

# Mismatch between midline shift and hematoma thickness as a prognostic factor of mortality in patients sustaining acute subdural hematoma

Matheus Rodrigues de Souza,<sup>1</sup> Caroline Ferreira Fagundes,<sup>1</sup> Davi Jorge Fontoura Solla,<sup>2,3</sup> Gustavo Carlos Lucena da Silva,<sup>1</sup> Rafaela Borin Barreto,<sup>1</sup> Manoel Jacobsen Teixeira,<sup>2</sup> Robson Luis Oliveira de Amorim,<sup>2</sup> Angelos G Kolias,<sup>4</sup> Daniel Godoy,<sup>5</sup> Wellingson Silva Paiva<sup>2,3</sup>

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/tsaco-2021-000707>).

<sup>1</sup>Department of Medicine, Mato Grosso State University, Caceres, Mato Grosso, Brazil

<sup>2</sup>Department of Neurology, University of São Paulo, São Paulo, Brazil

<sup>3</sup>Department of Neurology, University of Cambridge, Cambridge, UK

<sup>4</sup>Department of Clinical Neuroscience - Division of Neurosurgery, Addenbrooke's Hospital, Cambridge, UK

<sup>5</sup>Intensive Care Unit, San Juan Bautista Hospital, San Fernando del Valle de Catamarca, Argentina

## Correspondence to

Professor Wellingson Silva Paiva, Department of Neurology – Division of Neurosurgery, University of São Paulo, São Paulo, São Paulo, Brazil; [wellingsonpaiva@yahoo.com.br](mailto:wellingsonpaiva@yahoo.com.br)

Received 8 February 2021

Revised 5 April 2021

Accepted 11 April 2021

© Author(s) (or their employer(s)) 2021. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

**To cite:** de Souza MR, Fagundes CF, Solla DJF, et al. *Trauma Surg Acute Care Open* 2021;**6**:e000707.

## ABSTRACT

**Background** Acute subdural hematoma (ASDH) is a traumatic lesion commonly found secondary to traumatic brain injury. Radiological findings on CT, such as hematoma thickness (HT) and structures midline shift (MLS), have an important prognostic role in this disease. The relationship between HT and MLS has been rarely studied in the literature. Thus, this study aimed to assess the prognostic accuracy of the difference between MLS and HT for acute outcomes in patients with ASDH in a low-income to middle-income country.

**Methods** This was a post-hoc analysis of a prospective cohort study conducted in a university-associated tertiary-level hospital in Brazil. The TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis) statement guidelines were followed. The difference values between MLS and HT (Zumkeller index, ZI) were divided into three categories (<0.00, 0.01–3, and >3). Logistic regression analyses were performed to reveal the OR of categorized ZI in predicting primary outcome measures. A Cox regression was also performed and the results were presented through HR. The discriminative ability of three multivariate models including clinical and radiological variables (ZI, Rotterdam score, and Helsinki score) was demonstrated.

**Results** A total of 114 patients were included. Logistic regression demonstrated an OR value equal to 8.12 for the ZI >3 category (OR 8.12, 95% CI 1.16 to 40.01;  $p=0.01$ ), which proved to be an independent predictor of mortality in the adjusted model for surgical intervention, age, and Glasgow Coma Scale (GCS) score. Cox regression analysis demonstrated that this category was associated with 14-day survival (HR 2.92, 95% CI 1.38 to 6.16;  $p=0.005$ ). A multivariate analysis performed for three models including age and GCS with categorized ZI or Helsinki or Rotterdam score demonstrated area under the receiver operating characteristic curve values of 0.745, 0.767, and 0.808, respectively.

**Conclusions** The present study highlights the potential usefulness of the difference between MLS and HT as a prognostic variable in patients with ASDH.

**Level of evidence** Level III, epidemiological study.

## BACKGROUND

Acute subdural hematoma (ASDH) is a traumatic lesion commonly found secondary to traumatic

brain injury (TBI). The acceleration–deceleration resulting from trauma results in the rupture of the bridged veins, which causes the formation of hematoma.<sup>1–3</sup> Damage to brain tissue cannot be attributed only to ASDH, as this hematoma is commonly associated with cerebral edema, brain concussions, and diffuse axonal lesions, which can worsen patient prognosis.<sup>4–5</sup> Despite advances in prehospital and hospital support, this entity still has high mortality rates.<sup>6–8</sup> The mortality rate in the literature ranges from 40% to 70%.<sup>6–9 10</sup>

Several factors are associated with the prognosis of these patients, such as the Glasgow Coma Scale (GCS) score at admission, age, pupillary response, and associated traumatic injuries.<sup>11 12</sup> Radiological findings on CT, such as hematoma thickness (HT) and structures midline shift (MLS), have an important prognostic role and can be a determining factor for surgical management.<sup>13–17</sup>

MLS is caused by the hematoma itself and concomitant brain swelling.<sup>18</sup> The effect of brain swelling can be shown on the initial head CT scan by the relationship of the MLS and the HT. Disproportionately increased MLS compared with HT would raise concerns of brain tissue injury and edema, and hence a higher intracranial pressure (ICP) and a worse prognosis could be anticipated. HT, MLS, ICP, and other factors including the severity of brain atrophy are interrelated.<sup>18–20</sup>

The concept of brain swelling is not new. However, complex scoring systems that assess radiological findings as prognostic factors for TBI include MLS and hematoma data in isolation and not associated, such as the Rotterdam<sup>21</sup> and Helsinki<sup>22</sup> scores.

The relationship between HT and MLS has been little studied in the literature.<sup>18 19</sup> Zumkeller *et al*<sup>19</sup> were the first to evaluate the difference between them as prognostic factors for survival in a cohort of patients. Recently, Bartels *et al*,<sup>9</sup> in a retrospective cohort of 59 patients, determined that a difference between MLS and HT greater than 3 mm was associated with fatality. However, this parameter was not evaluated in a large sample and in low-income or middle-income countries (LMICs), a context of scarcity of resources that can benefit from simplified predictive models, thus requiring additional studies for external validation of its real

predictive value. Thus, this study aimed to assess the prognostic value of the difference between MLS and HT for acute outcomes in patients with ASDH in an LMIC.

## METHODS

### Study design

This was a post-hoc analysis of a previously conducted prospective cohort study. The study adhered to the principles of the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD), the TRIPOD statement.<sup>23</sup> All participants provided written informed consent to participate, and none of them were identified in this study.

### Patients and population

The study was conducted at the Clinics Hospital of São Paulo, a tertiary-level hospital located in the largest city of Brazil, serving a population of more than 12 million people. Data were collected from a prospective data bank registry of patients with TBI admitted to the emergency department between January 2012 and December 2015. Inclusion criteria were defined as age greater than or equal to 18 years and traumatic ASDH confirmed by CT. Exclusion criteria were spontaneous or subacute ASDH, bilateral ASDH, epidural hematoma and patients with poly-trauma. In our institution, any patient with intracranial abnormalities is eligible to be transferred to intensive care unit, which is subject to availability of bed. Therapeutic planning followed the recommendations provided by the Advanced Trauma Life Support and the guidelines provided by the Brain Trauma Foundation. Patients with non-operative management were submitted to a strict control of ICP, so when surgical evacuation is necessary it is immediately performed.

### Outcome and variables of interest

#### Clinical variables

Epidemiological data such as sex and age were assessed. Trauma mechanisms were analyzed and classified as road traffic injury, fall, violence, and others. The GCS postresuscitation care for hospital admission and pupillary response were also included.

#### Radiological variables

The diagnosis of ASDH was made based on the admission CT evaluation performed using a multidetector 64-channel CT scanner (Philips Medical Systems World Headquarters, Best, The Netherlands) by a neurosurgeon and confirmed by an experienced radiologist. The Rotterdam and Helsinki scores were calculated according to the original article that describes them.<sup>21 22</sup> These scores were chosen because they are complex models that include several radiological variables in their evaluation. Previous studies have already demonstrated that higher Helsinki and Rotterdam scores are associated with worse clinical outcomes in patients with TBI.<sup>8 16 18</sup> The Marshall CT class was not evaluated because it was not originally constructed for outcome prediction and was developed in a patient population managed with protocols of care from the early 1980s, where aggressive surgical management for high ICP was not a common approach.<sup>24</sup>

MLS was assessed in the axial plane at the level of the inter-ventricular foramen. This was measured as the longest perpendicular distance between the most displaced point of the pellucid septum and an imaginary sagittal line that associates the inner occipital protuberance and the frontal ridge.<sup>19 25</sup> HT was assessed as the longest distance between the inner table and the cortex.<sup>6</sup> Figure 1 shows an example of HT and MLS in a patient with



**Figure 1** The thickness of the acute subdural hematoma (red arrow) was measured on a CT scan as the largest distance between the cortex and the internal table; midline, orange line; midline shift, orange arrow. HT, hematoma thickness; MLS, midline shift.

ASDH. The HT was subtracted from the MLS to obtain the value described by Zumkeller *et al*<sup>19</sup>—the Zumkeller index (ZI=MLS–HT).

To assess its relationship with the outcome, a categorical variable with three cut-off points was created, categorized as ZI, using the authors' original work as a guide or key parameter.<sup>19</sup> The first category included patients whose MLS was lower than HT. The second category included patients whose calculation was between 0.01 mm and 3 mm. The third category included patients who had a difference of MLS–HT greater than 3 mm. This categorization takes into account the principle that there is an underlying brain swelling when MLS is greater than HT.

Patients were followed up during their hospital stay. The predictive value of the ZI and other variables was assessed for the primary outcome of 14-day mortality, based on reports in the literature for assessing acute outcomes of TBI.<sup>26 27</sup>

### Statistical analysis

Categorical variables were presented using relative and absolute frequencies for descriptive purposes. Normally distributed continuous data were presented as mean and SD, and otherwise by median and quartiles. Continuous data were tested for normality using the Shapiro-Wilk test.

Clinical and radiological variables were presented in each category of the ZI and were compared. Categorical data were compared using the  $\chi^2$  test. Normally distributed continuous data were compared using a one-way analysis of variance (ANOVA), and the post-hoc Tukey test was used to identify which pair had a significant difference. Data without normal distribution were compared using the Kruskal-Wallis test, and if the result was significant pairwise comparisons were performed.

Logistic regression analyses were performed to reveal the OR of the categorized ZI in predicting primary outcome measures.

Analyses considered unadjusted models and models adjusted for age, GCS, and surgical intervention. The estimated survival times for the three ZI categories were estimated using the Kaplan-Meier model and compared using the log-rank test. A Cox regression analysis was also performed and the results were presented as HR and 95% CI.

A multivariate model was used to assess the discriminatory ability of the ZI against the complex scores of Rotterdam and Helsinki. Three models were created, all of which included age and GCS added from the Helsinki or Rotterdam or ZI score. The discriminative ability of multivariable models was evaluated by calculating the area under the receiver operating characteristic (ROC) curve (AUC). Calibration was assessed using the Hosmer-Lemeshow test.

All tests were two-sided and a final p value <0.05 was considered statistically significant. Data were analyzed using the Statistical Package for Social Sciences (IBM SPSS Statistics for Windows V.25.0; IBM, Armonk, NY, USA), and ROC curve analysis was performed using MedCalc V.19.1.3 (MedCalc, NY, USA).

## RESULTS

### Patient characteristics

Overall, 114 patients were included in the study; 84.2% (n=96) were men and 15.8% (n=18) were women. The mean age was 47.7 years (SD 19.3). Regarding the trauma mechanism, 43.90% (n=50) were due to motor vehicle crashes, and the same percentage was associated with falls. A total of 64.90% (n=74) were categorized as severe TBI, and the others were classified as having moderate or mild TBI. Half of the admitted patients scored less than 6 points (IQR, 3–10) on the GCS.

The mean value of the ZI was -4.99 mm (SD: 6.80). In the categorical ZI assessment, 78.90% (n=90) of patients had negative values, 11.4% (n=13) between 0.01 mm and 3 mm, and 9.6% (n=11) greater than 3 mm. Of those who had values greater than 3 mm, 81.81% (n=9) died.

**Table 1** presents the main characteristics of the sample in each category of the ZI. The Kruskal-Wallis test demonstrated that there was an effect of ZI on the GCS, and pairwise comparison demonstrated that there was a difference between the first and third categories of the ZI (p=0.025). One-way ANOVA demonstrated the effect of ZI on MLS. The post-hoc Turkey test showed that, on average, MLS was different between the ZI categories of 1 and 2 and 1 and 3 (p<0.001 and p<0.001, respectively); however, there was no difference between categories 2 and 3 (p=0.507). Although there was a difference in MLS, no significant differences were found in HT. As for radiological scores, the Kruskal-Wallis test revealed an effect of the ZI under the Rotterdam and Helsinki scores. The pairwise comparison showed a statistically significant difference in the distribution of the values of the two scores between categories 1 and 3 of the ZI (p=0.004 and p=0.001, respectively). Finally, the  $\chi^2$  test showed that there was an association between the ZI and the presence of intraventricular hemorrhage (IVH), intracerebral hematoma (ICH), and 14-day mortality and in-hospital mortality outcomes.

### Prognostic value of MLS, HT, and ZI for 14-day mortality outcome

HT was significantly associated with clinical outcome (p=0.027). Logistic regression analysis showed that HT (OR 1.073, 95% CI 1.015 to 1.135; p=0.013) was a significant predictor of mortality. MLS was also associated with 14-day mortality

**Table 1** Clinical and radiological characteristics according to ZI category

	ZI <0	ZI 0–3 mm	ZI >3	P value
Age*	49.8 (19.6)	36.7 (12.9)	49.7 (15.6)	0.061
GCS†	6 (3–10)	5 (3–11)	3 (3–4)	0.031
Pupil reactivity				0.257
Both pupils	62.2 (56)	76.9 (10)	36.4 (4)	
One pupil	17.8 (16)	15.4 (2)	36.4 (4)	
Neither pupil	11.1 (2)	7.7 (1)	27.3 (3)	
TBI class				0.874
Mild	15.6 (14)	7.7 (1)	1 (9.1)	
Moderate	14.4 (13)	15.4 (2)	1 (9.1)	
Severe	64.4 (58)	53.8 (7)	81.1 (9)	
MLS, mm*	6.7 (5.45)	14.1 (7.8)	16.7 (5.1)	<0.001
HT, mm*	14.1 (7.12)	13.1 (7.9)	10.9 (7.7)	0.368
Rotterdam score†	5 (3–6)	5 (4.5–6)	6 (6–6)	0.002
Helsinki score†	6 (4–9)	9 (5–10)	11 (9–14)	0.001
Other injuries				
Fractures	42.2 (38)	46.2 (6)	63.6 (7)	0.401
tSAH	5.6 (5)	100 (13)	100 (11)	0.498
IVH	21.1 (19)	7.7 (1)	45.5 (5)	0.077
ICH	50 (45)	46.2 (6)	90.9 (10)	0.032
DC	81.1 (73)	92.3 (12)	90.9 (10)	0.466
Outcome				
14-day mortality	36.7 (33)	30.8 (4)	81.1 (9)	0.012
In-hospital mortality	48.9 (44)	46.2 (6)	90.9 (10)	0.027

\*Mean (SD).

†Median (IQR); all other variables: % (number).

DC, decompressive craniectomy; GCS, Glasgow Coma Scale; HT, hematoma thickness; ICH, intracerebral hematoma; IVH, intraventricular hemorrhage; MLS, midline shift; TBI, traumatic brain injury; tSAH, traumatic subarachnoid hemorrhage; ZI, Zunkeller index.

outcome (p=0.001) and was a significant predictor of mortality (OR 1.105, 95% CI 1.038 to 1.176; p=0.002).

The categorized ZI was associated with 14-day mortality outcome (p=0.012). Logistic regression demonstrated that this was a predictor of mortality with the reference category ZI >3 (OR 8.12, 95% CI 1.1651 to 40.01; p=0.01) (**table 2**). This category proved to be an independent predictor of mortality in the adjusted model for surgical intervention, age, and GCS (online supplemental table 1).

### Survival analysis

The Kaplan-Meier survival analysis demonstrated a statistically significant difference in the survival function at the different levels of the ZI categorized for the 14-day follow-up (log-rank p=0.008) (**figure 2**). Cox regression analysis demonstrated that the third category of ZI was associated with 14-day survival (HR 2.924, 95% CI 1.388 to 6.160; p=0.005), as shown in **table 2**. This category proved to be an independent predictor of 14-day survival in adjusted Cox regression for surgical intervention, age, and GCS (online supplemental table 2).

### Multivariable predictive models

Multivariate analysis was performed for all three models. Model 1 included age, GCS, and categorized ZI; model 2 included age, GCS, and Helsinki score; and model 3 included age, GCS, and Rotterdam score. All variables included were independent predictors of mortality. Models 1, 2, and 3 demonstrated an AUC equal to 0.747 (95% CI 0.654 to 0.826), 0.767 (95% CI

**Table 2** Univariate logistic and Cox regression values in predicting 14-day mortality outcome according to Zumkeller index categories

Zumkeller index	Logistic regression			Cox regression		
	OR	95% CI	P value	HR	95% CI	P value
<0.00*	–	–	0.033	–	–	0.014
0.01–3	0.768	0.219 to 2.689	0.679	0.854	0.303 to 2.412	0.766
>3	7.773	1.583 to 38.155	0.012	2.924	1.388 to 6.160	0.005

\*Zumkeller index values <0.00 were included as a reference category in the model.

0.676 to 0.843), and 0.808 (95% CI 0.721 to 0.878), respectively, as shown in figure 3. The test by DeLong *et al*<sup>28</sup> showed no significant differences between the AUC values ( $p>0.05$ ). All models demonstrated adequate calibration using the Hosmer-Lemeshow test ( $p>0.05$ ).

## DISCUSSION

The present study stands out for presenting the prognostic value of a variable that is little reviewed in the literature, “Zumkeller index,” which was associated with acute outcomes and which may suggest the presence of cerebral edema or other associated injuries in patients with ASDH. The data presented corroborate the assumption by Zumkeller *et al*<sup>19</sup> that an MLS that exceeds the thickness of the hematoma suggests the presence of associated cerebral edema and/or other parenchymal lesions, which contributes to worst clinical outcome.

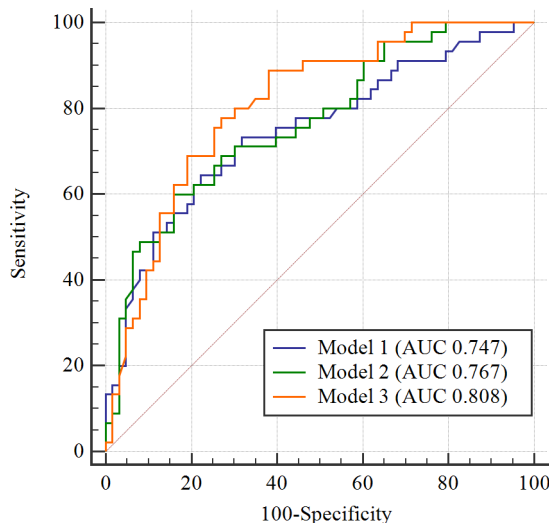
In a review of approximately 3000 autopsy cases after TBI, Tandon<sup>29</sup> concluded that ASDHs are rarely isolated lesions; in their study, 82% of the cases were associated with parenchymal lesions, which again demonstrates the importance of MLS evaluation. In our study, intraparenchymal lesions were found in 53.5% of patients, and a higher frequency of this finding was observed (90.9%) in patients who were classified as having a ZI >3. Several studies have associated the presence of ICH and its progression with poor prognosis.<sup>30–32</sup> The study by Cepeda *et al*<sup>33</sup> demonstrated that when studying the progression of ICH in patients with TBI, ASDH is associated more with this progression. In addition, it highlights the role of higher MLS values in the progression of ICH. In cases where the ZI was greater than 0, the role of MLS was notorious. Therefore, patients with these

findings and associated ICH have a greater risk of lesion progression. Cepeda *et al*<sup>33</sup> also demonstrated an unfavorable clinical outcome in 74% of patients with ICH progression, compared with 26% of those who did not. In addition, the number of patients undergoing decompressive craniectomy was significantly higher in patients with ICH progression (75% vs. 25%).

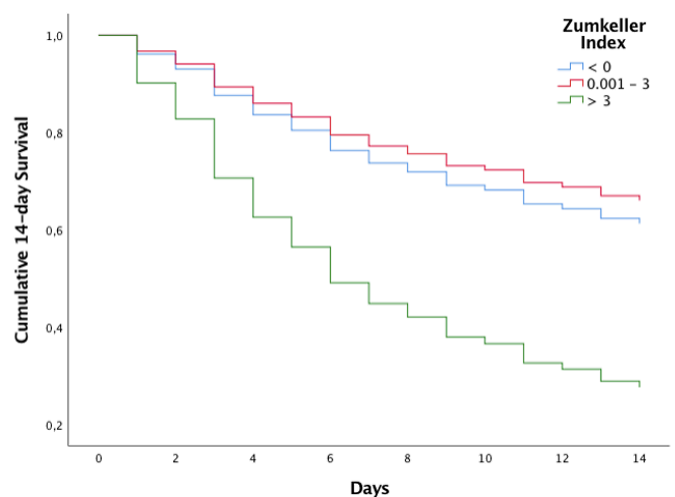
In our study, patients with ZI >3 had an increased frequency of IVH (45.5%) compared with 7.7% of patients with ZI between 0.001 and 3 and 21.1% of patients with negative ZI. According to the literature, the rate of occurrence of IVH in patients with moderate-to-severe TBI ranges between 7.1% and 22%.<sup>34–36</sup> The presumed possible mechanisms of IVH are an extension of intracerebral hemorrhage into the ventricular system or rupture of the subependymal veins, which can be deformed by the negative pressure at the time of injury.<sup>37</sup> Like ICH, several studies also associate IVH with a poor prognosis.<sup>21</sup> The study by Laleva *et al*<sup>36</sup> demonstrated that the main factor related to the onset of IVH is the presence of ICH on admission images. In our cohort, we observed high frequencies of the two lesions in patients with a ZI >3.

It was also observed that 100% of patients with a positive ZI had a traumatic subarachnoid hemorrhage (SAH). Diffuse bleeding resulting from rupture of the subarachnoid vessels in TBI is a predictor well described in the literature.<sup>38–40</sup> Similar to what happens in the rupture of aneurysms, traumatic SAH induces vasospasm and cerebral ischemia, which can trigger inflammatory and neurotoxic processes and contribute to brain swelling, which contributes to worsening the outcome of patients.<sup>41 42</sup>

However, in cases of isolated ASDH, the ZI may play a role as a prognostic factor of mortality because, without a parenchymal lesion, the MLS exceeding the HT may be due to brain swelling and impairment of cerebrovascular reactivity.



**Figure 2** ROC curves for the multivariate model including age, Glasgow Coma Scale and categorical Zumkeller index (model 1), Helsinki CT score (model 2), Rotterdam CT score (model 3). AUC, area under the ROC curve; ROC, receiver operating characteristic.



**Figure 3** Survival function for each category of Zumkeller index for 14-day mortality outcome.

The relationship between MLS and HT is promising in terms of prognosis and may help to estimate ICP. Recently, Liao *et al.*<sup>20</sup> constructed a model for ICP estimation based on a half-sphere finite-element model using only HT and MLS in ASDH. The ICP values obtained by the normogram created by the authors showed a high correlation with those measured, demonstrating an R<sup>2</sup> coefficient of 0.744. Using estimates like these and predictive models like ZI, neurosurgeons can do more with less. In patients with TBI with multiple traumas, estimating ICP and brain swelling also helps prioritize treatment of different regions of the body.

We highlight the high mortality rate of patients with an MLS >3 mm in relation to HT. In our series, there was 81.8% mortality within 14 days for these patients, an even higher rate than that found by Zumkeller *et al.*<sup>19</sup> When the entire length of hospital stay was assessed, 10 of the 11 patients categorized as ZI >3 died. Bartels *et al.*,<sup>9</sup> when studying this difference in a small cohort of patients, found a mortality rate of 100% when ZI was greater than 3 mm, which indicates the accuracy of this indicator for use in clinical practice. The authors further suggested that in these patients, the trauma resulted in greater damage than that generated by the hematoma, in addition to having an influence on the anatomy and physiology of the brain, resulting in an acute onset of swelling. This assumption helps to justify the poorer clinical presentation at admission of patients with positive ZI, demonstrated by significantly lower GCS values in the second and third categories of the ZI, as well as the poor pupillary response of patients with ZI >3. It should also be noted that values greater than 3 mm, in addition to being associated with a worse outcome, also implied a reduction in the estimated survival time.

Additionally, our results highlight the potential role of ZI as a variable for modeling studies, since a comparison with more complex scores such as Rotterdam<sup>21</sup> and Helsinki<sup>22</sup> demonstrated acceptable AUC values. We hypothesize that the values close to the three multivariate models created to assess the prediction of acute ZI outcomes against these scores are because the brain injuries covered by the scores, such as IVH, ICH, and SAH, are related to the positive values of MLS–HT. It should be noted that the intention of our work is not to suggest the replacement of other existing tomography scores because they can be used in the context of other brain injuries and include variables that are associated with the prognosis of TBI; our objective was to present a complementary index to these scores which assesses something not directly included in them. The objective of our multivariate analysis, which compared the ZI with these scores, was to demonstrate that the ZI has a discriminative ability similar to these more complex models, demonstrating its clinical utility in the context of outcome prediction.

To date, only two studies have evaluated the ZI: Zumkeller *et al.*,<sup>19</sup> who described the index, and Bartels *et al.*<sup>9</sup> Neither of these studies were conducted in LMICs, which have distinct epidemiological contexts from high-income countries. As we know, LMICs have the highest burden of neurotrauma; however, most of the scientific articles published in journals originate from high-income countries.<sup>43–45</sup> Interestingly, in Brazil, many centers already use this “Zumkeller index,” not as a prognostic variable but to decide whether to perform a primary decompressive craniectomy in the setting of ASDH.<sup>46</sup> As it is a post-hoc analysis of a prospective study, it is not possible to suggest the indication of decompressive craniectomies for patients with positive ZI. However, cerebral edema and/or associated injuries in this group of patients are notorious. We then suggest the proper management of intracranial

hypertension and that future studies of primary decompressive craniectomy address this variable.

Finally, regarding the epidemiological data for ASDH, the literature demonstrates that high mortality rates are more often associated with advanced ages.<sup>6 47–49</sup> Wilberger *et al.*,<sup>50</sup> in their study, demonstrated that the average age of non-survivors was 59 years, whereas that of survivors was 41 years, a finding similar to that seen in other studies.<sup>3 9</sup> In our study, the average age of survivors was 44.4 years and that of non-survivors was 53.4 years. Ryan *et al.*,<sup>51</sup> in their study, described falls as the main injury mechanism (57%), followed by automobile crash (23%), which was very close to the study by Leitgeb *et al.*,<sup>52</sup> which also presented falls as the main mechanism (51.9%), followed by automobile crash (22.2%). In the present study, the percentages of ASDH resulting from automobile crash and falls were the same (43.9%). Several authors have already demonstrated epidemiological differences in different socioeconomic contexts.<sup>53 54</sup> In LMICs, where traffic laws and enforcement are not as effective, automobile crash and trauma mechanisms related to aggression are predominant. Thus, we emphasize that the present study is the first to evaluate the MLS–HT relationship in an LMIC, which contributes to the process of external validation of its practical utility in different contexts.

### Study limitations

This study has some limitations. Despite an adequate number of patients for the proposed analyses, this study was restricted to a single center, which may limit the generalization of the findings. In addition, it is a post-hoc analysis of a prospective study. Thus, some variables, such as surgical intervention, could not be controlled. Despite this, we present an adjusted regression model for performing decompressive craniectomy associated with other clinical variables. Besides, to minimize bias of deaths from causes other than TBI, the primary outcome of our study was 14-day mortality. Several authors have already described that this is a useful time to assess prognosis in patients suffering from TBI. In a shorter follow-up period, it is possible to minimize other factors that could contribute to mortality, such as in-hospital infections and late complications. We encourage other authors from various centers around the world to assess the difference between MLS and HT for patients with ASDH and to investigate ZI in prospective cohorts as an indication of decompressive craniectomy. We emphasize the limitation of not providing data on the long-term outcomes of the study population. In future studies, the Glasgow Outcome Scale should be included. However, the difficulty of long-term monitoring of patients with TBI is not restricted to our study, which has been previously reported in the literature, mainly in LMICs.<sup>55 56</sup>

### CONCLUSION

The present study highlighted the potential usefulness of the difference between MLS and HT (the “Zumkeller index”) as a prognostic variable for patients with ASDH. A worse clinical presentation by GCS was demonstrated in patients with positive ZI, as well as a worse classification in the Rotterdam and Helsinki tomography scores. A higher frequency of other injuries associated with ASDH, such as SAH, IVH, and ICH, was found in patients with a ZI greater than 3. In addition, the present study demonstrated a lower survival rate in this group of patients. We advocate that such an index be used in future modeling studies or evaluate its potential in future studies of primary decompressive craniectomies.

**Contributors** MRDs: study design, data analysis and interpretation, drafting of the article, and editorial oversight. CFF: study design, data analysis, article preparation, and editorial oversight. DJFS: study design, data analysis and interpretation, and review. GCLdS, RBB: abstract preparation, data collection, and drafting of the article. MJT: review of the article and editorial oversight. RLOdA: conception and design, data collection, and review of the article. AGK: drafting of the article, review, and final approval of the article. DG: study design, data analysis and interpretation, drafting of the article, review, and final approval of the article. WSP: conception and design, data collection, analysis and interpretation, drafting of the article, review, and final approval of the article.

**Funding** This research was partially funded by the National Council for Scientific and Technological Development (CNPq), Brazil. DJFS, WSP and AGK are supported by the NIHR Global Health Research Group on Neurotrauma, which was commissioned by the National Institute for Health Research (NIHR) using UK aid from the UK Government (project 16/137/105). The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

**Competing interests** DJFS reports grants and non-financial support from National Institute for Health Research (NIHR), during the conduct of the study. RLOdA reports grants from the National Council for Scientific and Technological Development (CNPq), Brazil, during the conduct of the study. AGK reports grants and non-financial support from NIHR, grants and non-financial support from the School of Clinical Medicine, University of Cambridge, and grants and non-financial support from Royal College of Surgeons of England, during the conduct of the study. WSP reports grants and non-financial support from NIHR, during the conduct of the study.

**Patient consent for publication** Not required.

**Ethics approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Research Ethics Committee of the University of São Paulo School of Medicine Hospital das Clínicas; registry: 46831315.3.0000.0068) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. All data relevant to the study are included in the article or uploaded as supplementary information. All personal identifiers found in the data will be removed prior to sharing.

**Open access** This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

## REFERENCES

- Kiboi JG, Kitunguu PK, Angwenyi P, Mbuthia F, Sagina LS. Predictors of functional recovery in African patients with traumatic intracranial hematomas. *World Neurosurg* 2011;75:586–91.
- Kolias AG, Scotton WJ, Belli A, King AT, Brennan PM, Bulters DO, Eljamel MS, Wilson MH, Papadopoulos MC, Mendelow AD, et al. Surgical management of acute subdural hematomas: current practice patterns in the United Kingdom and the Republic of Ireland. *Br J Neurosurg* 2013;27:330–3.
- Taussky P, Hidalgo ET, Landolt H, Fandino J. Age and salvageability: analysis of outcome of patients older than 65 years undergoing craniotomy for acute traumatic subdural hematoma. *World Neurosurg* 2012;78:306–11.
- Tsang KK-T, Whitfield PC. Traumatic brain injury: review of current management strategies. *Br J Oral Maxillofac Surg* 2012;50:298–308.
- Karibe H, Hayashi T, Hirano T, Kameyama M, Nakagawa A, Tominaga T. Surgical management of traumatic acute subdural hematoma in adults: a review. *Neurol Med Chir* 2014;54:887–94.
- Bauchner G, Troude L, Pauly V, Bernard F, Zieskiewicz L, Roche P-H. Predictive factors of poor prognosis after surgical management of traumatic acute subdural hematomas: a single-center series. *World Neurosurg* 2019;126:e944–52.
- Evans LR, Jones J, Lee HQ, Gantner D, Jaison A, Matthew J, Fitzgerald MC, Rosenfeld JW, Hunn MK, Tee JW. Prognosis of acute subdural hematoma in the elderly: a systematic review. *J Neurotrauma* 2019;36:517–22.
- Alagoz F, Yildirim AE, Sahinoglu M, Korkmaz M, Secer M, Celik H, Yel C, Guvenc Y, Uckun OM, Narin F, et al. Traumatic acute subdural hematomas: analysis of outcomes and predictive factors at a single center. *Turk Neurosurg* 2017;27:187–91.
- Bartels RHMA, Meijer FJA, van der Hoeven H, Edwards M, Prokop M. Midline shift in relation to thickness of traumatic acute subdural hematoma predicts mortality. *BMC Neurol* 2015;15:1–6.
- Howard MA, Gross AS, Dacey RG, Winn HR. Acute subdural hematomas: an age-dependent clinical entity. *J Neurosurg* 1989;71:858–63.
- Koç RK, Akdemir H, Öktem IS, Meral M, Menkü A. Acute subdural hematoma: outcome and outcome prediction. *Neurosurg Rev* 1997;20:239–44.
- Perel P, Arango M, Clayton T, Edwards P, Komolafe E, Poccock S, Roberts I, Shakur H, Steyerberg E, et al. MRC CRASH Trial Collaborators. Predicting outcome after traumatic brain injury: practical prognostic models based on large cohort of international patients. *BMJ* 2008;336:425–9.
- Servadei F, Nasi MT, Giuliani G, Cremonini AM, Cenni P, Zappi D, Taylor GS. CT prognostic factors in acute subdural haematomas: the value of the 'worst' CT scan. *Br J Neurosurg* 2000;14:110–6.
- Won YD, Na MK, Ryu J-I, Cheong J-H, Kim J-M, Kim C-H, Han M-H. Radiologic factors predicting deterioration of mental status in patients with acute traumatic subdural hematoma. *World Neurosurg* 2018;111:e120–34.
- Zhu GW, Wang F, Liu WG. Classification and prediction of outcome in traumatic brain injury based on computed tomographic imaging. *J Int Med Res* 2009;37:983–95.
- Maas AIR, Steyerberg EW, Butcher I, Dammers R, Lu J, Marmarou A, Mushkudiani NA, McHugh GS, Murray GD. Prognostic value of computerized tomography scan characteristics in traumatic brain injury: results from the impact study. *J Neurotrauma* 2007;24:303–14.
- Hawryluk GWJ, Rubiano AM, Totten AM, O'Reilly C, Ullman JS, Bratton SL, Chesnut R, Harris OA, Kisson N, Shutter L, et al. Guidelines for the management of severe traumatic brain injury: 2020 update of the decompressive craniectomy recommendations. *Neurosurgery* 2020;87:427–34.
- Moussa WMM, Khedr WM, Elwany AH. Prognostic significance of hematoma thickness to midline shift ratio in patients with acute intracranial subdural hematoma: a retrospective study. *Neurosurg Rev* 2018;41:483–8.
- Zumkeller M, Behrmann R, Heissler HE, Dietz H. Computed tomographic criteria and survival rate for patients with acute subdural hematoma. *Neurosurgery* 1996;39:708–12.
- Liao C-C, Liao H-C, Lai F, Xiao F. A nomogram for estimating intracranial pressure using acute subdural hematoma thickness and midline shift. *Sci Rep* 2020;10:21787.
- Maas AIR, Hukkelhoven CWPM, Marshall LF, Steyerberg EW. Prediction of outcome in traumatic brain injury with computed tomographic characteristics: a comparison between the computed tomographic classification and combinations of computed tomographic predictors. *Neurosurgery* 2005;57:1173–81.
- Raj R, Siironen J, Skrifvars MB, Hernesniemi J, Kivisaari R. Predicting outcome in traumatic brain injury: development of a novel computerized tomography classification system (Helsinki computerized tomography score). *Neurosurgery* 2014;75:632–46.
- Collins GS, Reitsma JB, Altman DG, Moons KGM. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. *BMC Med* 2015;13:1.
- Steyerberg EW, Mushkudiani N, Perel P, Butcher I, Lu J, McHugh GS, Murray GD, Marmarou A, Roberts I, Habbema JDF, et al. Predicting outcome after traumatic brain injury: development and international validation of prognostic scores based on admission characteristics. *PLoS Med* 2008;5:1251–61.
- Bullock MR, Chesnut R, Ghajar J, Gordon D, Hartl R, Newell DW, Servadei F, Walters BC, Wilberger JE. Surgical management of acute subdural hematomas. *Neurosurgery* 2006;58:S2-16–S2-24.
- Roozenbeek B, Chiu Y-L, Lingsma HF, Gerber LM, Steyerberg EW, Ghajar J, Maas AIR. Predicting 14-day mortality after severe traumatic brain injury: application of the impact models in the brain trauma Foundation TBI-trac@ New York state database. *J Neurotrauma* 2012;29:1306–12.
- Perkins NJ, Schisterman EF. The Youden index and the optimal cut-point corrected for measurement error. *Biom J* 2005;47:428–41.
- DeLong ER, DeLong DM, Clarke-Pearson DL, DeLong ER, Carolina N. Comparing the areas under two or more correlated receiver operating characteristic curves: a nonparametric approach. *Biometrics* 1988;44:837–45.
- Tandon PN. Acute subdural haematoma: a reappraisal. *Neurol India* 2001;49:3–10.
- Chang EF, Meecker M, Holland MC. Acute traumatic intraparenchymal hemorrhage: risk factors for progression in the early post-injury period. *Neurosurgery* 2007;61:647–56.
- Narayan RK, Maas AIR, Servadei F, Skolnick BE, Tillinger MN, Marshall LF, et al. Traumatic Intracerebral Hemorrhage Study Group. Progression of traumatic intracerebral hemorrhage: a prospective observational study. *J Neurotrauma* 2008;25:629–39.
- Alahmadi H, Vachrajani S, Cusimano MD. The natural history of brain contusion: an analysis of radiological and clinical progression. *J Neurosurg* 2010;112:1139–45.
- Cepeda S, Gómez PA, Castaño-Leon AM, Martínez-Pérez R, Munarriz PM, Lagares A. Traumatic intracerebral hemorrhage: risk factors associated with progression. *J Neurotrauma* 2015;32:1246–53.
- Abraszko RA, Zurynski YA, Dorsch NW. The significance of traumatic intraventricular haemorrhage in severe head injury. *Br J Neurosurg* 1995;9:769–74.
- Atzema C, Mower WR, Hoffman JR, Holmes JF, Killian AJ, Wolfson AB, et al. National Emergency X-Radiography Utilization Study (NEXUS) II Group. Prevalence and prognosis of traumatic intraventricular hemorrhage in patients with blunt head trauma. *J Trauma* 2006;60:1010–7.
- Laleva M, Gabrovsky N, Naseva E, Velinov N, Gabrovsky S. Delayed intraventricular hemorrhage in moderate-to-severe traumatic brain injury: prevalence, associated risk factors, and prognosis. *Acta Neurochir* 2016;158:1465–72.

- 37 Mata-Mbemba D, Mugikura S, Nakagawa A, Murata T, Kato Y, Tatewaki Y, Li L, Takase K, Ishii K, Kushimoto S, *et al*. Intraventricular hemorrhage on initial computed tomography as marker of diffuse axonal injury after traumatic brain injury. *J Neurotrauma* 2015;32:359–65.
- 38 Mendelow AD, Teasdale G, Jennett B, Bryden J, Hessel C, Murray G. Risks of intracranial haematoma in head injured adults. *Br Med J* 1983;287:1173–6.
- 39 Greene KA, Marciano FF, Johnson BA, Jacobowitz R, Spetzler RF, Harrington TR. Impact of traumatic subarachnoid hemorrhage on outcome in nonpenetrating head injury. Part I: a proposed computerized tomography grading scale. *J Neurosurg* 1995;83:445–52.
- 40 Thelin EP, Nelson DW, Vehviläinen J, Nyström H, Kivisaari R, Siironen J, Svensson M, Skrifvars MB, Bellander B-M, Raj R. Evaluation of novel computerized tomography scoring systems in human traumatic brain injury: an observational, multicenter study. *PLoS Med* 2017;14:e1002368.
- 41 Armin SS, Colohan ART, Zhang JH. Traumatic subarachnoid hemorrhage: our current understanding and its evolution over the past half century. *Neurol Res* 2006;28:445–52.
- 42 Hellewell S, Semple BD, Morganti-Kossmann MC. Therapies negating neuroinflammation after brain trauma. *Brain Res* 2016;1640:36–56.
- 43 Langer A, Díaz-Olavarrieta C, Berdichevsky K, Villar J. Why is research from developing countries underrepresented in international health literature, and what can be done about it? *Bull World Health Organ* 2004;82:802–3.
- 44 Kolas AG, Rubiano AM, Figaji A, Servadei F, Hutchinson PJ. Traumatic brain injury: global collaboration for a global challenge. *Lancet Neurol* 2019;18:136–7.
- 45 Neurotrauma.world. NIHR global health research group on neurotrauma. 2016. <http://neurotrauma.world/> (21 Oct 2019).
- 46 de Amorim R, de Andrade A, Paiva W, Faleiro R, Monteiro R. Management of diffuse lesions in traumatic brain injury in Brazil. *Austin Neurosurg Open Access* 2014;1:1011.
- 47 Kim K-H. Predictors for functional recovery and mortality of surgically treated traumatic acute subdural hematomas in 256 patients. *J Korean Neurosurg Soc* 2009;45:143–50.
- 48 Kotwica Z, Brzeziński J. Acute subdural haematoma in adults: an analysis of outcome in comatose patients. *Acta Neurochir* 1993;121:95–9.
- 49 Phuenpathom N, Choomuang M, Ratanalert S. Outcome and outcome prediction in acute subdural hematoma. *Surg Neurol* 1993;40:22–5.
- 50 Wilberger JE, Harris M, Diamond DL. Acute subdural hematoma: morbidity, mortality, and operative timing. *J Neurosurg* 1991;74:212–8.
- 51 Ryan CG, Thompson RE, Temkin NR, Crane PK, Ellenbogen RG, Elmore JG. Acute traumatic subdural hematoma. *J Trauma Acute Care Surg* 2012;73:1348–54.
- 52 Leitgeb J, Mauritz W, Brazinova A, Janciak I, Majdan M, Wilbacher I, Rusnak M. Outcome after severe brain trauma due to acute subdural hematoma. *J Neurosurg* 2012;117:324–33.
- 53 Roozenbeek B, Maas AIR, Menon DK. Changing patterns in the epidemiology of traumatic brain injury. *Nat Rev Neurol* 2013;9:231–6.
- 54 De Silva MJ, Roberts I, Perel P, Edwards P, Kenward MG, Fernandes J, Shakur H, Patel V, . CRASH Trial Collaborators. Patient outcome after traumatic brain injury in high-, middle- and low-income countries: analysis of data on 8927 patients in 46 countries. *Int J Epidemiol* 2009;38:452–8.
- 55 Teasdale GM, Pettigrew LE, Wilson JT, Murray G, Jennett B. Analyzing outcome of treatment of severe head injury: a review and update on advancing the use of the Glasgow outcome scale. *J Neurotrauma* 1998;15:587–97.
- 56 Wisborg T, Montshiwa TR, Mock C. Trauma research in low- and middle-income countries is urgently needed to strengthen the chain of survival. *Scand J Trauma Resusc Emerg Med* 2011;19:62.