Original Article

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Surgery Section

Predictive Value of CT Perfusion Parameters in Traumatic Brain Injury Patients: A Longitudinal Study

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ABSTRACT

Introduction: Traumatic Brain Injury (TBI) is the most common cause of mortality and morbidity worldwide. Moreover, cerebral contusions, Subdural Haemorrhages (SDH), Extradural Haemorrhages (EDH), and Subarachnoid Haemorrhage (SAH), which are secondary injuries that occur due to alterations in cerebral haemodynamics, remain unevaluated and unchecked by plain non contrast scans. Timely delineation of the cerebral perfusion status of the patient can assist in modifying treatment plans and could lead to a better recovery of the patient.

Aim: To assess the cerebral haemodynamics of patients with TBI at admission and evaluate the predictive value of Computed Tomography (CT) perfusion.

Materials and Methods: The present prospective longitudinal study was conducted in the Department of Radiodiagnosis and Neurosurgery, Jawaharlal Nehru Medical College and Hospital (JNMCH), Aligarh Muslim University (AMU), Aligarh, Uttar Pradesh, India, from September 2019 to September 2020. A total of 40 participants were included in the study using a purposive sampling method. CT Perfusion (CTP) was performed within 72 hours of head injury, followed by Glasgow Outcome at Discharge Scale (GODS) assessments at discharge and one month later. Cerebral perfusion parameters such as Cerebral Blood Flow (CBF), Cerebral Blood Volume (CBV), Mean Transit Time (MTT), and Time To Peak (TTP) were measured, and correlations were established using Spearman's rank correlation coefficients to determine the relationship of GODS with CTP parameters.

Results: The mean age of study subjects was 35.8±13.4 years, with a median (25^{th}-75^{th} percentile) of 32 (25-42.75). Among a total of 40 patients, 22 (55%) were males and 18 (45%) were females. Significant positive correlations were observed between GODS at discharge and CBF (mL/100 gm/min) at presentation, CBV (mL/100 gm/min) at presentation, and the number of normal/hyperemic territories, with correlation coefficients of 0.398, 0.329, and 0.504, respectively. A significant negative correlation was found between GODS at discharge and TTP (seconds) at presentation, with a correlation coefficient of -0.392. Similarly, significant positive correlations were observed between GODS at one month with CBF (mL/100 gm/min) at presentation and the number of normal/hyperemic territories, with correlation coefficients of 0.407 and 0.827, respectively. A significant negative correlation was seen between GODS at one month and MTT (seconds) at presentation, with a correlation coefficient of -0.344. CBV (mL/100 gm/min) at presentation exhibited a sensitivity of 100%, followed by MTT (seconds) at presentation (71.43%), and CBF (mL/100 gm/min) at presentation (57.14%). Conversely, CBF (mL/100 gm/min) at presentation showed a specificity of 92.31%, followed by TTP (seconds) at presentation (92.31%), and CBV (mL/100 gm/min) at presentation (53.85%). In predicting unfavourable outcomes, MTT (seconds) at presentation had the lowest specificity of 7.69%.

Conclusion: Perfusion CT provides additional information compared to Non Contrast Computed Tomography (NCCT) with insights into the pericontusional areas. Therefore, it can be a potential tool in the evaluation of TBI. Perfusion parameters have prognostic value, and thus, this modality should be studied with a larger sample size for more precise results.

Keywords: Cerebral blood flow, Cerebral blood volume, Computed tomography, Glasgow outcome at discharge scale, Mean transit time

INTRODUCTION

A sudden trauma can lead to brain damage, causing a type of acquired brain injury called TBI. TBI can occur as a result when an object brutally and abruptly hits the head or an object punctures the skull and then enters the brain tissue. The Centre for Disease Control and Prevention (CDC) describes TBI as a penetrating head injury or a disturbance in the normal brain function that results from a jolt, bump, or blow to the head [1]. In developed countries, the incidence of TBI is noted to be around 200 per 100,000 population every year [2]. Every year in India, around 1.5-2 million people meet with traumatic injuries, and about one million succumb to death. The leading cause of TBIs is road traffic injuries (60%), followed by injuries due to falls (20%-25%) and violence (10%) [3]. In approximately, 15%-20% of TBIs, alcohol is found to be the etiological factor [3]. The pathogenesis of TBI is an intricate process, which is the result of primary and secondary injuries, causing either permanent or temporary neurological loss. The primary injury is directly linked to the external impact on the brain, whereas the secondary deficit can occur after a few minutes to days after the primary impact. The secondary injury incorporates chemical, molecular and inflammatory cascades that can lead to cerebral damage in the future [4].

Non Contrast CT (NCCT) has emerged as one of the most frequently used imaging technologies for assessing TBI, as it easily identifies fractures related to traumatic injuries, intracranial injuries and swellings, haemorrhage, collections of extra-axial fluid and radio-opaque foreign objects [5]. There is agreement and verification that NCCT is the first diagnostic imaging method for patients with acute or moderate to severe TBI [5]. Recent neuroimaging advances have shown promising results in the evaluation of TBI. One of them is perfusion CT.

Perfusion CT provides easily accessible methods to assess brain vascular status and, by calculating MTT, CBV, and CBF for various

areas, can recognise areas of abnormal anointing and ischaemia [6]. In patients with severe TBI, the perfusion image provides insight into regional brain changes due to TBI, with great benefit in detecting regional trends [7]. To the best of the authors knowledge, only limited studies are available that utilised and compared CTP parameters with clinical outcomes in patients of the Indian subset population. Thus, the present study was conducted to demonstrate how cerebral perfusion CT of the brain can provide additional information in head injury patients to predict their functional outcome.

MATERIALS AND METHODS

The present prospective longitudinal study was conducted in the Department of Radiodiagnosis and Neurosurgery, Jawaharlal Nehru Medical College and Hospital, AMU, Aligarh, Uttar Pradesh, India, from September 2019 to September 2020. Permission from the Institutional Ethics Committee was obtained before the start of the study (D.No.133/FM/IEC). The study population consisted of individuals aged over 18 years with complaints of significant head injury and reduced Glasgow Coma Scale (GCS) scores who underwent NCCT at admission. A purposive sampling method was used, and a total of 40 participants were included in the study.

Inclusion criteria: Patients aged >18 years and <60 years who presented to JNMCH with traumatic head injuries were included in the study. The screening of patients was conducted by Neurosurgery resident doctors on duty, and those with GCS scores less than 13 were referred for imaging to the Radiology Department for NCCT scan and CTP brain were included in the study.

Exclusion criteria: Patients with intoxication, abnormal renal function tests, pregnant women, known allergies to contrast media, patients requiring General Anaesthesia (GA) or difficult examinations, and patients with other significant systemic injuries such as Blunt Trauma Abdomen (BTA), Blunt Trauma Chest (BTC) were excluded from the study.

Study Procedure

Computed tomography perfusion was performed in cine mode within 72 hours of admission on a 128-slice CT scanner (Revolution EVO 128, GE Healthcare, USA). Patients were positioned supine with proper body immobilisation. A power injector was used for contrast administration. Initially, an unenhanced CT was performed with 5 mm thick transverse sections using technical parameters of 120 KVp and 200 Mas. Perfusion CT was then performed immediately after the NCCT.

During intravenous contrast administration, a 40-second series of 40 gantry rotations at a rate of one rotation per second was performed in cine mode. For perfusion CT, the acquisition conditions were 80 KVp and 100 mAs. The scan was started five seconds after a power injector (MEDRAD® Salient, Bayer AG, Germany) injected 40 mL of iodinated contrast material (Iohexol; 300 mg/mL of iodine) into the antecubital vein at a rate of 4-4.5 mL/sec, followed by a 20 mL saline chase. Four 5 mm slices were taken above the orbit in the direction of the vertex, paired with similar regions of CT that were not enhanced.

The CTP parameters were calculated using commercially available post-processing software platforms provided by GE Medical Systems. It includes CBF, CBV, MTT, and TTP. On perfusion CT postprocessing colour maps, absolute values of CBV, CBF, MTT, and TTP were recorded in the pericontusional area by drawing Region of Interest (ROI) circles of approximately 15×15 mm to determine the presence and absence of ischaemia. For descriptive purposes, the cut-off values for ischaemia were set at 20 mL/100 gm/min for CBF and 2 mL/100 gm/min for CBV, while it was eight seconds for MTT. Additionally, qualitative analysis was conducted through visual assessment of colour maps to determine the presence of territories showing overall normal or increased perfusion, recorded on a scale of 0 to 6. Clinical data of the patients were prospectively collected from the Department of Neurosurgery. GCS was recorded at presentation and at discharge [8]. The pattern of injury was noted, and the presence or absence of mass effect was evaluated.

Furthermore, using the Glasgow Outcome Discharge Score (GODS) v6/12/12, the neurosurgeon recorded the patient's functional outcome at discharge and at the one-month follow-up. Patient status was assessed on a scale of 8, and for the study's purposes, patients were categorised into two groups: Favourable outcome with a GODS score of 5-8 and unfavourable outcome with GODS scores of 1-4, representing good and limited recovery, respectively [Table/Fig-1]. As the Glasgow Outcome Scale Extended (GOSE) has the same description as GODS, the GODS at discharge scale was used to assess functional outcomes [9].

GODS score	Description
01	Dead
02	Not conscious
03	Lower severe disability
04	Upper severe disability
05	Lower moderate disability
06	Upper moderate disability
07	Lower good recovery
08	Upper good recovery

[Table/Fig-1]: Glasgow Outcome at Discharge Scale (GODS) (v6/12/12).

STATISTICAL ANALYSIS

Categorical variables were presented as numbers and percentages, while continuous data were reported as mean±SD (Standard Deviation) and as median with 25th and 75th percentiles (interquartile range). The normality of the data was verified using the Kolmogorov-Smirnov test. Spearman's rank correlation coefficient was used to determine the correlation of GODS with CTP parameters. The receiver operating characteristic curve was employed to find the cut-off values of CTP parameters at presentation for predicting unfavorable outcomes.

RESULTS

Total of 58 subjects were initially enrolled in the study, out of which 18 subjects were excluded from the final analysis group due to various exclusion factors. Among the 40 patients included, 22 (55%) were males and 18 (45%) were females. The mean age of the study subjects was 35.8±13.4 years, with a median (25th-75th percentile) of 32 (25-42.75). The mode of injury for the majority of patients (95%) was Road Traffic Accidents (RTA), while assault was the mode of injury in only two out of 40 patients (5%).

Out of 40 patients at one month of follow-up using GODS/GOSE, 14 patients had limited recovery, whereas 26 patients had good recovery. However, at the time of discharge, only two out of 40 patients had GODS ≥5. The mean value of GODS at one month of the study was 4.55±2.01 with a median (25th-75th percentile) of 5.5 (3.75-6). Various descriptive values of perfusion parameters are shown in [Table/Fig-2].

CT Perfusion (CTP) parameters at presentation	Mean±SD	Median (25th-75th percentile)
Cerebral Blood Flow (CBF) (mL/100 gm/min)	14.69±12.91	10.7 (7.475-14.775)
Cerebral Blood Volume (CBV) (mL/100 gm/min)	1.25±0.53	1.2 (0.9-1.425)
Mean Transit Time (MTT) (seconds)	7.54±3.61	6 (5.125-10.475)
Time To Peak (TTP) (seconds)	13.88±2.41	13.95 (12.275-14.775)

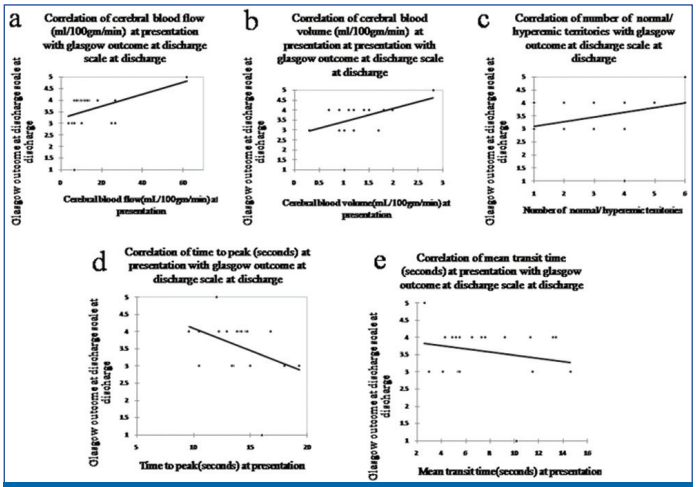
[Table/Fig-2]: The descriptive statistics of CT Perfusion (CTP) parameters at presentation of study subjects at presentation.

In the present study, 12 (30%) patients had normal/hyperemic territories; four in four territories patients, three territories in eight (20%) patients, five territories in six (15%) patients and six territories in six (15%) patients. The number of normal/hyperemic territories was 1 and 2 in only four patients each (10%).

A significant positive correlation was seen between GODS at discharge with CBF (mL/100 gm/min) at presentation, CBV (mL/100 gm/min) at presentation, and the number of normal/hyperemic territories with a correlation coefficient of 0.398, 0.329, and 0.504, respectively [Table/Fig-3,4a-e].

Variables	Cerebral Blood Flow (CBF) (mL/100 gm/min) at presentation	Cerebral Blood Volume (CBV) (mL/100 gm/min) at presentation	Mean Transit Time (MTT) (seconds) at presentation	Time To Peak (TTP) (seconds) at presentation	Number of normal/ hyperemic territories at presentation
Glasgow Outcome at Discharge Scale (GODS) at discharge					
Correlation coefficient	0.398	0.329	-0.126	-0.392	0.504
p-value	**0.012**	**0.038**	0.436	**0.013**	**0.001**

[Table/Fig-3]: Correlation of Glasgow Outcome at Discharge Scale (GODS) at discharge with CT perfusion parameters.
The p-value in bold font indicates statistically significant value



[Table/Fig-4]: Correlation of different perfusion parameters at presentation with Glasgow outcome at discharge scale at discharge.

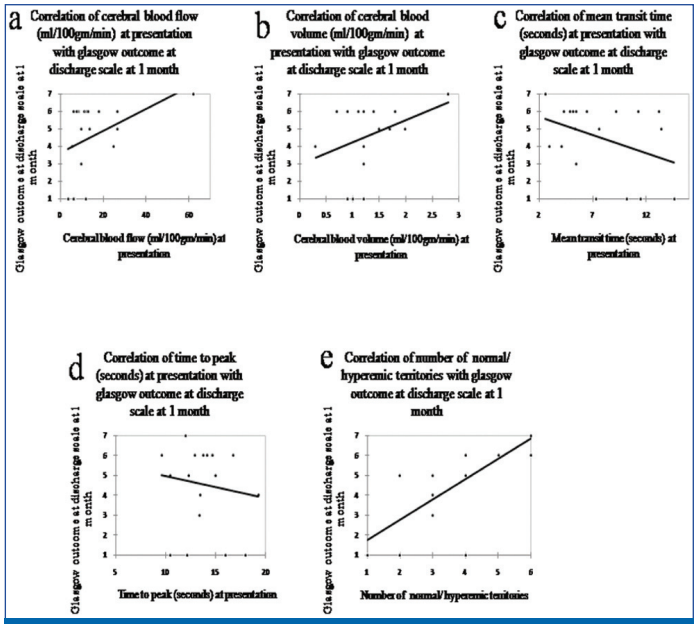
A significant positive correlation was seen between GODS at one month with CBF (mL/100 gm/min) at presentation and the number of normal/hyperemic territories at presentation with correlation coefficients of 0.407 and 0.827, respectively. A significant negative correlation was seen between GODS at one month and MTT (seconds) at presentation with a correlation coefficient of -0.344 [Table/Fig-5,6a-e].

Variables	Cerebral Blood Flow (CBF) (mL/100 gm/min) at presentation	Cerebral Blood Volume (CBV) (mL/100 gm/min) at presentation	Mean Transit Time (MTT) (seconds) at presentation	Time To Peak (TTP) (seconds) at presentation	Number of normal/ hyperemic territories at presentation
Glasgow Outcome at Discharge Scale (GODS) at 1 month					
Correlation coefficient	0.407	0.199	-0.344	-0.083	0.827
p-value	**0.010**	0.218	**0.030**	0.610	**<0.0001**

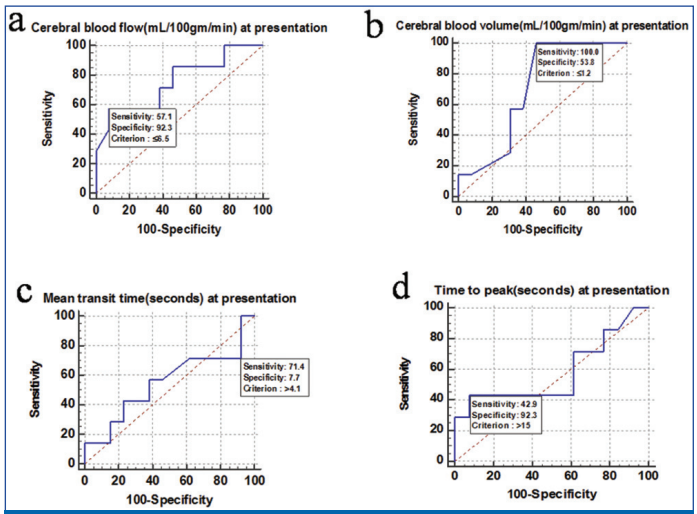
[Table/Fig-5]: Correlation of Glasgow Outcome at Discharge Scale (GODS) at one month with CT Perfusion (CTP) parameters.

Receiver Operating Curves (ROC) were also generated to determine the cut-off of a variety of parameters to predict an unfavorable outcome. Above the diagonal line, ROC curves are thought to have a decent discriminating capacity to forecast an undesirable outcome. The discriminatory power of CBF (mL/100 gm/min) at presentation (AUC 0.753; 95% CI: 0.591 to 0.875) and CBV (mL/100 gm/min) at presentation (AUC 0.703; 95% CI: 0.538 to 0.837) was acceptable [Table/Fig-7a-d].

CBV (mL/100 gm/min) at presentation had a sensitivity of 100%, followed by MTT (seconds) at presentation (71.43%) [Table/Fig-3c], CBF (mL/100 gm/min) at presentation (57.14%). On the other hand,



[Table/Fig-6]: Correlation of different perfusion parameters at presentation with Glasgow outcome at discharge scale at one month.



[Table/Fig-7]: Receiver Operating Curves (ROC) determining the cut-off of a variety of parameters to predict unfavourable outcome.

CBF (mL/100 gm/min) at presentation had a specificity of 92.31%, followed by TTP (seconds) at presentation (92.31%) [Table/Fig-3d], CBV (mL/100 gm/min) at presentation (53.85%). In the prediction of an unfavourable outcome, MTT (seconds) at presentation had the lowest specificity of 7.69%.

The highest Positive Predictive Value (PPV) was found in CBF (mL/100 gm/min) at presentation (80%), and the highest Negative Predictive Value (NPV) was found in CBV (mL/100 gm/min) at presentation (100%) [Table/Fig-8].

Glasgow Outcome at Discharge Scale (GODS) at 1 month	Cerebral Blood Flow (CBF) (mL/100 gm/min) at presentation	Cerebral Blood Volume (CBV) (mL/100 gm/min) at presentation	Mean Transit Time (MTT) (seconds) at presentation	Time To Peak (TTP) (seconds) at presentation
Area under the ROC curve (AUC)	0.753	0.703	0.549	0.577
Standard error	0.0862	0.0822	0.105	0.108
95% Confidence interval	0.591 to 0.875	0.538 to 0.837	0.384 to 0.707	0.411 to 0.731
p-value	**0.0034**	**0.0134**	0.6389	0.4778
Cut-off	≤6.5	≤1.2	>4.1	>15
Sensitivity (95% CI)	57.14% (28.9-82.3%)	100% (76.8-100.0%)	71.43% (41.9-91.6%)	42.86% (17.7-71.1%)
Specificity (95% CI)	92.31% (74.9-99.1%)	53.85% (33.4-73.4%)	7.69% (0.9-25.1%)	92.31% (74.9-99.1%)

PPV (95% CI)	80% (44.4-97.5%)	53.8% (33.4-73.4%)	29.4% (15.1-47.5%)	75% (34.9-96.8%)
NPV (95% CI)	80% (61.4-92.3%)	100% (76.8-100.0%)	33.3% (4.3-77.7%)	75% (56.6-88.5%)
Diagnostic accuracy	80%	70%	30%	75%

[Table/Fig-8]: Receiver operating characteristic curve to find cut-off of CT Perfusion (CTP) parameters at presentation for predicting unfavourable outcome.

DISCUSSION

Perfusion CT provides comparable information to various diagnostic modalities, with added advantages of easy availability, short acquisition time, and low radiation dose [10]. By calculating MTT, CBV and CBF for different areas, perfusion CT offers readily available methods for examining brain perfusion and identifying areas of abnormal perfusion and ischaemia [11]. It has been revealed that CTP has focused on measuring MTT, CBF and CBV, with CBF being observed as the most significant parameter of perfusion that predicts the Glasgow Outcome Score (GOS) [6].

In the present study, a significant positive correlation was observed between GODS at discharge with CBF (mL/100 gm/min) and CBV (mL/100 gm/min) at presentation. Additionally, a significant negative correlation was seen between GODS and TTP (seconds) at presentation.

Wintermark M et al., also assessed unenhanced cerebral CT results and perfusion CT scans in connection to the GOS score at three months [12]. They found that perfusion CT revealed a certain pattern regarding patient outcomes, showing either normal cerebral perfusion or hyperemia in patients with a satisfactory prognosis and oligaemia in patients with an unsatisfactory outcome. The number of arterial territories with low regional CBV on perfusion CT was identified as an independent prognostic factor (p-value=0.008). Other factors such as mean arterial pressure at the scene of the accident (p-value=0.083), base excess at admission (p-value=0.002), the presence of skull fractures (p-value=0.041), and signs of herniation (p-value=0.013) on admission unenhanced cerebral CT were also highlighted. Perfusion CT demonstrates a range of brain perfusion alterations in patients with juxtadural collections, cerebral oedema, or intracranial hypertension.

Bindu TS et al., in a study of mild head injury, observed that a higher CBV/CBF was correlated with a higher GOS [13]. Conducted as the first study in India comparing CTP with GOS in head injury patients, they found these results. In contrast to these studies, the present research correlated the perfusion characteristics of the pericontusional oedema region with the patient's functional scale at discharge as well as at short-term one-month follow-up. Out of all perfusion parameters, CBF and CBV in the pericontusional region and the number of normal/hyperemic territories at presentation were found to have acceptable discriminatory ability in predicting outcomes. It was observed that with higher values of CBV (mL/100 gm/min) at presentation, the risk of an unfavourable outcome significantly decreased.

Limitation(s)

The present study was conducted with a limited sample size. Therefore, future studies are required to include more patients, better stratification of age groups, and an equal distribution of the sex ratio. In the current study, follow-up was conducted for one month, which could be a limitation, as various studies have revealed that a longer follow-up may have shown alterations in GOS. Different influencers of CBF and intracranial pressures include temperature, sedatives and the partial pressure of CO_2 in arterial blood. CTP itself is also susceptible to motion artifacts.

CONCLUSION(S)

It is possible to detect anomalies in individuals with TBI using perfusion CT in conjunction with a normal NCCT at the time of admission. Perfusion anomalies are associated with the severity of injury as measured by the GCS score. In patients with suboptimal outcomes as recorded by the GODS scores, a dramatic decrease in CBF and CBV was observed. Future studies should be conducted to validate the results of the present study and establish the use of perfusion CT methods in TBI. Furthermore, the connection of perfusion CT parameters with neuropsychological data and complaints needs to be thoroughly investigated.

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