Gastrointestinal Failure Score in Children with Traumatic Brain Injury

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Research article

Keywords: gastrointestinal failure (GIF) score, traumatic brain injury, children

Posted Date: June 25th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-36656/v1

Version of Record: A version of this preprint was published at BMC Pediatrics on May 4th, 2021. See the published version at https://doi.org/10.1186/s12887-021-02673-5.

Abstract

Purposes

To review the value of the gastrointestinal failure (GIF) score in children with different degrees of traumatic brain injury (TBI) by analyzing the correlation between outcome and gastrointestinal function.

Methods

A total of 165 children with TBI who were diagnosed and treated in the surgical intensive care unit (SICU) for longer than 72 h between August 2017 and 2019 were retrospectively analyzed. Admission parameters were sex, age, Glasgow Coma Scale (GCS) score, body mass index (BMI), leukocyte count, C-reactive protein (CRP), hemoglobin (Hb) and hematocrit (Hct), blood glucose, lactic acid, procalcitonin (PCT), albumin, plasma osmotic pressure, prothrombin time (PT) and activated partial thromboplastin time (APTT). In order to predict outcome, Sequential Organ Failure Assessment (SOFA) score, Pediatric Clinical Illness Score (PCIS) and mean GIF score for the first three days were also combined.

Results

The percent of patients with gastrointestinal dysfunction on the first day was 78.8%. Food intolerance (FI) developed in 36.4% and intra-abdominal hypertension (IAH) in 21.8% of patients. The GIF score and mean GIF score for the first three days in children with different degrees of TBI were significantly different ($P<0.05$); they were also significantly different between those who died and those who survived ($P<0.05$). The mean GIF score for the first three days was identified as an independent risk factor for mortality (odds ratio>1, 95% confidence interval=1.457 to 16.016, $P<0.01$), as was the PCIS. Receiver operating characteristic (ROC) curve analysis suggested that the mean GIF score for the first three days had the same calibrating power as the PCIS in discriminating the risk of death of children.

Conclusion

The incidence of gastrointestinal dysfunction in children with TBI is high. The GIF score has its ability to judge gastrointestinal system. The mean GIF score for the first three days has high prognostic value for ICU mortality in the SICU.

Introduction

Traumatic brain injury (TBI) has the highest mortality and morbidity of all types of trauma and represents a serious threat to the life and physical health of children. Due to their young age, low crisis awareness and poor self-protection ability, children with TBI require monitoring and treatment in intensive care units (ICUs). The gastrointestinal tract is the only system that is jointly controlled by the central nervous system, enteric nerves and autonomic nerves. It performs adaptive activities to the internal and external environment through complex and fine regulation to achieve physiological functions. Children in ICUs with gastrointestinal bleeding, dysfunction or failure often endure prolonged hospital stays, with

increased mortality [1]. In clinical practice, gastrointestinal tract-related problems frequently occur in TBI children that are hospitalized in the ICU, and gastrointestinal function is closely related to prognosis. However, there is currently no accurate definition and standard criteria for gastrointestinal dysfunction. The variety of existing scoring systems that determine the severity of the disease of pediatric patients rarely involve the evaluation of gastrointestinal function [2]. Therefore, the importance of gastrointestinal function in children with TBI is often underestimated; furthermore, it is difficult to conduct systematic evidence-based medical analysis of gastrointestinal dysfunction in children with TBI. The gastrointestinal failure (GIF) score is as an objective indicator used to evaluate gastrointestinal dysfunction [3]; the score indicates gastrointestinal function, which can be classified into different levels similar to other scoring systems for organ function failure. The clinical value and high reliablity to predict outcome of the GIF score has been verified in intensive care patients and in digestive system diseases [4–6]. Therefore, this study collected clinical and prognostic data of children with TBI admitted to the surgical intensive care unit (SICU) in our hospital, and a GIF score was obtained. The purpose of this study was to reveal the importance of gastrointestinal dysfunction and its impact on the prognosis of children with TBI and to provide reliable evidence for the evaluation of gastrointestinal function in children with TBI.

Materials And Methods

2.1 Ethics

Informed consent forms were signed by the patients and/or parents, and this project was approved by the ethics committee of Children's Hospital of Nanjing Medical University(NO.202001004-1). All treatment followed the medical principle. All of the data were handled anonymously before analysis.

2.2 Inclusion and exclusion criteria

The inclusion criteria were as follows: a) admitted to the hospital less than 24 h after injury; b) accurate GCS scoring could be performed; c) craniocerebral injury confirmed by computed tomography (CT) in our hospital; and d) no history of previous craniocerebral or gastrointestinal diseases or surgery.

The exclusion criteria were as follows: a) neonates; b) TBI combined with primary gastrointestinal injury; c) admitted to the hospital more than 24 h after injury or died within several hours of being admitted; d) hospital stay shorter than 72 h; and e) TBI combined with organ failure, serious metabolic disorders and other basic diseases.

2.3 Clinical information

A total of 165 children with TBI who were diagnosed and treated for at least 72 h in the SICU between August 2017 and September 2019 were screened for inclusion in this prospective observational study. The parameters recorded on admission were as follows: sex, age, body mass index (BMI), Glasgow Coma Scale (GCS) score, leukocyte count, C-reactive protein (CRP) count, hemoglobin (Hb) and hematocrit (Hct), blood glucose (Glu), lactic acid (Lac), procalcitonin (PCT), albumin (ALB), plasma osmotic pressure

(POP), prothrombin time (PT) and activated partial thromboplastin time (APTT). The Sequential Organ Failure Assessment (SOFA) score and Pediatric Clinical Illness Score (PCIS) were recorded daily. Gastrointestinal function of the patients was evaluated daily by the GIF score as follows [3]: 0=normal gastrointestinal function; 1=enteral feeding with under 50% of calculated need or no feeding 3 days after abdominal surgery; 2=food intolerance (FI) or intra-abdominal hypertension (IAH); 3=FI and IAH; and 4=abdominal compartment syndrome (ACS). The SOFA scores, PICS and mean GIF scores for the first three days were combined to predict outcome. The primary outcome parameter was ICU mortality.

There are a few caveats. Enteral feeding was provided as early as possible according to each child's condition. The criteria for the diagnosis of FI were failure of enteral feeding or occurrence of recurrent vomiting, high gastric residual volumes, intestinal obstruction, severe diarrhea, abdominal pain, or bloating that could not be resolved. Intra-abdominal pressure (IAP) was measured via empty bladder in the supine position, using the closed loop system repeated measurements technique when the child developed FI [7]. The IAP was measured at least twice per day when normal. When IAP was higher than 12 mmHg, it changed to four times per day at different points . IAH was defined as persistent IAP 12 mmHg or higher. ACS was defined as persistent IAP 20 mmHg or greater, accompanied by new organ failure. Mean and maximum IAP values were documented daily, and the first mentioned of two was used to calculate the daily GIF score.

2.4 Statistical analysis

SPSS 19.0 (Professional Edition) was used for data analysis. Data are presented as the mean ± standard (`x±s), if not stated otherwise. Differences between two groups were determined by the two-sample T test for continuous variables and by the chi-square test (or Fisher's exact probability) for categorical variables. one-way ANOVA was used for the comparison of multiple means. The GIF score for the first three days were calculated as the mean individual score for 3 days for every child. Risk factors for ICU mortality were identified by univariate analyses of admission parameters, and these with $p < 0.1$ were entered into a multiple logistic regression model to identify independent risk factors. Receiver operating characteristic (ROC) curves were used to determine the likelihood ratios for the abilities of the GIF score, SOFA score and PCIS to predict ICU mortality. $P < 0.05$ was considered statistically significant.

Results

3.1 This study included 165 children (103 boys (62.4%) and 62 girls (37.6%)) with an average age of 4 years and 11 months. There were 35 patients (21.2%) without gastrointestinal dysfunction on the first day of hospital admission, and 130 patients (78.8%) with gastrointestinal dysfunction, of which 34 had insufficient feeding (20.6%), 60 had FI (36.4%), and 36 had IAH or ACS (21.8%). There were 80 children with TBI with stress ulcers (48.5%) and 114 children with secondary gastrointestinal dysfunction after TBI (69.1%).

Children were divided into two groups based on whether or not FI occurred on the first day of admission. There were 69 children (41.8%) with a GIF score <2 on the first day and 96 children (58.2%) with a GIF score ≥2. There were significant differences in GCS and GIF scores on the first day, mean GIF scores for the first three days of admission, SOFA scores, and PCIS between the two groups ($p<0.05$), and mortality (a prognostic indicator) was also significantly different between the two groups (Table 1).

According to the GCS score at admission, the children were divided into the severe group (GCS score, 3-8 points), the moderate group (GCS score, 9-12 points) and the mild group (GCS score, 13-15 points); the incidence rates of stress ulcers among the three groups were 85.9%, 4.3%, and 0% ($p<0.05$), respectively, and the incidence rates of secondary gastrointestinal dysfunction were 100%, 82.6%, and 38%, respectively. The GIF score on the first day and the mean GIF score for the first three days were significantly different among the three groups ($p <0.05$). Mortality was significantly different among children with different degrees of TBI (Table 2).

According to the in-hospital outcome (died or survived), the children were divided into the death group and the survival group. The data were statistically analyzed, and the results showed that the clinically relevant indicators, such as GCS score, leukocyte count, Hb, Glu, pH, lactate, ALB, PT, APTT, SOFA score, PCIS, GIF score on the first day and mean GIF score for the first three days were significantly different between the two groups ($p<0.05$), while CRP, Hct, PCT, and POP were not significantly different ($p\geq0.05$, Table 3).

3.2 Multivariate regression and receiver operating characteristic (ROC) curve analyses

To determine the risk of death for children with TBI using the SOFA score, PCIS, GIF score on first day of admission and mean GIF score for first three days of admission, the above parameters were analyzed using binary multivariate logistic regression to establish a death prediction model. The overall accuracy rate of this model in predicting death was 90.9%. Among the four scoring methods, PCIS and mean GIF score for the first three days were included in the mortality prediction model, and the odds ratio (OR) values were > 1, indicating independent risk factors for death (Figure 1). The ROC analysis of the PCIS and the mean GIF score for the first three days showed that the area under the curve was 0.795 and 0.819, respectively, and that both had good predictive ability for the death of children with TBI (Figure 2).

Discussion

The major pathological change in the gastrointestinal tract following TBI is gastrointestinal mucosal ischemia, which usually manifests as stress ulcers and gastrointestinal bleeding. The incidence of stress ulcers in adult TBI patients is as high as 41-75%, and 17% of stress ulcers gradually develop into severe gastrointestinal bleeding in patients with severe TBI [8]. In this study, the incidence of stress ulcers in children with TBI was 48.5%. With the increase in TBI severity, the incidence of stress ulcers gradually increased, and the incidence in severe cases was 85.9%, suggesting that gastrointestinal mucosal ischemia is a common clinical complication of TBI children, a result similar to previous reports. After

major trauma, the nervous, endocrine, and immune systems are fully mobilized to activate numerous adaptive responses, and blood distribution can be readjusted to ensure the perfusion of vital organs, such as the heart and brain. Therefore, the gastrointestinal mucosa is in a state of hypoperfusion, and secondary ischemia, anoxia, acidosis, reperfusion injury, and accumulation of inflammatory mediators aggravate the structural damage to the gastrointestinal mucosa, resulting in the spread of focal small ulcers and further aggravation of gastrointestinal dysfunction, directly triggering the development of a series of intestinal events such as FI [9]. Based on whether FI was present, children were divided into two groups: GIF score <2 and GIF score ≥2. GSC scores, SOFA scores, PCIS, and mortality were significantly different between the two groups. Although the application of SOFA scores to children still has not reached a consensus [10], compared with the PCIS scoring system, which is widely accepted in the field of pediatrics, the two methods are consistent in assessing TBI severity. These results suggested that children with GIF scores ≥2 had poorer systemic pathological conditions and higher mortality. The causes of these findings were analyzed. It was found that the intestinal mucosa morphology had changed within a short time after trauma, including epithelial cell detachment and apoptosis, rupture of the villi, edema of interstitial tissue and the lamina propria, interruption of tight junctions, etc., and that the mucosal barrier had lost its protective function [11]. Additionally, the intestinal flora was completely disordered within a few hours after injury, and the microbial composition and relative abundance changed significantly. The number of beneficial microbiota decreased, the pathogenic flora, with relatively increased invasiveness and virulence, dominated the intestinal tract, and the diversity and stability of the microbial ecological system were destroyed. This dysbacteriosis also greatly affected gastrointestinal function. The infection risk and the mortality rate of pediatric patients were greatly increased [12].

Second, the main manifestations of gastrointestinal dysfunction after TBI are inadequate motility and impaired digestion and absorption of water and nutrients, leading to a negative N balance and malnutrition. The clinical manifestations are usually gastric retention, abdominal distension and high intra-abdominal pressure [13]. However, it is hard to provide an objective evaluation of gastrointestinal dysfunction in clinical practice because there is still a lack of quantitative standards to classify severity although there are numerous relevant research reports and many scholars have defined gastrointestinal dysfunction and continuously improved and unified the definition [14-15]. GIF scores provide a quantification evaluation for the varying degrees of gastrointestinal dysfunction and objectively and accurately reflect gastrointestinal functional status. In this study, 135 children with TBI (78.8%) had gastrointestinal dysfunction on the first day of admission, including 34 cases of insufficient feeding (20.6%), 60 cases of FI (36.4%), and 36 cases of IAH or ACS (21.8%), suggesting that gastrointestinal dysfunction in children with TBI is very common in clinical practice and should receive increased attention. Furthermore, according to GCS score, children were divided into severe, moderate and mild groups. The incidence of secondary gastrointestinal dysfunction increased with injury severity, and GIF score on the first day and the mean GIF score for the first three days were significantly different among the three groups, suggesting that TBI severity is directly related to GIF score, indicating that TBI causes gastrointestinal dysfunction. Because the children included in this study did not have primary gastrointestinal injury, the complex neuroendocrine network named brain-gut axis played an important

role in regulating gastrointestinal function. When the gastrointestinal tract is stimulated, such as with food and nutrients, children with TBI are unable to receive all types of information normally, due to direct impairment of the central nervous system. After misintegration, the autonomic nerves and the endocrine system transmit regulatory information to effector cells in the gastrointestinal tract, thereby resulting in regulatory dysfunction of the gastrointestinal mucosa, smooth muscle, blood vessels and glands [16-17]. Meanwhile, after damage to the central nervous system, many brain-gut peptides are secreted abnormally. They cannot function as neurotransmitters to exert normal information transmission and transfer effects between the brain and enteric nerves and effector cells, protect gastrointestinal tissues and the nerve plexus, and stimulate gastrointestinal motility. Various pathways in the brain-gut axis are blocked, and the important targets do not bind with brain-gut peptides, resulting in abnormal sphincter tone and smooth muscle contraction and slow gastric emptying and intestinal motility [18]. In addition, patients are in a state of stress after trauma, and emotions fluctuate greatly. The patients are affected by changes in the biopsychology and neuroendocrine systems. Gastrointestinal hormone levels and secretion are disordered, visceral sensitivity and epithelial permeability are increased, endotoxin is translocated, and intestinal flora are imbalanced [19-20]. Therefore, feedback from the gastrointestinal tract to the central nervous system is abnormal, causing gastrointestinal dysfunction.

In this study, the main indicator for evaluating the prognosis of children was mortality. Univariate analysis of the group of patients who died and the group of patients who survived showed that the clinical indicators GCS score, leucocyte count, Hb, Glu, lactate, ALB, PT, and APTT were significantly different between the two groups ($P < 0.05$), suggesting that the degree of brain injury, hematology, internal environment, and coagulation in the children who died were all worse than those in the children who survived; furthermore, the SOFA scores and PCIS for the children who died were higher than those for the children who survived. Meanwhile, the GIF score on the first day and mean GIF score for the first three days for the children who died were significantly higher than those for the children who survived, suggesting that the children who died had a worse gastrointestinal functional status than that of the children who survived. Although the GIF score can be used as an independent risk factor in the prediction of the risk of death in critically ill patients [21], it focuses on gastrointestinal function at the time of injury. However, the condition of a child develops and changes during hospitalization. The GIF score cannot be limited only on the first day. Therefore, the role of the GIF score on the first day in predicting death during the entire ICU stay is limited [22]. The mean GIF score for the first three days can be used to dynamically observe and assess changes in gastrointestinal dysfunction during peak disease development, providing better continuity. Researchers such as Reintam et al. [3] found that GIF scores had higher application value in the assessment of gastrointestinal function in critically ill patients; the mean GIF score for the first three days was more important in predicting death than was the GIF score on the first day. In this study, the GIF score on the first day, the mean GIF score for the first three days, the SOFA score, and the PCIS were used as test factors, and multivariate regression analysis was included to assess the predictive value of the four factors. The mean GIF score for the first three days was considered an independent risk factor. The reliability of the GIF score on the first day was relatively low, suggesting that although the GIF score can be used as an objective indicator, the effectiveness and accuracy of dynamic observation and

scoring are even higher; therefore, the mean GIF score for the first three days is better than the GIF score on the first day for evaluating the gastrointestinal function of children with TBI. One limitation of this study is that the SOFA score may be inapplicable to low-age infants and toddlers in terms of the items assessed [23-25], and it is easy to evaluate the normal or nonquiet state as the pathological state by mistake, leading to an increase in the SOFA score. In terms of predicting the risk of death, the accuracy and reliability of the SOFA score are not ideal. PCIS, as a recognized and commonly used effective means in the field of pediatric critical care, fully integrates the physiological and morbidity characteristics of children at different ages, more accurately, objectively and comprehensively reflects the disease condition, can be used to predict the risk of death and provides a reliable basis for the implementation of a rational clinical treatment plan [26-27]. In this study, the PCIS scoring system was also included in the death prediction equation. As two independent risk factors for the death prediction equation, the mean GIF score for the first three days had a predictive ability of death comparable to that for the PCIS, and when survival curves of the two score systems were generated, the areas under the curve were 0.795 and 0.819, respectively. They both had good predictive ability for risk of death, once again confirming the clinical significance of the GIF score in diagnosing gastrointestinal dysfunction in children with TBI and further emphasizing the importance of continuous monitoring and dynamic observation of the gastrointestinal status of children at different time points. Organ dysfunction in critically ill patients should be scored dynamically [28].

In summary, gastrointestinal dysfunction has a high incidence rate in children with TBI. The GIF score can accurately classify and objectively assess gastrointestinal status. A high GIF score is significantly correlated with ICU mortality. As an independent risk factor, the mean GIF score for the first three days has a higher predictive value for the prediction of ICU mortality; this result can provide guidance for the clinical evaluation and treatment of gastrointestinal dysfunction in children with TBI.

Abbreviations

TBI=traumatic brain injury; SICU=surgical intensive care unit; GCS=Glasgow Coma Scale; BMI =body mass index; CRP=C-reactive protein; Hb=hemoglobin; Hct=hematocrit; PCT=procalcitonin; PT=prothrombin time; APTT=activated partial thromboplastin time; SOFA=Sequential Organ Failure Assessment; PCIS=Pediatric Clinical Illness Score; GIF=gastrointestinal failure; FI=food intolerance; IAH=intra-abdominal hypertension; ACS=abdominal compartment syndrome; IAP= Intra-abdominal pressure; ROC=receiver operating characteristic.

Declarations

Conflict of interest statement:

Ying Zhou and other co-authors have no conflict of interest.

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Tables

Table 1 Admission and outcome parameters for GIF score <2 and GIF score ≥2

Parameters	GIF score <2	GIF score ≥2	p
Number (%)	69(41.8)	96(58.2)	
Age	4.82±4.23	4.96±3.64	t=0.23，p=0.82
BMI (kg/m^2)	17.11±3.37	16.56±3.36	t=-1.03，p=0.30
GCS	12.29±2.00	5.54±2.83	t=17.91，p=0.00
First day GIF score	0.49±0.50	2.38±0.49	t=-24.02，p=0.00
Mean GIF score for the first three days	0.31±0.36	2.07±0.38	t=-29.86，p=0.00
SOFA score	2.87±1.80	7.52±3.06	t=-12.23，p=0.00
PCIS score	94.09±6.17	75.02±11.24	t=13.96，p=0.00
Mortality (%)	0	41.67	X^2=37.95^2，p=0.00

Unit of measure provided in parentheses.

Table 2 Admission and outcome parameters for different degrees

Parameters	Severe	Moderate	Mild	p
Number (%)	92(55.8)	23(13.9)	50(30.3)	
Age	4.70±3.57	5.08±4.63	5.05±4.03	F=0.18 p=0.84
BMI (kg/m^2)	16.46±2.99	18.08±5.06	16.81±2.96	F=2.17 p=0.12
Stress ulcer (%)	85.90	4.30	0.00	X^2=116.48^2 p=0.00
First day GIF score	2.28±0.56	0.96±0.56	0.60±0.95	F=104.16 p=0.00
Mean GIF score for the first three days	2.02±0.44	0.57±0.38	0.42±0.75	F=165.62 p=0.00
Mortality (%)	43.5	0	0	X^2=41.90^2 p=0.00

Unit of measure provided in parentheses.

Table 3 Admission and outcome parameters for the Died and Survived groups

Parameters	Total	Died	Survived	p
Number (%)	165 (100)	40 (24.2)	125 (75.8)	
Male (%)	103 (62.4)	26 (25.2)	77 (74.8)	χ^2=0.15
Female (%)	62 (37.6)	14 (22.6)	48 (77.4)	P=0.70
Age	4.88±3.89	4.14±3.63	5.12±3.96	t=-1.38 p=0.17
BMI (kg/m^2)	16.79±3.36	16.70±3.23	16.82±3.42	t=-0.19 p=0.85
GCS	8.36±4.18	3.88±1.52	9.80±3.71	t=-14.45 p=0.00
leukocyte count (*10^9/L)	17.48±7.81	24.10±7.98	15.37±6.48	t=7.00 p=0.00
CRP (μg/ml)	13.25±24.13	13.03±23.90	13.32±24.29	t=-0.07 p=0.95
Hb (g/L)	100.16±22.49	91.93±25.55	102.80±20.86	t=-2.44 p=0.02
Hct (%)	30.34±6.86	28.44±7.54	30.96±6.54	t=–1.90 p=0.06
PCT (ng/ml)	2.49±6.07	3.58±7.72	2.14±5.44	t=1.10 p=0.28
Glu (mmol/L)	11.65±6.83	19.61±6.53	9.11±4.61	t=9.46 p=0.00
Lac (mmol/L)	6.40±5.87	15.03±4.72	3.64±2.62	t=14.56 p=0.00
ALB (g/L)	39.68±6.91	36.86±7.13	40.59±6.62	t=-3.05 p=0.00
POP (mOsm/kg·H2O)	299.38±11.87	302.69±15.26	298.32±10.41	t=-5.47 p=0.59
PT (s)	14.07±3.81	16.64±5.24	13.24±2.79	t=3.93 p=0.00
APTT (s)	42.53±27.99	60.49±34.85	36.79±22.73	t=4.03 p=0.00
SOFA score	5.58±3.47	9.68±2.51	4.26±2.62	t=11.50 p=0.00
PCIS	82.99±13.34	66.05±6.00	88.42±10.08	t=-17.09 p=0.00
First day GIF score	1.59±1.05	2.43±0.50	1.32±1.04	t=9.03 p=0.00

Mean GIF score for the first three days	1.33±0.95	1.55±0.83	1.06±0.93	t=2.95 p=0.00

Unit of measure provided in parentheses.

Figures

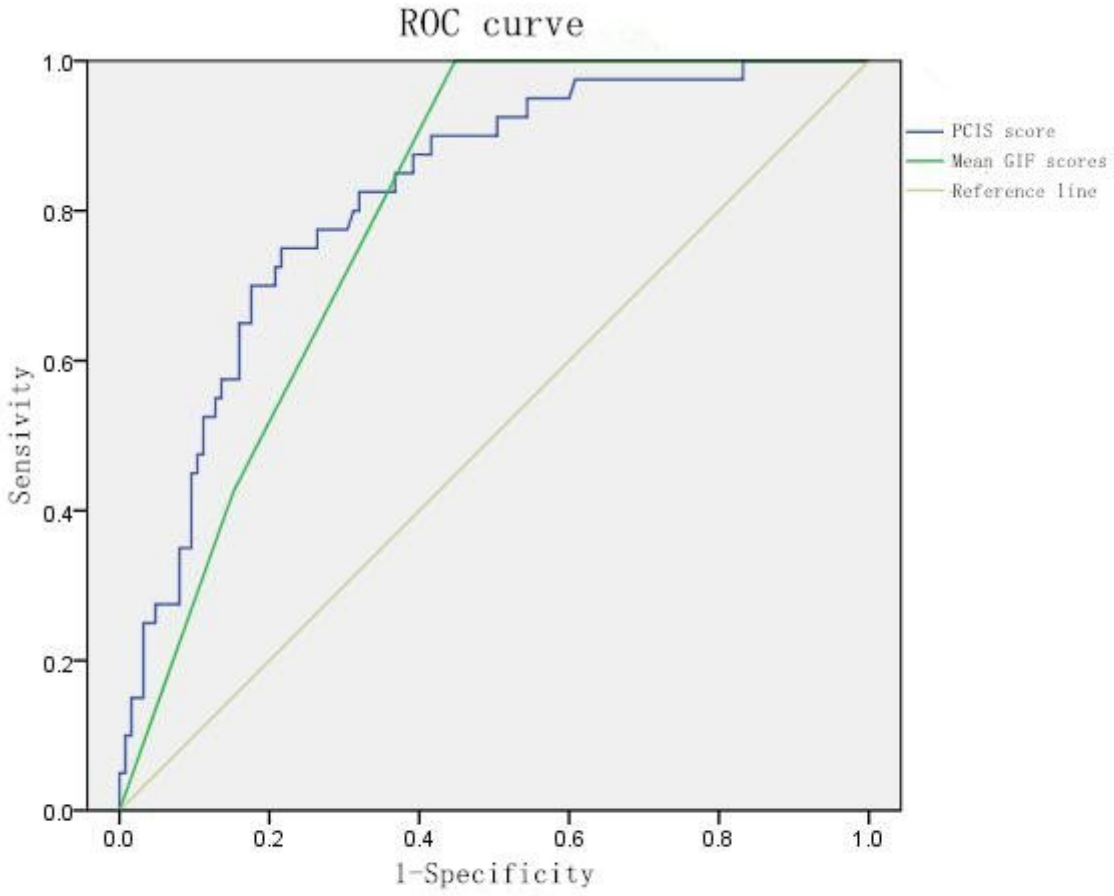

Figure 1

The ROC analysis of the PCIS and the mean GIF score for the first three days showed that the area under the curve was 0.795 and 0.819, respectively, and that both had good predictive ability for the death of children with TBI

Figure 1 Logistic regression analysis for different scores

	B	SE	Wals	df	Sig	Exp(B)	95% CI of EXP(B)	
							Lower limit	Upper limit
SOFA score	-0.14	0.17	0.70		0.40	0.87	0.63	1.20
PCIS	0.25	0.06	15.64	1	0.00	1.29	1.14	1.46
First day GIF score	-0.66	0.68	0.94	1	0.33	0.52	0.14	1.97
Mean GIF score for the first three days	1.58	0.61	6.63	1	0.01	4.83	1.46	16.02
constant	-17.96	5.87	9.37	1	0.00	0.00		

Figure 2

Among the four scoring methods, PCIS and mean GIF score for the first three days were included in the mortality prediction model, and the odds ratio (OR) values were > 1, indicating independent risk factors for death