6 (18%) passed away. CT findings showed brain contusion in 27 (82%) cases, subarachnoid hemorrhage (SAH) in 22 (67%) cases, intracerebral hemorrhage in 14 (42%) cases, subdural hemorrhage (SDH) in 10 (30%) cases, brain herniation in 9 (27%) cases, extradural hemorrhage (EDH) in 6 (18%) cases, brainstem injury in 6 (18%) cases, pneumocephalus in 5 (15%) cases, hydrocephalus in 2 (6%) cases and cerebellar injury in 1 (3%) case. There was no detected significance for the patient's mortality outcome concerning CT scan Marshal score, CT scan Rotterdam score, and MRI Adams grade. Conclusion: Road traffic accidents account for a high percentage of DAI among young males (15-25 years), and a high percentage of our studied population improved. We detected no significance in patient's mortality outcome in relation to Marshal, Rotterdam and Adams grading scores.

Keywords: Diffuse axonal injury, outcome, CT, MRI, Rotterdam score, Marshal score, Adams grading

Introduction

Traumatic brain injury (TBI) can result in axonal damage. Diffuse axonal injury (DAI) is microscopic damage linked to shear and tensile forces to the axons in the brain neural tracts, corpus callosum, and brainstem [1]. DAI that is biomechanically caused by rotational acceleration-deceleration forces at impact is characterized by widespread axonal injury in the superficial and deep white substance [2]. Pathophysiological changes in DAI are comprised of mechanical axonal violation, transport inter-

ruption, edema, and proteolysis with secondary physiological changes [3]. Clinically, it is defined by coma lasting 6 hours or more after TBI, excluding cases of swelling or ischemic brain lesions [4]. Survivors often display debilitating motor, sensory and cognitive symptoms, leading to reduced quality of life and a profound economic burden to society [5, 6]. If the brain is impaired functionally and not totally damaged, the brain may slowly resume its function as the neural connections are remodeled with an improvement of the patient's clinical condition [7].

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In Saudi Arabia (KSA), road traffic accidents and injury are estimated at a rate of 28.8 per 100,000. Yet, there have been no data on the clinical characteristics and outcome of DAI in KSA. Thus, this study was designed to determine the characteristics and outcome of traumatic DAI in correlation to Marshall, Rotterdam and Adams grading scores.

CT scan Marshall score [8]

The Marshall score of TBI is a CT scan-derived metric using only a few features and has been shown to predict outcomes in patients with TBI.

It places patients into one of six grades (I to VI) of increasing severity based on findings on non-contrast CT scans of the brain. Higher grades have a worse prognosis and survival. It is primarily concerned with two features:

1. Degree of swelling, as determined by midline shift and/or compression of basal cisterns.
2. Presence and size of contusions/hemorrhages referred to as "high or mixed density lesions".

- Diffuse injury I

- no visible intracranial pathology

- Diffuse injury II

- midline shift of 0 to 5 mm
- basal cisterns remain visible
- no high or mixed density lesions $>25 \text{ cm}^3$

- Diffuse injury III (swelling)

- midline shift of 0 to 5 mm
- basal cisterns compressed or completely effaced
- no high or mixed density lesions $>25 \text{ cm}^3$

- Diffuse injury IV (shift)

- midline shift $>5 \text{ mm}$
- no high or mixed density lesions $>25 \text{ cm}^3$

- Evacuated mass lesion V

- any lesion evacuated surgically

- Non-evacuated mass lesion VI

- high or mixed density lesions $>25 \text{ cm}^3$

- not surgically evacuated

CT scan Rotterdam grade [9]

A more recent system attempts to address some of the recognized limitations of the Marshall system, such as struggling to classify patients who have injuries of multiple types.

It includes four independently graded elements. Like the Marshall system, it includes:

1. Degree of basal cistern compression.
2. Degree of midline shift.

However, it does not include contusions but rather restricts mass lesions to epidural, intraventricular, and subarachnoid hematomas.

Each of these is given a grade, and these grades are tallied, with the addition of 1 to the total. In other words, a completely normal-appearing scan has a Rotterdam grade of 1, and the worse possible Grade is 6, which makes it comparable to the Marshall system:

- basal cisterns

- 0: normal
- 1: compressed
- 2: absent

- midline shift

- 0: no shift or $\leq 5 \text{ mm}$
- 1: shift $>5 \text{ mm}$

- epidural mass lesion

- 0: present
- 1: absent

- intraventricular blood or traumatic SAH

- 0: absent
- 1: present

MRI Adams grade [10, 11]

A classification based on MRI findings proposed in 1989.

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- Grade 1 (lobar): diffuse axonal injury lesions confined to the lobar white matter, especially grey-white matter junction
 - most common sites: parasagittal regions of frontal lobes, periventricular temporal lobes
 - less common sites: parietal and occipital lobes, internal and external capsules, cerebellum
- Grade 2 (callosal): diffuse axonal injury lesions in the corpus callosum, almost invariably in addition to the lobar white matter
 - most common sites: posterior body and splenium of the corpus callosum
 - less common sites: anterior body and rostrum of corpus callosum (usually in conjunction with posterior involvement)
 - usually unilateral and eccentric but may be bilateral and symmetric
- Grade 3 (brainstem): diffuse axonal injury lesions in the brainstem, almost invariably in addition to the lobar white matter and corpus callosum
 - most common sites: dorsolateral midbrain, upper pons, and superior cerebellar peduncles

Methods

This was a retrospective cross-sectional study, with data collected from the medical records of patients with traumatic head injury who were admitted between 2017 and 2020 at a tertiary care hospital, in the southern region of Saudi Arabia. This study was approved by Ethics and Internal Review Board at Aseer Central Hospital with approval number: 20200410 On April 15, 2022.

Patients eligible for inclusion in the study had to have a history of TBI with Glasgow Coma Scale (GCS) grades of ≤ 14 at admission, aged more than 14 years, and had a computed tomography (CT) scan or MRI of DAI. The study criteria excluded patients who had Traumatic head Injury with mass lesions in the brain, who had psychiatric disorders, and patients who were younger than 14 years.

Data regarding age, gender, cause of trauma, associated brain findings, and outcome according to gender, year of admission, Rotterdam CT score, Marshal CT score, and MRI Adams grade were collected and analyzed. To exclude inter-observer variations, all CT and MRI scans were reported by one radiologist with 15 years of post-board experience.

Statistical analysis

After data were extracted, it was revised, coded, and fed to statistical software IBM SPSS version 22 (SPSS, Inc. Chicago, IL). All statistical analysis was done using two-tailed tests. A *P*-value of less than 0.05 was considered to be statistically significant.

Results

The study included 33 DAI patients whose ages ranged from 15 to 60 years (15-25 years: [17 cases = 52%], 26-36 years: [11 cases = 33%], above 36 years: [5 cases = 15%]) with majority of patients being males (30 case = 91%) with 3 females (9%). Number of admission cases per year was 15, 10, 7 and 1, in 2017, 2018, 2019, and 2020, respectively. Causes of trauma were road traffic accidents (RTA) (31 cases = 94%) and fall from height (2 cases = 6%). Regarding outcome, twenty-one patients (64%) improved (discharged home) [19 males, 2 females], 6 (18%) patients transferred to a peripheral hospital for long term nursing care [6 males, 0 females] while 6 (18%) patients expired [5 males, 1 female]. **Table 1.**

Description of CT findings associated with DAI is shown from higher incidence to the lower in **Table 2.** They include: brain contusion [27 cases = 81.81%], subarachnoid hemorrhage (SAH) [22 cases = 66.66%], intracerebral hemorrhage [14 cases = 42.42%], subdural hemorrhage (SDH) [10 cases = 30.30%], brain herniation [9 cases = 27.27%], extradural hemorrhage (EDH) [6 cases = 18.18%], brainstem injury [6 cases = 18.18%], pneumoencephalus [5 cases = 15.15%], hydrocephalus [2 cases = 6.06%] and cerebellar injury [1 case = 3.03%].

CT scan Marshal Grade showed the highest distribution in grade III [15 cases = 45.45%] followed by [9 cases = 27.27%], [4 cases = 12.12%], [3 cases = 9.1%], [1 case = 3%] and [1

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Table 1. Descriptive statistics

Variables	Number	%
Age (in years)		
15-25	17	52%
26-36	11	33%
Above 36	5	15%
Gender		
Male	30	91%
Female	3	9%
Year of admission		
2017	15	45.45%
2018	10	30.30%
2019	7	21.21%
2020	1	3.03%
Cause of trauma		
RTA	31	94%
Fall from height	2	6%
Outcome		
Improved	21	64%
Male	19	
Female	2	
Transferred	6	18%
Male	6	
Female	0	
Expired	6	18%
Male	5	
Female	1	

Table 2. Description of CT findings associated with DAI

Variable	Number	%
Brain contusion	27	81.81%
Subarachnoid hemorrhage	22	66.66%
Intracerebral hemorrhage	14	42.42%
Subdural hemorrhage	10	30.30%
Brain herniation	9	27.27%
Extradural hemorrhage	6	18.18%
Brainstem injury	6	18.18%
Pneumocephalus	5	15.15%
Hydrocephalus	2	6.06%
Cerebellar injury	1	3.03%

case = 3%] in grades II, VI, I, IV and V respectively. Similarly, CT scan Rotterdam grade showed the highest distribution in grade IV: [15 cases = 45.45%] followed by Grade VII [8 cases = 24.24%], grade III [6 = 18.18%], grade V [2 cases = 6.06%] then grades 1 and VI [1 case for each = 3.03%]. MRI was done only in

Table 3. CT scan Marshal and Rotterdam and MRI Adams grading: No. and %

Variable	Number	%
CT scan Marshal Grade		
Grade I	3	9%
Grade II	9	27%
Grade III	15	46%
Grade IV	1	3%
Grade V	1	3%
Grade VI	4	12%
CT scan Rotterdam Grade		
Grade I	1	3%
Grade II	8	24%
Grade III	6	18%
Grade IV	15	46%
Grade V	2	6%
Grade VI	1	3%
MRI Adam grading		
No MRI done	7	21%
Grade I	3	9%
Grade II	14	43%
Grade III	9	27%

26 cases (78, 78%), and MRI Adams grade showed the highest distribution in Grade II [14 cases, 42.42%] followed by Grade III [9 cases, 27.27%] and then Grade I [3 cases, 9.09%], shown in **Table 3**. No significance was detected for the patient's outcome in relation to CT scan Marshal Grade ($P = 0.337$), CT scan Rotterdam Grade ($P = 0.148$), and MRI Adam grade ($P = 0.167$). **Table 4**.

A one-way ANOVA was performed to compare the effect of the independent variables on the dependent variable; for Marshal grade. It revealed that there was a statistically significant difference in Marshal grade and brain contusion ($F = 6.089$, $P = 0.001$), pneumocephalus ($F = 8.209$, $P = 0.000$), Rotterdam grade ($F = 21.982$, $P = 0.000$) and MRI Adam grade ($F = 3.796$, $P = 0.010$). On the other hand, no statistical significant difference was detected in Marshal grade and age ($F = 0.21$, $P = 0.959$), SAH ($F = 2.591$, $P = 0.49$), intracerebral hemorrhage ($F = 2.53$, $P = 0.53$), SDH ($F = 1.457$, $P = 0.237$), brain herniation ($F = 2.33$, $P = 0.70$), EDH ($F = 0.781$, $P = 0.572$), brainstem injury ($F = 1.797$, $P = 0.147$), Hydrocephalus ($F = 0.627$, $P = 0.681$), cerebellar injury ($F = 0.21$, $P = 0.959$). **Table 5**.

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Table 4. Patient's outcome in relation to CT scan Marshal, Rotterdam, and MRI Adam grading

Variable	Outcome		
	Improved: No. & % within the Grade, % of total patients	Transferred: No., % within the Grade, % of total patients	Expired: No., % within the Grade, % of total patients
CT scan Marshal Grade			
Grade I	1, 33.3%, 3%	0, 0%, 0%	2, 66.6%, 6%
Grade II	7, 77.77%, 21%	1, 11.11%, 3%	1, 11.11%, 3%
Grade III	10, 66.66%, 30%	3, 20%, 9%	2, 13.33%, 6%
Grade IV	1, 100%, 1%	0, 0%, 0%	0, 0%, 0%
Grade V	0, 0%, 0%	1, 100%, 3%	0, 0%, 0%
Grade VI	2, 50%, 6%	1, 25%, 3%	1, 25%, 3%
CT scan Rotterdam Grade			
Grade I	0, 0%, 0%	0, 0%, 0%	1, 100%, 3%
Grade II	6, 75%, 18%	0, 0%, 0%	2, 25%, 6%
Grade III	4, 66.7%, 12%	2, 33.3%, 6%	0, 0%, 0%
Grade IV	9, 60%, 27%	4, 26.7%, 12%	2, 13.3%, 6%
Grade V	2, 100%, 6%	0, 0%, 0%	0, 0%, 0%
Grade VI	0, 0%, 0%	0, 0%, 0%	1, 100%, 0%
MRI Adam grading			
No MRI done	4, 57.14%, 12%	0, 0%, 0%	3, 42.86%, 9%
Grade I	3, 100%, 9%	0, 0%, 0%	0, 0%, 0%
Grade II	8, 57.14%, 24%	5, 35.71%, 15%	1, 7.15%, 3%
Grade III	6, 66.66%, 18%	1, 11.11%, 3%	2, 22.22%, 6%

Similarly, one-way ANOVA revealed that there was a statistically significant difference in Rotterdam grade and age ($F = 2.918$, $P = 0.031$), brain contusion ($F = 3.637$, $P = 0.012$), SAH ($F = 3.881$, $P = 0.009$), SDH ($F = 3.089$, $P = 0.025$), brain herniation ($F = 2.10$, $P = 0.028$), EDH ($F = 0.899$, $P = 0.496$), pneumocephalus ($F = 2.410$, $P = 0.063$), Hydrocephalus ($F = 5.470$, $P = 0.001$) and MRI Adam grade ($F = 2.678$, $P = 0.043$). On the other hand, no statistical significant difference was detected in Rotterdam grade and intracerebral hemorrhage ($F = 1.926$, $P = 0.123$), brainstem injury ($F = 2.321$, $P = 0.071$), cerebellar injury ($F = 0.884$, $P = 0.505$). **Table 5.**

Last of all, one-way ANOVA revealed that there was a statistically significant difference in MRI Adam grade and cerebellar injury ($F = 4.39$, $P = 0.11$), SAH ($F = 4.72$, $P = 0.008$) and SDH ($F = 5.46$, $P = 0.004$). However, no statistical significant difference was detected in Rotterdam grade and age ($F = 1.392$, $P = 0.265$), brain contusion ($F = 1.921$, $P = 0.148$), intracerebral hemorrhage ($F = 0.393$, $P = 0.759$), brain herniation ($F = 0.139$, $P = 0.936$), EDH ($F = 0.433$,

$P = 0.731$), brainstem injury ($F = 0.714$, $P = 0.552$), pneumocephalus ($F = 0.505$, $P = 0.682$), Hydrocephalus ($F = 0.504$, $P = 0.683$).

Table 5.

Discussion

The objective of our study was to focus on DAI, appraise the outcome and describe associated brain CT findings, categorize CT scan Marshal and Rotterdam scores and MRI Adams grading and find out any possible association between brain CT findings and different grading systems in DAI patients from a tertiary hospital in KSA.

The majority of our patients (30 patients, 91%) were males, similar to previous studies that found (70 patients, 89.7% [7]), (101 patients = 94.4% [12]), (97 patients, 72.9%) [13] that most of their patients were males. The younger population was more affected in our study, with 52% being between 15 and 25 years of age. Similar statistics for age were seen in other studies, with 43.6% [7], 48.59% [12], and 45.1% [13] being between the ages of 18 and 30 years.

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Table 5. One-way ANOVA: DAI grades versus other variables

Variable	ANOVA (CT Marshal grade versus other variables)		ANOVA (CT Rotterdam Grade versus other variables)		ANOVA (MRI Adam grade versus other variables)	
	F	P	F	P	F	P
Age	0.21	0.959	2.918	0.031*	1.392	0.265
Brain contusion	6.089	0.001*	3.637	0.012*	1.921	0.148
Subarachnoid hemorrhage	2.591	0.49	3.881	0.009*	4.72	0.008*
Intracerebral hemorrhage	2.53	0.53	1.926	0.123*	0.393	0.759
Subdural hemorrhage	1.457	0.237	3.089	0.025*	5.46	0.004*
Brain herniation	2.33	0.70	2.10	0.028*	0.139	0.936
Extradural hemorrhage	0.781	0.572	0.899	0.496*	0.433	0.731
Brainstem injury	1.797	0.147	2.321	0.071	0.714	0.552
Pneumocephalus	8.209	0.000*	2.410	0.063	0.505	0.682
Hydrocephalus	0.627	0.681	5.470	0.001*	0.504	0.683
Cerebellar injury	0.21	0.959	0.884	0.505	4.39	0.11*

*diffuse axonal injury grades versus age and other radiological finding.

In our study, the most prevailing cause of DAI was RTA (94%), while fall from height accounted only for 6%. Similarly, previous studies [5, 7, 13] found RTA to account for a high percentage of DAI (83.8%, 60%, and 51.9% respectively). This may be due to the high incidence of the shearing forces associated with RTA as brain movement lags behind skull movement with subsequent tearing of the nerve axons and disruption of nerve communication [14].

The greater percentage of our studied patients improved (64%) with no association seen between gender distribution and outcome of DAI, similar to previous studies [7, 13]. There was a significant decrease in the number of TBI and hence DAI cases in the year 2020 compared to the previous three years investigated in our study. This may be attributed to the international lockdown due to the SARS COV2 pandemic (COVID-19) with a decline of RTA [15].

DAI describes multifocal brain damage, hemorrhagic and/or non-hemorrhagic, predominantly affecting gray-white matter junction resulting from axonal stretch and/or shear strain due to rotation and/or acceleration-deceleration forces in the frontal lobes (as the rotational axis of the head is posterior, hence creating higher anterior momentum), corpus callosum, internal capsules, thalamus, midbrain and/or pons [16-18].

DAI findings depicted on CT or MR images are the signpost revealing underlying axonal injury

[19, 20]. Conversely, cognitive and neurological impairment due to DAI is, sometimes, disproportionate to the CT brain imaging abnormalities [21]. On CT, identification of DAI is dependent upon the presence of foci of hemorrhage at the sites of white matter bundles within the cerebrum and brainstem [22, 23]. Our study showed that most CT findings associated with DAI were brain contusion (81.8%) (**Figure 1A**), subarachnoid hemorrhage (66.66%), intracerebral hemorrhage (42.42%), subdural hemorrhage (30.30%), brain herniation (27.27%), extradural hemorrhage (18.18%), brainstem injury (18.18%), pneumocephalus (15.15%), hydrocephalus (6.06%), and cerebellar injury (3.03%). The fraction of the different CT brain findings in our study is not uniform with previous studies [16, 24-27], but the percentage of DAI cases was still comparable with those studies. This may be attributed to the wide variety of brain injuries that can cause DAI and due to different patterns of TBI between different study populations. Still, it was shown that some brain findings on CT are correlated well with DAI, such as midline SAH (61% sensitivity and 82% specificity) [16], with significant progression of contusions [28], and intraventricular hemorrhage (with univariate and multivariate odds ratios of 3.7 and 4.2) [29].

Detection of no significance non-contrast brain CT imaging is the cornerstone of initial investigation following TBI [16], while DAI is poorly identified with this modality, especially in non-hemorrhagic lesions, and is only able to detect

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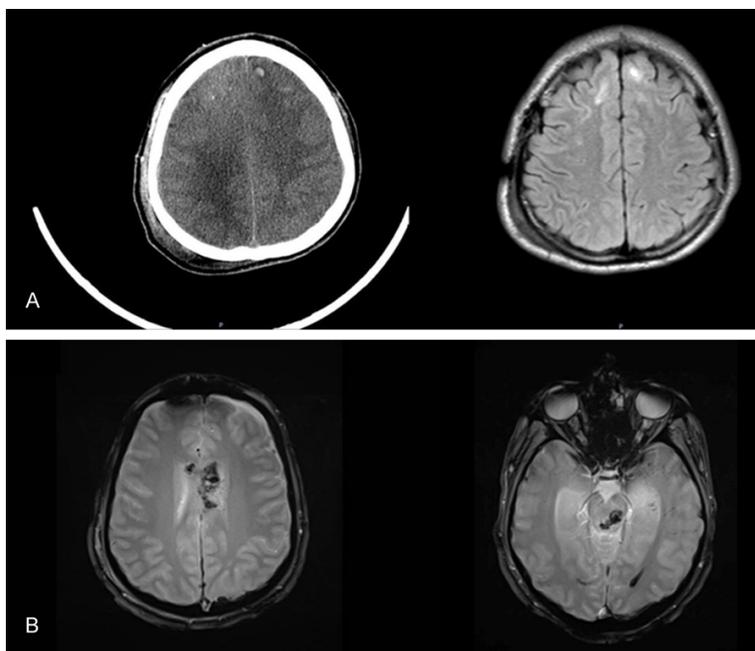


Figure 1. A: CT and MRI showed diffused axonal injury with hemorrhagic contusions at the grey-white matter junction. B: Gradient echo MRI showing the effect of hemosiderin deposition in the corpus callosum and midbrain (Adams grade 3).

19% of such lesions, compared to 92% using MRI (**Figure 1B**) [30]. On the other hand, although brain MRI imaging serves as the best imaging modality for DAI detection [31], the time frame for its execution delays its utilization, particularly in ventilated sick patients [32]. Also, notably, it should be renowned that even with modern MRI scanners, the absenteeism of DAI signs does not unconditionally exclude the presence of axonal injury. So, CT remains the first available imaging choice for assessment of TBI and prediction of the outcome [33, 34]. Previous studies [35-37] showed that the Marshall score is worthy in predicting the outcome, but the Rotterdam score with its individual CT parameters was shown to surpass it due to its incorporation of individual CT parameters underlying the CT classification [38]. Our results, are in contrast to those previous studies, and show no apparent association between Marshall, Rotterdam, and MRI Adams scores with mortality rate.

We used the One-Way ANOVA to compare the means of Marshall, Rotterdam, and MRI Adams grades with each other as well as with age and different brain lesions. The Rotterdam Grade was correlated with more variables (age, brain

contusion, subarachnoid hemorrhage, Intracerebral hemorrhage, subdural hemorrhage, Brain herniation, extradural hemorrhage, and hydrocephalus) compared to Marshall Grade (brain contusion and pneumocephalus) and to Adam MRI grade (Subarachnoid hemorrhage, Subdural hemorrhage, Cerebellar injury). This correlation analysis is heterogeneous between different studies [26, 39-43] and therefore confusing. This may be partially illuminated if we think it through, that DAI occurs mainly due to the forces associated with rapid acceleration-deceleration rather than to the direct impact on the brain itself [44]. The CT findings correlated with DAI are characteristically limited to microhemorrhages within the subcortical and cerebral

white matter (Grade I), corpus callosum (Grade II), and brainstem (Grade III) [45]. Accordingly, patients with DAI might have cognitive impairment that looks disproportionate to the imaging lesions shown on CT [16]. On the other hand, MRI grading is more sensitive than CT in visualizing microscopic amounts of blood-related to DAI [46] and it may have a good future role in predicting the length of coma in DAI patients [47, 48].

Our study demonstrated a correlation between Marshall, Rotterdam, and MRI Adams grades. Although Marshall CT grading has strong predictive power, greater discrimination (and hence more strong correlation) is obtained when the individual CT parameters are included in the Rotterdam score model [38]; however, MRI grading was shown to be a better predictor of neurological outcome in DAI compared to the CT obtained grading. Indeed, conventional Brain MRI has low resolution and can only detect DAI in approximately half of DAI cases [51] as 80% of DAI lesions are microscopic or nonhemorrhagic [52, 53]. By contrast, diffusion tensor imaging (DTI) has been shown to have higher sensitivity for the detection of DAI lesions than that of conventional brain MRI

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[54, 55]. Furthermore, diffusion tensor tractography, which is a derivative of DTI, enables three-dimensional (3-D) visualization and estimation of specific neural tracts with the advantage that the characteristics of an entire neural tract can be determined and analyzed providing marked improvements in detecting the site and extent of DAIs within the examined tracts [55, 56]; however, studies to launch DTI-based diagnostic criteria for DAI are required.

There are some limitations to our study. First, our cohort does not represent the pediatric population who may have TBI and be imperiled to DAI. In addition, our sample is only representative of one tertiary hospital in the southern region of KSA, with a relatively small number of included patients. Further similar multicenter studies that include pediatric patients are warranted to obtain more visible and comprehensive results. Afterward, with the retrospective design of our study, we were not capable of controlling the timing, as well as the technical specifications of the CT and MRI scan. However, we do not expect slight variations in the timing of CT and MRI to have a significant impact on our used grading systems, given the stability of DAI imaging studies.

Conclusion

Road traffic accidents account for a high percentage of DAI among young males (15-25 years), while a high rate of our studied population improved (64%). No detected significance was found for the patient's mortality outcome concerning CT scan Marshal score, CT scan Rotterdam score, and MRI Adams grade.

Disclosure of conflict of interest

None.

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