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Evaluation of Admission Brain Computed Tomography Findings to Predict the Long-Term Outcomes of Patients with Traumatic Brain Injury

Avaliação de achados em tomografia de crânio admissional para predizer o prognóstico a longo prazo de paciente com trauma cranioencefálico

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Abstract

Objective To evaluate the admission brain computed tomography (CT) scan findings in patients with traumatic brain injury (TBI) in a low- and middle-income country (LMIC) to predict long-term neurological outcomes.

Materials and Methods Patients admitted to a tertiary emergency hospital between March 2017 and April 2018 who had suffered a TBI and had undergone a brain CT scan within 12 hours of the trauma were prospectively evaluated. All of the patients who were hospitalized for at least 24 hours were contacted by phone after 12 months to evaluate their neurological condition.

Results We achieved a 12-month follow-up with 180 patients, most of them male (93.33%). The brain changes identified by CT, such as brain contusion (BC; $p = 0.545$), epidural hemorrhage (EDH; $p = 0.968$) and skull base fracture (SBF; $p = 0.112$) were not associated with worse neurological outcomes; however, subdural hemorrhage (SDH; $p = 0.041$), subarachnoid hemorrhage (SAH; $p \leq 0.001$), brain swelling (BS; $p \leq 0.001$), effacement of cortical sulci (ECS; $p = 0.006$), effacement of basal cisterns (EBC; $p \leq 0.001$), depressed skull fracture (DSF; $p = 0.017$), and a brain midline shift > 5 mm ($p = 0.028$) were associated with worse outcomes.

Keywords
- traumatic brain injury
- computed tomography
- outcome
- developing countries

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Conclusion Findings such as SAH, BS and DSF were independent predictors of worse neurological outcomes. The rate of 70% of patients lost to follow-up shows the difficulties of conducting long-term research in LMICs.

Resumo

Objetivo Avaliar as variáveis de tomografia computadorizada (TC) cerebral admissional em pacientes com trauma cranioencefálico (TCE) em um país de baixa e média renda (PBMR) para prever os resultados neurológicos de longo prazo.

Materiais e Métodos Foram avaliados prospectivamente pacientes admitidos em um hospital terciário de emergência entre março de 2017 e abril de 2018, que sofreram TCE e realizaram tomografia de crânio em até 12 horas após o trauma. Todos os pacientes que permaneceram internados por pelo menos 24 horas foram contatados por telefone após 12 meses para avaliação de sua condição neurológica.

Resultados Conseguimos um acompanhamento de 12 meses com 180 pacientes, a maioria deles do sexo masculino (93,33%). As alterações cerebrais identificadas pela TC, como contusão cerebral (CC; $p = 0{,}545$), hemorragia peridural (HPD; $p = 0{,}968$) e fratura da base do crânio (FBC; $p = 0{,}112$) não foram associadas a piores desfechos neurológicos; no entanto, hemorragia subdural (HSD; $p = 0{,}041$), hemorragia subaracnóidea (HSA; $p \leq 0{,}001$), edema cerebral (EC; $p \leq 0{,}001$), apagamento de sulcos corticais (ASC; $p = 0{,}006$), apagamento de cisternas (AC; $p \leq 0{,}001$), fratura craniana deprimida (FCD; $p = 0{,}017$) e desvio da linha média do cérebro > 5 mm ($p = 0{,}028$) foram associados a piores resultados.

Conclusão Achados como HSA, EC e FCD foram preditores independentes de piores desfechos neurológicos. A taxa de perda de acompanhamento de 70% indica as dificuldades de se conduzir pesquisas de longo prazo em PBMRs.

Palavras-chave
- lesão cerebral traumática
- tomografia computadorizada
- prognóstico
- países em desenvolvimento

Introduction

Traumatic brain injury (TBI) is defined as a change in brain function or other evidence of encephalopathy caused by an external force.[1] These injuries can be caused by a bump, blow, or jolt to the head, or they may be penetrating head injuries that disrupt the normal function of the brain.[2] They represent an important public health problem, and are a significant cause of morbidity and mortality, especially among men and young adults.[3–5] Data from the TBI Model Systems National Data and Statistical Center (TBINDSC) in the United States, show that, in 2017, the cases among male patients greatly outnumbered those among female patients, accounting for more than 73% of all TBIs reported.[6] Patients who survive a moderate to severe TBI often experience a broad spectrum of cognitive and behavioral changes due to diffuse injury. These deficits include slow information processing, as well as impaired long-term memory, attention, functional memory, executive functions, social cognition, and self-awareness.[1]

Upon admission to the hospital, the severity of the TBI is commonly graded according to the Glasgow Coma Scale (GCS), a measure of the level of consciousness. This is purely a descriptive scale; it does not provide any structural information on potential intracranial lesions.[7,8] Due to its accessibility and speed, computed tomography (CT) is the routine imaging modality used to assess structural lesions in acute TBI;[8] it is important in the early identification of patients with significant intracranial damage at risk of deterioration, but CT can also identify lesions that are relevant to the patient's prognosis and rehabilitation but do not necessarily require neurosurgical intervention.[9] Knowledge of the relationship between the clinical signs presented by the patient in the first hours after trauma and the morphological changes identified by brain CT is important for the early diagnosis of TBI; however, CT has to be used with caution due to the increased risk of developing cancer resulting from exposure to ionizing radiation, especially in children.[10]

In 1991, Marshall et al.[11] used tomographic findings to classify patients with TBI. Initially, the purpose of the classification was descriptive; however, it also started to be used as a predictor of mortality. The study[11] used the term *diffuse brain injury*, which was divided into four categories: Marshall I, without any changes on brain CT; and Marshall II, III and IV, with certain degrees of brain damage. In the original study, the authors[11] noticed a direct relationship between the diagnosis of TBI and the mortality rate; however, other studies[12–15] have shown that the status of the basal cisterns, the midline shift, traumatic subarachnoid or intraventricular hemorrhage, and the presence of different types of mass lesions could produce a more accurate prognostic prediction. Other classifications were later created, such as the Rotterdam CT score (2005), which reweighted the components of the Marshall CT classification and added traumatic subarachnoid hemorrhage (tSAH)

and intraventricular hemorrhage, becoming part of the International Mission for Prognosis and Analysis of Clinical Trials in TBI (IMPACT) outcome model for TBI patients.[12,13] More recently, new CT classifications have emerged, including the Stockholm CT score, in 2010,[14] and the Helsinki CT score, in 2014.[15] However, none of these scales have been extensively evaluated.

To objectively assess the functionality of patients with TBI, Jennett and Bond[16] (1975) developed the Glasgow Outcome Scale (GOS),[7,16,17] which was modified over time to provide a more detailed categorization, becoming the Glasgow Outcome Scale-Extended (GOSE),[17,18] a global scale for the functional evaluation of TBI patients.[19]

The purpose of the present study was to evaluate the potential association between morphological brain changes identified through CT and the long-term functional neurological outcomes of patients with TBI.

Materials and Methods

Study Design

We conducted a prospective cohort study of TBI patients admitted to a Brazilian tertiary hospital – Hospital de Urgências de Sergipe Governador João Alves Filho. Patients were recruited between March 2017 and April 2018 and were followed up until 12 months after the injury.

Sample

The study included patients who had suffered a TBI, were referred to the emergency unit to undergo a brain CT scan within 12 hours of the injury, and were then admitted to the hospital for at least 24 hours. After 12 months, we attempted to contact all the patients by phone.

Exclusion Criteria

We excluded patients who: reported or presented CT changes from a previous TBI; had other neurological or neurosurgical conditions, were aged $\leq$ 18 years; did not agree to participate in the study (or whose legal guardian/next of kin did not agree); and had suffered the head trauma more than 12 hours before the Brain CT scan.

Data Collection

All data about the admission brain CT scan were collected during the study period, including the grade on the Marshall classification and 12 radiological variables (brain contusion, epidural hemorrhage, subdural acute hemorrhage, subarachnoid hemorrhage, brain swelling, basal cistern effacement, cortical sulci effacement, brain midline shift $>$ 5 mm, brain midline shift $<$ 5 mm, skull fracture, depressed skull fracture, and skull base fracture). Twelve months later, the patients/next of kin were contacted by phone and assessed through a structured questionnaire to obtain the GOSE score: 1–death; 2–vegetative state; 3–severe disability (low); 4–severe disability (high); 5–moderate disability (low); 6–moderate disability (high); 7–good recovery (low); and 8–good recovery (high). They were then divided into 2 groups: good recovery (GOSE score $\geq$ 7) and poor recovery (GOSE score $<$ 7).

Statistical Analysis

Data were systematized, analyzed, and statistically tested using the IBM SPSS Statistics for Windows (IBM Corp., Armonk, NY, United State) software, version 23.0. The variables were expressed as absolute and relative frequencies, and median, arithmetic mean, and standard deviation (SD) values. The results of interest were analyzed using the Chi-squared (χ^2) test and logistic regression. A multivariate analysis was performed to create a model of the CT variables regarding the functional outcomes at the 12-month follow-up. Values of $p < 0.05$ were considered statistically significant.

Results

From the initial 600 subjects who had suffered a TBI and had undergone CT, we achieved a 12-month follow up with 180 (30%) patients (►**Fig. 1**). Most patients were male (93.3%), with a mean age of 36 (SD: $\pm$ 16.2) years. As aforementioned, the patients were divided into two groups: good recovery (42.7%), defined by a GOSE score $\geq$ 7; and poor recovery (56.3%), defined by a GOSE score $<$ 7 (38.9% had moderate to severe disability, 0.56% were in a vegetative state, and 17.8% had died). At baseline, 168 patients (93.3%) presented pathological findings on the brain CT and 12 (6.7%) prresented completely normal images. Among the patients with TBI-related CT alterations, 99 (58.9%) had a good recovery (GOSE score $\geq$ 7), while 69 patients had disability or death (GOSE score $<$ 7). The distribution of the patients in terms of functionality is shown in ►**Table 1**.

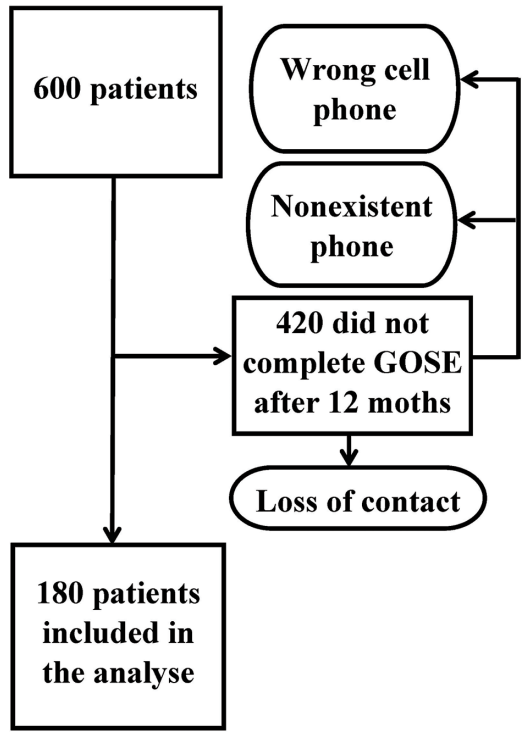

Fig. 1 Flowchart of the data cohort and the 180 patients included in the study.

Table 1 Demographics, changes in computer tomography in the patients included, and associations with neurological outcomes

Variable	Included patients: GOSE score < 7 ($n = 103$)	Included patients: GOSE score ≥ 7 ($n = 77$)	*p*-value
Ages in years: mean ± standard deviation	36.6 ± 16.2)	36.06 ± 16.2)	0.738
Sex: n (%)			0.637
Male	87 (84)	63 (82)	
Female	16 (16)	14 (18)	
Changes on CT: n (%)	99 (96)	69 (90)	0.083
Contusion	57 (56)	39 (51)	0.545
EDH	23 (22)	17 (22)	0.968
SDH	33 (32)	14 (18)	**0.041**
SAH	69 (67)	30 (39)	**< 0.001**
Swelling	23 (22)	03 (04)	**< 0.001**
Effacement of cortical sulci	44 (43)	18 (23)	**0.006**
Effacement of basal cisterns	17 (17)	01 (01)	**< 0.001**
Brain midline shift > 5 mm	20 (19)	06 (08)	**0.028**
Brain midline shift < 5 mm	15 (15)	05 (07)	0.084
Skull fracture	65 (63)	34 (44)	**0.011**
Depressed skull fracture	17 (17)	04 (05)	**0.017**
Skull base fracture	60 (59)	36 (47)	0.112
Marshall grade 1	13 (13)	15 (19)	0.219
Marshall grade 2	51 (50)	52 (67)	**0.019**
Marshall grade 3	21 (20)	04 (05)	**0.003**
Marshall grade 4	17 (17)	11 (15)	**0.040**

Abbreviations: CT, computed tomography; EDH, epidural hemorrhage; GOSE, Glasgow Outcome Scale-Extended; SDH, subdural hemorrhage; SAH, subarachnoid hemorrhage.
Note: *p*-values in bold indicate statistical significance.

Brain CT and Neurological Prognosis

There were no significant associations regarding brain contusions ($p = 0.545$), epidural hemorrhage ($p = 0.968$), skull base fractures ($p = 0.112$), and a worse outcome. In patients with a GOSE score < 7 there was an increased frequency of subdural hemorrhage ($p = 0.041$) and subarachnoid hemorrhage ($p \leq 0.001$). Conditions that are related with increased intracranial pressure and a worse neurological prognosis, such as brain swelling ($p \leq 0.001$), effacement of cortical sulci ($p = 0.006$), effacement of basal cisterns ($p \leq 0.001$), and brain midline shift > 5 mm ($p = 0.028$) were also observed. Skull fracture ($p = 0.011$) and depressed skull fracture ($p = 0.017$) were also associated with worse outcomes at 12 months. A summary of all changes in the brain CT scans (including the Marshall grade) and the associations with neurological outcomes are shown in ►**Table 1**.

After a multivariate analysis of the CT variables, only the presence of subarachnoid hemorrhage, swelling, and depressed skull fracture were independent predictors of outcomes (►**Table 2**).

Secondary Analysis

Age, baseline GOSE scores, and the main baseline CT variables were analyzed for the group of patients lost to follow-up, and no statistically significant differences were found (►**Table 3**).

Table 2 Computed tomography variables that were independent predictors of outcome after a multivariate analysis

Variable	Odds ratio	95% confidence interval	*p*-value
Subarachnoid hemorrhage	2.38	1.24–4.55	0.009
Swelling	4.39	1.20–15.99	0.025
Depressed skull fracture	3.30	1.02–10.70	0.046

Table 3 Comparison of baseline clinical and radiological findings of the patients recruited regarding loss or not to follow-up

Variable	Not lost to follow-up ($n = 180$)	Lost to follow-up ($n = 420$)	*p*-value
Ages in years: mean ± standard deviation	36.5 ± 16.1)	34.75 ± 16.5)	0.23
Sex: n (%)			0.77
Male	354 (84.3)	150 (83.3)	
Severe traumatic brain injury: n (%)	159 (37.9)	66 (36.7)	0.81
Changes on computed tomography: n (%)			
Subdural hemorrhage	119 (28.3)	47 (26.2)	0.70
Subarachnoid hemorrhage	217 (51.7)	99 (55.0)	0.45
Swelling	50 (11.9)	26 (14.4)	0.56
Effacement of cortical sulci	148 (35.2)	62 (34.4)	0.79
Effacement of basal cisterns	77 (18.3)	39 (21.7)	0.59
Brain midline shift > 5 mm	49 (11.67)	26 (14.4)	0.52
Skull fracture	233 (55.5)	99 (55.0)	0.79
Depressed skull fracture	62 (14.8)	22 (12.2)	0.46
Marshall grade 1	72 (17.1)	28 (15.56)	0.89
Marshall grade 2	250 (59.52)	103 (57.22)	0.78
Marshall grade 3	47 (11.2)	25 (13.9)	0.72
Marshall grade 4	50 (11.9)	22 (12.2)	0.93

Discussion

The present study investigated the associations involving morphological changes in the brain identified by CT and the functional outcomes after 12 months measured through the GOSE, which was chosen because it is the most cited and accepted scale to measure functional outcomes following TBI. A simplified Portuguese version of the scale has been validated for use in Brazil.[20–22] It is a very flexible scale that can help to improve follow-up, as it can be applied face to face or by telephone. McMillan et al.[19] found no differences between these two interview modalities in terms of results. Rainer et al.,[23] in 5-year prospective cohort, reported that the best functional improvement occurs 6 to 12 months after the TBI, data that supports the time chosen by us to conduct the follow-up. In the present study, 12 months after the TBI, we found that 42.7% of the patients had good recovery, a figure that is in agreement with the results of the study by Samanamalee et al.[24]

Regarding the Marshall CT classification in a study with a large sample ($n = 2269$), Mass et al.[13] (2005) confirmed that it had a good predictive value, although they recommended making more use of the characteristics underlying the classification and including other predictors, such as intraventricular and traumatic subarachnoid hemorrhage, as well as a clearer differentiation between basal and mass lesions, to produce a better prognostic tool. The results of the present study are in line with most of the results found by Mass et al.,[13] showing the importance of including the effacement of basal cisterns ($p < 0.001$), midline shift > 5 mm ($p < 0.028$) and subarachnoid hemorrhage ($p < 0.001$); however, unlike Mass et al.,[13] we did not find epidural hemorrhage to be associated with better outcomes and intravascular hemorrhage to be related to worse outcomes. In fact, we found a similar percentage of patients with these abnormalities in both groups in the present study, with no association with the outcomes.[13] According to Gennarelli et al.,[25] the worst TBI they observed was subdural hematoma, as it was not only responsible for the majority of all deaths in their series of patients, but it was associated with the greatest impact on quality of life among the survivors. Another study, also conducted in Brazil, Amorim et al.[26] reported an associations regarding epidural, subdural, subarachnoid, and intracerebral hemorrhage and higher levels of mortality in 14 days, as well as with worse GCS scores, findings similar to those of the present study.

Increased intracranial pressure due to a mass effect from swelling or hematoma can lead to displacement of the brain parenchyma into a different compartment, resulting in a worse prognosis. The signs of increased pressure that were analyzed on the CT scans in the present study included brain swelling, effacement of cortical sulci and basal cisterns, and brain midline shift > 5 mm. These alterations were related to functional decline, especially basal cistern effacement, which was the variable most associated with poor recovery. Cordobés et al.[27] found a mortality rate of 76% in the presence of basal cistern effacement. Murphy et al.[28] showed that basal cistern effacement had a close relationship with increased intracranial pressure, being an important independent prognosis factor in first hours after a TBI.

Vascular injury with hemorrhage is an important complication in TBI, and it can be caused by several mechanisms.

Arterial lesions as a result of a direct laceration or skull base fracture are among the most common causes, leading to other complications, such as cerebrospinal fluid leak, which increases the risk of developing meningitis or orthostatic headaches months to years after the lesion.[29] Although a basilar skull fracture was not associated with either good or poor recovery in the data ($p = 0.112$) of the present study, we found that depressed skull fracture, which could indicate a high-energy trauma and a possible parenchyma lesion, was associated with poor recovery ($p = 0.017$). Most of the studies on TBI prognosis[10,11,13] do not report skull fracture as an important indicator of neurological prognosis. In the present study, among the CT variables, depressed skull fracture was found to be an independent predictor of outcome; however, this anomalous finding should be interpreted with caution, and needs to be better evaluated in future studies.

The present cohort study has some limitations which could reduce the impact of our findings. The successful follow-up rates were lower than expected when compared with other studies, such as that the one by Rainer et al.,[23] which reported a loss of only 56% with the same follow-up period, against the rate of 70% observed in the present study. The main reason for the low level of successful follow-up in the present study was the lack of correct contact information in medical records and difficulty accessing the patients' data in general. In low- middle-income countries (LMICs), long-term follow-up may be more challenging than in high-income countries, since telecommunication networks, including mobile phone use and the internet, are not as developed.[26] Moreover, the regular contact that may be maintained by patients visiting rehabilitation centers in countries with better resources is more difficult in LMICs such as Brazil, where the health infrastructure is less developed, as described by Conforto et al.[30,31] Despite the rate of patients lost to follow-up, no statistically significant differences were observed regarding the baseline characteristics of the individuals in the follow-up group and lost to follow-up group. A final limitation is the fact that external factors, such as socioeconomic condition, level of schooling, access to a multidisciplinary team (physiotherapist, physiatrist, or occupational therapist), which could affect functional recovery in the long term, were not assessed in the present study. These important variables could be included in future studies. One important strength of the study was the fact that we used self-reported measures, such as the GOSE, in the follow-up. These are important, as they introduce the direct perspective of the patients, which is often missing in studies which only include provider-driven measures, thus introducing a potential bias.

Conclusion

The present study showed that subarachnoid hemorrhage, brain swelling, and depressed skull fracture were the main morphological abnormalities identified on admission CT scans and the strongest independent predictors of functional outcomes measured at follow-up 12 months after the TBI. Although there was an important rate of patients lost to follow-up, a common difficulty in studies in LMICs, there were no statistically significant differences at baseline regarding the characteristics of the overall sample and the follow-up group. Further studies with larger samples and longer follow-up are warranted to provide a higher level of evidence regarding the important variables identified in the present study.

Ethical Considerations

The present study was approved by the Ethics Committee of Fundação Universidade Federal de Sergipe (in accordance with the Helsinki Declaration, revised in 1983), and all patients or their legal guardian/next of kin signed an informed consent form.

Authors Contribution

All authors contributed to the conception and design of the study. Material preparation and data collection and analysis were performed by RSD, TCSM, IFSL, JNCN, LAS, BFOS,RLOA, and AMPO. The first draft of the manuscript was written by RSD, and all authors commented on previous versions of the manuscript. The final draft of the manuscript was written by LAS. All authors read and approved the final manuscript.

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Conflict of Interests

The authors have no conflict of interests to declare.

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