

Role of Transcranial Doppler Ultrasound Pulsatility Index as a Predictor of Outcome in Moderate to Severe Brain Injury

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ABSTRACT

Background: Elevated intracranial pressure (ICP) is a critical determinant of outcome in patients with moderate to severe brain injury. While invasive monitoring remains the gold standard, Transcranial Doppler (TCD) ultrasound offers a promising non-invasive alternative. This study investigates the prognostic utility of TCD-derived Pulsatility Index (PI) alongside other neuro-monitoring parameters in predicting outcomes in brain-injured patients.

Methods: In this prospective observational study, 50 adult patients admitted to intensive care units with moderate to severe traumatic or spontaneous brain injury (GCS ≤ 13) were enrolled. TCD assessments were performed serially up to day 7, measuring PI, estimated ICP (eICP), and resistive index (RI). Invasive ICP monitoring was also conducted. The primary outcome was the Glasgow Outcome Scale-Extended (GOS-E) at 28 days, dichotomized into favorable (5–8) and unfavorable (1–4) outcomes. Secondary outcomes included ICU stay, MV duration, and mortality.

Results: PI showed significant associations with outcomes. On day 3, PI correlated negatively with GOS-E ($r = -0.288$, $P = 0.045$), while on day 7, it correlated positively with ICU stay ($r = 0.536$, $P < 0.001$) and ventilation duration ($r = 0.435$, $P = 0.004$). Mortality was significantly associated with elevated PI on days 1, 3, and 5 ($P < 0.01$). ROC analysis revealed day 7 RI had the highest prognostic accuracy (AUC = 0.769), followed by eICP (AUC = 0.754) and PI (AUC = 0.747). Multivariate regression identified Marshall score as the sole independent predictor of GOS-E ($P = 0.001$).

Conclusions: TCD-derived PI is a valuable non-invasive marker that correlates with clinical outcomes in brain-injured patients. Its integration with standard monitoring may enhance prognostication, especially when invasive methods are contraindicated.

KEYWORDS: Pulsatility Index, Transcranial Doppler, Intracranial Pressure, Brain Injury, Prognosis.

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INTRODUCTION

The concept of intracranial pressure (ICP) has evolved significantly since the late 18th century. In 1783, Scottish anatomist Alexander Monro provided the first detailed account of ICP, proposing that the brain resides within a rigid, incompressible skull, where blood volume must remain constant 1. He posited that a continuous venous outflow was necessary to accommodate the incoming arterial blood. This foundational theory was later substantiated by George Kellie, forming the basis of what became known as the Monro-Kellie doctrine. However, both early formulations failed to incorporate the cerebrospinal fluid (CSF), a critical component of intracranial volume regulation 2.

The role of CSF in intracranial dynamics was elucidated by François Magendie in 1842 through animal experiments, establishing the presence of a fluid-filled system in the brain. This understanding was further advanced by George Burrows, who incorporated CSF into the Monro-Kellie doctrine in 1846, emphasizing a compensatory relationship between the volumes of blood and CSF. Any increase in one component would be balanced by a reduction in another to maintain stable intracranial volume and pressure 3.

The modern interpretation of the Monro-Kellie hypothesis was shaped by Harvey Cushing in 1926. He recognized that in adults with closed cranial sutures, the total intracranial volume remains constant, comprising approximately 1300 mL of brain tissue, 110 mL of blood, and 60–80 mL of CSF in young adults, or slightly more in the elderly due to cerebral atrophy. When this delicate balance is disrupted—such as by trauma, hemorrhage, or edema—ICP rises, leading to secondary brain injury and poor neurological outcomes 4, 5.

ICP is now widely accepted as a critical parameter in the neurocritical care of patients with moderate to severe traumatic brain injury. It serves as a reflection of the volume and compliance of intracranial contents 6. While direct ICP measurement is invasive and not always feasible, non-invasive alternatives such as Transcranial Doppler (TCD) ultrasound offer valuable surrogate markers. Among these, the pulsatility index (PI), derived from cerebral blood flow velocity, has emerged as a promising indicator of intracranial compliance and cerebral perfusion dynamics 7.

Hence, the aim of this work is to determine the role of TCD-PI as a predictor of outcome in moderate to severe brain injury.

PATIENTS AND METHODS

Study design and setting

This prospective observational study was conducted at the Critical Care Medicine Units of Cairo University Hospital and Al-Amria General Hospital over a 12-month period from June 2022 to June 2023. The study was approved by the institutional ethics committee of the Faculty of Medicine, Cairo University. Informed consent was obtained from the next of kin of each enrolled patient prior to participation.

Study Population

Fifty adult patients (≥ 18 years) of both sexes, admitted to the ICU with moderate to severe brain injury were enrolled. Eligible cases included patients with cerebral hemorrhagic stroke or traumatic brain injury (TBI) who presented post-resuscitation with a Glasgow Coma Scale (GCS) score ≤ 13 . Patients were excluded if they were expected to die within the first 24 hours post-injury, had systolic blood pressure < 90 mmHg, oxygen saturation $< 92\%$, were pregnant, or had conditions impeding TCD insonation such as surgical dressings, soft tissue hematomas, or skull base fractures with CSF leak. Patients who experienced cardiac arrest (in- or out-of-hospital) before performing TCD, or those with severe extracranial injuries, were also excluded.

Clinical Assessment and Management

Following enrollment, each patient underwent initial stabilization, including assessment of airway, breathing, and circulation. Supportive measures such as oxygen therapy, endotracheal intubation, intravenous fluid resuscitation, or vasopressor administration were applied as needed. A detailed medical history was obtained, followed by a thorough physical examination. All patients received standard management for TBI as per the American Association of Neurological Surgeons guidelines, and for spontaneous hemorrhagic stroke as per the American Heart Association/American Stroke Association recommendations.

Laboratory and Radiologic Investigations

Baseline investigations included complete blood count, renal and liver function tests, arterial blood gases (including $\text{PaO}_2/\text{FiO}_2$), and routine chest X-ray and abdominal ultrasound. Non-contrast brain CT scans were performed on admission (Day 1), repeated at 48 hours (Day 3), and again on Day 5 or as clinically indicated. Radiological classification was performed using the Marshall CT classification and Rotterdam CT scoring systems.

Monitoring and Follow-Up

Vital signs including body temperature, heart rate, respiratory rate, blood pressure, and oxygen saturation were continuously monitored at the bedside. Intake and output were documented. Neurological status was assessed daily for 14 days using the GCS. Patient morbidity and mortality were also recorded.

Intracranial Pressure and TCD Assessment

Invasive ICP monitoring was conducted via a ventricular catheter connected to an external pressure monitoring and drainage system. ICP readings were documented every other day until the catheter was removed. TCD ultrasonography was performed using the GE Healthcare Venue Go™ device with a 3S phased array probe via the transtemporal window. TCD was first conducted within 24 hours of ICU admission after hemodynamic and respiratory stabilization and then repeated every other day up to Day 7.

TCD measurements were obtained from the middle cerebral artery (MCA) at a depth of 40–65 mm. Peak systolic velocity (PSV), end-diastolic velocity (EDV), and mean flow velocity (mFV) were recorded across at least ten cardiac cycles. The **PI** was calculated using the formula: $\text{PI} = (\text{PSV} - \text{EDV}) / \text{mFV}$. The **estimated ICP (eICP)** was derived using the Bellner formula: $\text{eICP} = (11.1 \times \text{PI}) - 1.43$ mmHg. The **Resistance Index (RI)** was also calculated: $\text{RI} = (\text{PSV} - \text{EDV}) / \text{PSV}$.

At the time of each TCD exam, concurrent data including arterial PaCO_2 (from ABG within 15 minutes), blood pressure (systolic, diastolic, mean), heart rate, temperature, and GCS were collected.

Outcome Measures

The **primary outcome** was the Glasgow Outcome Score Extended (GOSE) at 28 days. For statistical modeling, GOSE was dichotomized into favorable (scores 5–8) versus unfavorable (scores 1–4) outcomes. **Secondary outcomes** included the duration of mechanical ventilation, length of hospital stay, ICU mortality, and overall, in-hospital mortality.

Statistical methods

Data management and statistical analysis were done using SPSS version 27 (IBM, Armonk, New York, United States). Quantitative data were assessed for normality using the Shapiro-Wilk test and direct data visualization methods. According to normality, quantitative data were summarized as means and standard deviations or medians and ranges or IQR. Categorical data were summarized as numbers and percentages. Quantitative data were compared between the groups using independent t Test and Mann-Whitney U Test for parametric and non-parametric variables, respectively. Categorical data were compared using the Chi-square or Fisher's exact test. Spearman's rank correlation assessed associations between outcome measures (GOS-E, ICU stay, MV duration) and neuro-monitoring parameters (Marshall scale, PI, RI, eICP, invasive ICP) across time points. ROC curve analysis evaluated the predictive accuracy of selected parameters for prolonged MV (> 14 days) and mortality, reporting AUC, cutoff, sensitivity, specificity, PPV, and NPV. Linear regression analysis (univariate and stepwise multivariate) identified independent predictors of GOS-E, presenting coefficients (B), 95% CI. All statistical tests were two-sided. P-values less than 0.05 were considered significant.

RESULTS

The median age was 34 years (IQR: 26–47), with a predominant male representation (84%). Comorbidities were present in a subset of patients, with diabetes mellitus (32%) and hypertension (24%) being the most common. The primary cause of injury was trauma (76%), while spontaneous causes accounted for 24%. Regarding vital signs, the mean heart rate was 111.1 ± 6.80 bpm, mean arterial pressure was 81.40 ± 4.92 mmHg, respiratory rate was 16.80 ± 2.89 breaths/min, and mean body temperature was $37.27 \pm 0.22^\circ\text{C}$. Arterial blood gas analysis showed a mean PaCO_2 of 39.48 ± 3.39 mmHg and a mean PaO_2 of 95.74 ± 20.26 mmHg. Neurologically, the mean GCS was 9.10 ± 1.97 and the mean FOUR score was 11.32 ± 2.57 . Table 1

Table 1: General characteristics of the studied patients (n = 50)

General characteristics		
Age (years)	Median (IQR)	34 (26 - 47)
Gender		
Male	n (%)	42 (84)
Female	n (%)	8 (16)
Comorbidities		
DM	n (%)	16 (32)
Hypertension	n (%)	12 (24)
IHD	n (%)	3 (6)
HF	n (%)	1 (2)
Liver disease	n (%)	2 (4)
Kidney disease	n (%)	1 (2)
Cause of injury		
Spontaneous	n (%)	12 (24)
Trauma	n (%)	38 (76)
Vital signs		
HR (bpm)	Mean $\pm$ SD	111.1 ± 6.80
MAP (mmHg)	Mean $\pm$ SD	81.40 ± 4.92
RR (breaths/min)	Mean $\pm$ SD	16.80 ± 2.89
Temperature ($^\circ\text{C}$)	Mean $\pm$ SD	37.27 ± 0.22
ABG		
PaCO_2 (mmHg)	Mean $\pm$ SD	39.48 ± 3.39
PO_2 (mmHg)	Mean $\pm$ SD	95.74 ± 20.26
GCS	Mean $\pm$ SD	9.10 ± 1.97
Four score	Mean $\pm$ SD	11.32 ± 2.57

n: number, IHD: Ischemic heart disease, HF: Heart failure, HR: Heart rate, MAP: Mean arterial pressure, RR: Respiratory rate, ABG: Arterial blood gases, PaCO_2 : Partial pressure of carbon dioxide, PaO_2 : Partial pressure of oxygen, GCS: Glasgow Coma Scale, FOUR: Full Outline of UnResponsiveness score, $^\circ\text{C}$: degrees Celsius.

The mean Marshall scale showed a gradual decline over time, decreasing from 3.70 on day 1 to 3.51 on day 3 and 3.28 on day 5. Similarly, mean PI initially rose slightly from 1.17 on day 1 to 1.18 on day 3, followed by a steady decrease to 1.12 on day 5 and 1.06 on day 7. The mean eICP also declined progressively from 15.05 mmHg on day 1 to 14.81, 13.06, and 10.53 mmHg on days 3, 5, and 7, respectively. RI peaked at day 3 (0.72) after starting at 0.61 on day 1, then dropped to 0.65 on day 5 and returned to 0.61 by day 7. A similar declining pattern was observed in invasive ICP, which decreased from 11.40 mmHg on day 1 to 11.16, 10.11, and 9.91 mmHg on days 3, 5, and 7, respectively. Figure 1 A-E

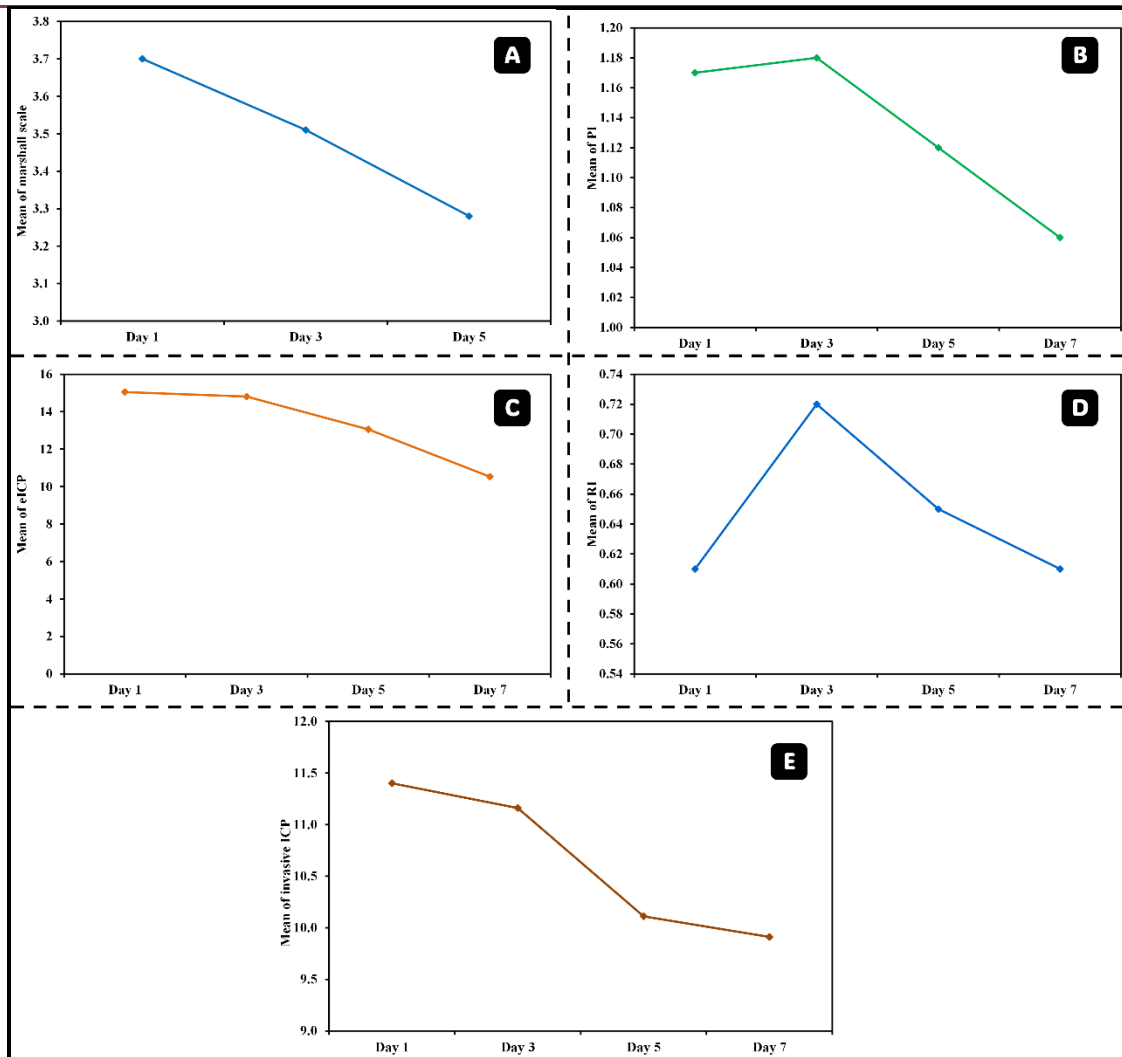


Figure 1: Mean A) Marshall CT score, B) PI, C) eICP, D) RI, and E) ICP

Table 2: Outcomes in the studied patients (n = 50)

Outcomes		
GOS-E	Median (IQR)	5.0 (3.0 - 7.0)
Poor (1 - 4)	n (%)	23 (46)
Good (5 - 8)	n (%)	27 (54)
Length of ICU stay	Median (IQR)	19.0 (12.0 - 26.0)
Duration of MV	Median (IQR)	8.0 (3.0 - 13.0)
Mortality		
Yes	n (%)	7 (14)
No	n (%)	43 (86)

n: number, GOS-E: Extended Glasgow Outcome Scale, ICU: Intensive Care Unit, MV: Mechanical ventilation, IQR: Interquartile range. A significant positive correlation was observed between GOS-E and GCS ($r_s = 0.320$, $P = 0.024$), as well as between GOS-E and FOUR score ($r_s = 0.850$, $P < 0.001$). Figure 2 A-B

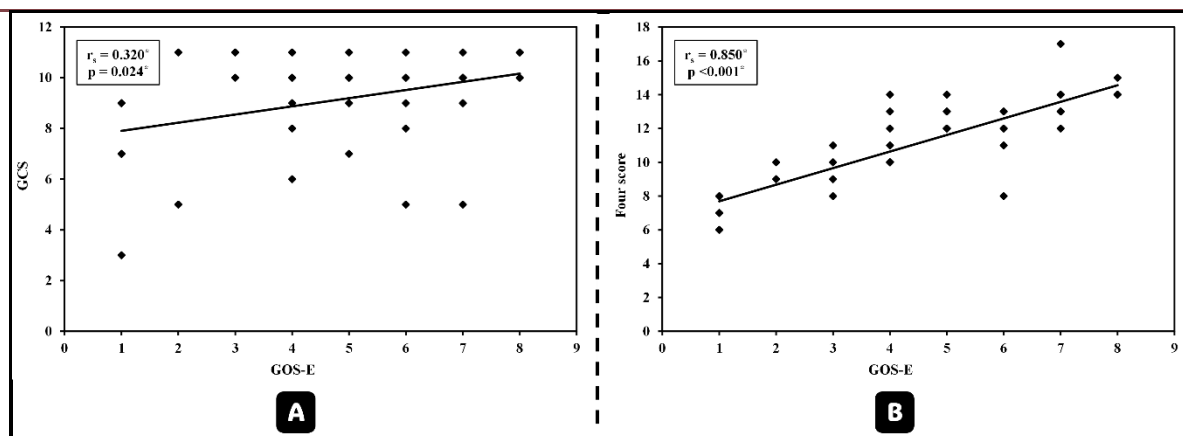


Figure 2: Correlation between outcome score (GOS-E) and both GCS (A) and FOUR score (B) on day 1

Marshall scale on days 1, 3, and 5 revealed significant negative correlations with GOS-E ($r = -0.598, -0.677$, and -0.587 respectively; all $P < 0.001$), and significant positive correlations with duration of MV ($r = 0.281, 0.309$, and 0.34 respectively; all $P < 0.05$). No significant correlations were observed with ICU stay duration. PI showed a significant negative correlation with GOS-E only on day 3 ($r = -0.288, P = 0.045$) and significant positive correlations with ICU stay ($r = 0.536, P < 0.001$) and MV duration ($r = 0.435, P = 0.004$) on day 7. Table 3

RI revealed significant positive correlations with ICU stay and MV duration on days 1, 5, and 7 (r ranging from 0.299 to 0.522 ; $P < 0.05$), while no significant correlations were noted with GOS-E. eICP showed significant negative correlations with GOS-E on days 1 and 3 ($r = -0.321$ and -0.316 , respectively; $P < 0.05$), and significant positive correlations with ICU stay and MV duration on days 3, 5, and 7 ($r = 0.306$ – 0.491 ; $P < 0.05$). Table 3

Invasive ICP correlated negatively with GOS-E on days 1 and 3 ($r = -0.425$ and -0.466 ; $P = 0.002$ and 0.001 , respectively) and showed significant positive correlations with ICU stay and MV duration on days 5 and 7 ($r = 0.308$ – 0.523 ; $P < 0.05$). Table 3

Table 3: Correlation between Marshall Scale, PI, RI, eICP, and invasive ICP with length of ICU stay, duration of MV, and GOS-E on different days of assessment.

		ICU stay length		MV duration		GOS-E	
	n	rs	p	rs	p	rs	p
Marshall scale							
Day 1	50	0.234	0.102	0.281	0.048*	-0.598	<0.001*
Day 3	49	0.136	0.352	0.309	0.031*	-0.677	<0.001*
Day 5	47	0.147	0.323	0.34	0.019*	-0.587	<0.001*
PI							
Day 1	50	0.086	0.551	0.13	0.367	-0.128	0.375
Day 3	49	0.12	0.411	0.193	0.183	-0.288	0.045*
Day 5	47	0.203	0.172	0.176	0.237	-0.078	0.601
Day 7	43	0.536	<0.001*	0.435	0.004*	0.028	0.861
RI							
Day 1	50	0.34	0.016*	0.309	0.029*	-0.257	0.072
Day 3	49	-0.161	0.269	-0.123	0.4	-0.278	0.053
Day 5	47	0.315	0.031*	0.299	0.041*	-0.224	0.131
Day 7	43	0.522	<0.001*	0.444	0.003*	-0.024	0.88
eICP							
Day 1	50	0.195	0.175	0.115	0.428	-0.321	0.023*
Day 3	49	0.306	0.032*	0.262	0.069	-0.316	0.027*
Day 5	47	0.329	0.024*	0.322	0.027*	-0.223	0.132
Day 7	43	0.491	0.001*	0.406	0.007*	0.012	0.941
Invasive ICP							
Day 1	50	0.122	0.398	0.213	0.137	-0.425	0.002*
Day 3	49	0.234	0.105	0.358	0.012*	-0.466	0.001*
Day 5	47	0.308	0.035*	0.406	0.005*	-0.215	0.147
Day 7	43	0.523	<0.001*	0.431	0.004*	0.031	0.845

n: number, rs: Spearman correlation coefficient, PI: Pulsatility Index, RI: Resistive Index, eICP: Estimated Intracranial Pressure, ICP: Intracranial Pressure, GOS-E: Extended Glasgow Outcome Scale, ICU: Intensive Care Unit, MV: Mechanical Ventilation, *: Significant P-value.

Patients who died exhibited significantly lower GCS scores (7.0 [3.0–9.0] vs. 10.0 [5.0–11.0], $P = 0.004$) and FOUR scores (7.0 [6.0–8.0] vs. 12.0 [8.0–17.0], $P < 0.001$) compared to survivors. Non-survivors also had significantly higher Marshall scale scores on day 1 (6.0 [3.0–6.0] vs. 4.0 [1.0–5.0], $P = 0.010$), day 3 (5.0 [4.0–5.0] vs. 3.0 [1.0–5.0], $P = 0.007$), and day 5 (4.5 [4.0–6.0] vs. 3.0 [1.0–5.0], $P = 0.038$).

Furthermore, PI values were significantly elevated in non-survivors on day 1 (2.70 [0.70–3.00] vs. 0.80 [0.70–3.20], $P = 0.009$), day 3 (2.50 [0.90–2.90] vs. 1.00 [0.70–2.80], $P = 0.002$), and day 5 (2.75 [1.0–3.0] vs. 0.90 [0.70–2.90], $P = 0.003$). Similarly, RI values were significantly higher in non-survivors across day 1 ($P < 0.001$), day 3 ($P = 0.012$), and day 5 ($P = 0.042$). Notably, both eICP and invasive ICP were markedly elevated in patients who died compared to survivors at all measured time points (all $P < 0.01$).

Table 4: GCS, FOUR score, Marshall scale, PI, RI, eICP, and invasive ICP between survivors and non-survivors

	Mortality		P-value
	Yes (n = 7)	No (43)	
GCS	7.0 (3.0 - 9.0)	10.0 (5.0 - 11.0)	0.004*
Four score	7.0 (6.0 - 8.0)	12.0 (8.0 - 17.0)	<0.001*
Marshall Scale			
Day 1	6.0 (3.0 - 6.0)	4.0 (1.0 - 5.0)	0.010*
Day 3	5.0 (4.0 - 5.0)	3.0 (1.0 - 5.0)	0.007*
Day 5	4.50 (4.0 - 6.0)	3.0 (1.0 - 5.0)	0.038*
PI			
Day 1	2.70 (0.70 - 3.0)	0.80 (0.70 - 3.20)	0.009*
Day 3	2.50 (0.90 - 2.90)	1.0 (0.70 - 2.80)	0.002*
Day 5	2.75 (1.0 - 3.0)	0.90 (0.70 - 2.90)	0.003*
RI			
Day 1	0.72 (0.63 - 1.0)	0.57 (0.38 - 0.78)	<0.001*
Day 3	0.83 (0.74 - 1.0)	0.72 (0.53 - 0.83)	0.012*
Day 5	0.90 (0.57 - 1.0)	0.61 (0.49 - 0.83)	0.042*
eICP			
Day 1	31.90 (17.0 - 38.0)	8.70 (6.70 - 39.0)	<0.001*
Day 3	31.90 (14.8 - 54.3)	9.40 (6.70 - 31.20)	<0.001*
Day 5	26.45 (14.9 - 31.9)	10.0 (6.70 - 31.20)	0.002*
Invasive ICP			
Day 1	28.90 (18.0 - 42.0)	7.0 (6.0 - 35.0)	<0.001*
Day 3	25.0 (15.0 - 29.0)	9.0 (6.0 - 25.0)	<0.001*
Day 5	21.0 (10.0 - 31.0)	9.0 (6.0 - 19.0)	<0.001*

n: number, GCS: Glasgow Coma Scale, FOUR: Full Outline of UnResponsiveness score, PI: Pulsatility Index, RI: Resistive Index, eICP: Estimated Intracranial Pressure, ICP: Intracranial Pressure, *: Significant P-value.

ROC curve analysis was performed to assess the prognostic performance of various parameters on day 7. RI showed the highest predictive ability with a significant AUC of 0.769 (95% CI: 0.617–0.921), suggesting good prognostic accuracy. The best cutoff was >0.5613 , yielding a sensitivity of 91.67%, specificity of 58.06%, PPV of 45.8%, and NPV of 94.7%. eICP followed with an AUC of 0.754 (95% CI: 0.601–0.907), and at a cutoff >8.5 , it showed sensitivity of 91.67%, specificity of 58.06%, PPV of 45.8%, and NPV of 94.7%. Invasive ICP and PI also demonstrated significant predictive values with AUCs of 0.743 and 0.747, respectively. For both, the best cutoffs were >8 and >0.9 , respectively, with sensitivity of 83.33%, specificity of 64.52%, PPV of 47.6%, and NPV of 90.9%. Figure 3

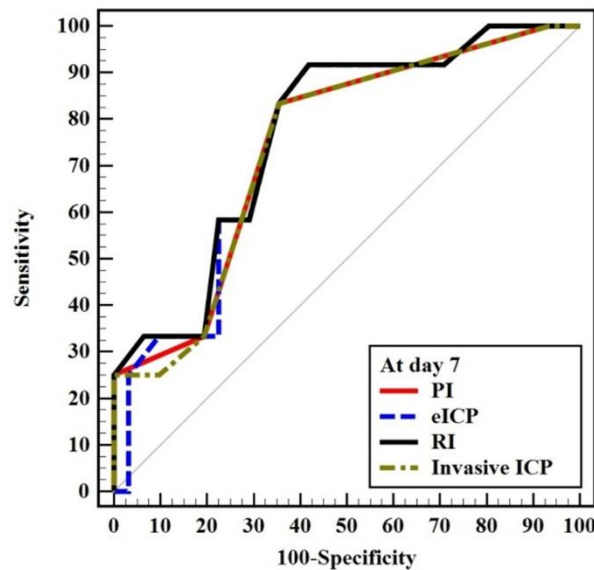


Figure 3: ROC curve analysis of different parameters on day 7 to predict prolonged duration of mechanical ventilation (>14 days) among patients (n = 12 vs. 31)

ROC curve analysis demonstrated that invasive ICP consistently showed the highest prognostic accuracy for predicting mortality across all time points. On day 1, invasive ICP exhibited an excellent AUC of 0.975 (95% CI: 0.937–1.000), followed by RI (AUC = 0.894), eICP (AUC = 0.885), and GCS (AUC = 0.831). PI and Marshall scale also showed good performance (AUCs = 0.802 and 0.796, respectively). Figure 4-A

On day 3, invasive ICP remained the strongest predictor with an AUC of 0.973 (95% CI: 0.931–1.000), followed by eICP (AUC = 0.942), PI (AUC = 0.874), and Marshall scale (AUC = 0.833). RI and GCS also maintained acceptable discriminatory performance. Figure 4-B

By day 5, invasive ICP continued to demonstrate outstanding prognostic value (AUC = 0.965, 95% CI: 0.897–1.000) with 100% specificity and PPV. eICP and PI followed with AUCs of 0.930 and 0.913, respectively, while RI and Marshall scale remained moderately predictive (AUCs = 0.808 and 0.811). Figure 4-C

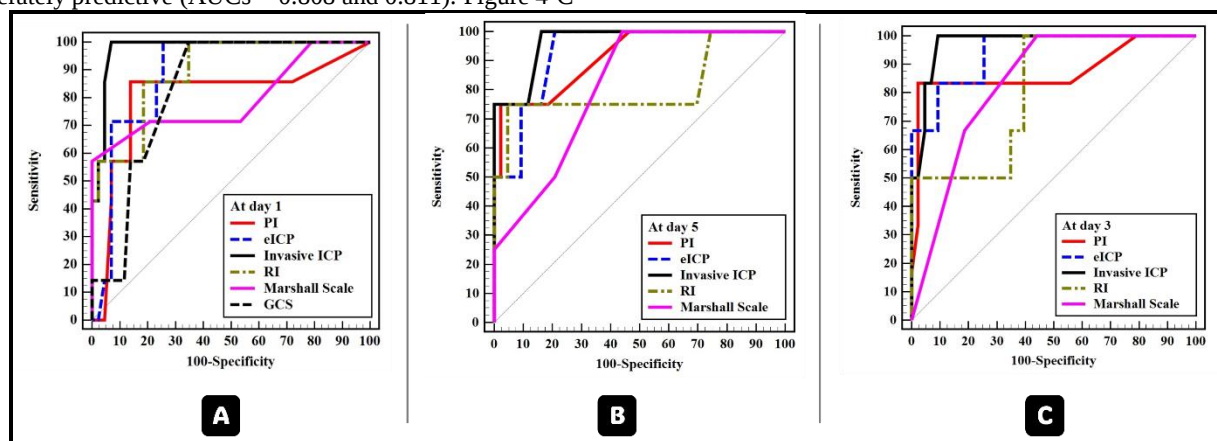


Figure 4: ROC curves for days A) 1, B) 3, and C) 5 to predict mortality

In the multivariate linear regression analysis, Marshall scale at day 1 was the only independent predictor of GOS-E. Each unit increase in Marshall score was associated with a 0.903-point decrease in GOS-E score (B = -0.903, 95% CI: -1.403 to -0.403, P = 0.001). Table 5

Table 5: Linear regression analysis for prediction of GOS-E

	Univariate	Multivariate	B (95% CI)	P-value
	B (95% CI)	P-value		
Age (years)	-0.035 (-0.082 - 0.012)	0.141		
Presence of comorbidities	-1.200 (-2.445 - 0.045)	0.059		
Cause of injury				
Spotaneous	-0.373 (-1.878 - 1.132)	0.621		
Trauma	0.373 (-1.132 - 1.878)	0.621		
Marshall scale at day 1	-1.075 (-1.475 - -0.674)	<0.001*	-0.903 (-1.403 - -0.403)	0.001*
PI at day 1	-0.821 (-1.616 - -0.025)	0.043*	-0.247 (-1.168 - 0.675)	0.592
RI at day 1	-7.694 (-12.895 - -2.494)	0.005*	-0.007 (-7.692 - 7.678)	0.999
eICP at day 1	-0.070 (-0.129 - -0.011)	0.021*	-0.031 (-0.101 - 0.040)	0.389
Invasive ICP at day 1	-0.117 (-0.173 - -0.060)	<0.001*	-0.022 (-0.112 - 0.067)	0.617

GOS-E: Extended Glasgow Outcome Scale, B: Regression coefficient, CI: Confidence Interval, PI: Pulsatility Index, RI: Resistive Index, eICP: Estimated Intracranial Pressure, ICP: Intracranial Pressure, *: Significant P-value.

DISCUSSION

Traumatic and spontaneous brain injuries remain a leading cause of mortality and long-term disability in neurocritical care. Elevated ICP is a pivotal determinant of clinical outcomes, yet its invasive monitoring carries procedural limitations [8]. Non-invasive surrogates such as the TCD-derived PI, RI, and eICP have emerged as promising tools [9].

In our study, we demonstrated that elevated PI, RI, eICP, and invasive ICP significantly correlated with prolonged ICU stay, extended mechanical ventilation, lower GOS-E scores, and increased mortality. On day 7, $PI > 0.9$ predicted prolonged mechanical ventilation with 83.3% sensitivity and 64.5% specificity. Invasive ICP > 20 mmHg showed excellent diagnostic accuracy for mortality on day 1 (AUC = 0.975), while PI and eICP yielded comparable prognostic value (AUCs = 0.802 and 0.885, respectively). Only the Marshall CT scale at day 1 remained an independent predictor of outcome in multivariate regression.

Regarding mortality, supporting our findings, Bellner et al. [10] reported a strong correlation between PI and ICP ($r = 0.938$, $P < 0.001$), with elevated PI associated with increased mortality. Similarly, Chandankhede et al. [11] found that patients with mean ICP > 20 mmHg had significantly higher mortality (47%) compared to those below this threshold (17%, $P < 0.0001$). Mei et al. [12] also demonstrated that elevated PI values were predictive of hospital mortality. These results reinforce the prognostic relevance of PI and ICP in early mortality stratification.

Regarding functional outcome (GOS-E), in line with our results, Splavski et al. [13] reported a significant negative correlation between PI and GOS-E ($r = -0.722$; $P < 0.01$), indicating that a one-unit increase in PI led to an expected 2.6-point drop in GOS-E. Chandankhede et al. [11] similarly observed that higher ICP values were associated with lower GOS-E scores at 2 weeks and 2 months. These findings corroborate the inverse relationship between cerebral hemodynamic compromise and long-term neurological recovery.

Regarding MV duration, Haddad et al. [14] showed that elevated ICP significantly prolonged ventilation duration (coefficient = 5.66 days; 95% CI: 3.45–7.88; $P < 0.0001$), consistent with our observation that higher PI and RI values were associated with extended ventilator support. Although few studies specifically correlate PI with ventilation time, Gura et al. [15] highlighted that 35% of neurocritical patients required tracheostomy due to prolonged respiratory dependence, indirectly supporting this association.

Regarding ICU length of stay, our findings are supported by Haddad et al. [14], who found that each unit increase in ICP was linked to an additional 5.62 days in ICU (95% CI: 3.27–7.98; $P < 0.0001$). In contrast, Lazaridis et al. [16] did not find a significant association between ICP and ICU stay ($P = 0.4$), potentially due to their higher mean ICP (19.8 ± 11.2 mmHg) and differing patient severity, which may have led to earlier deaths or discharges.

Regarding correlation between PI and invasive ICP, consistent with our data, Voulgaris et al. [17] identified a strong positive correlation between PI and invasive ICP ($r = 0.64$; $P < 0.001$) in severe TBI patients. Rasulo et al. [18] found 100% sensitivity of TCD-derived ICP in identifying invasive ICP > 20 mmHg, supporting the accuracy of PI and eICP. Similarly, Kazimierska et al. [19] found significant correlations between mean ICP and Marshall CT scores ($r = 0.20$; $P = 0.023$), validating our multimodal correlation model.

Regarding RI correlations with ICP, supporting our observations, Klingelhöfer et al. [20] reported that RI significantly increased with rising ICP, with a correlation coefficient of 0.873 ($P < 0.001$). Likewise, Goraj et al. [21] found a significant correlation between RI and intraparenchymal ICP ($r = 0.614$; $P < 0.001$). Despite being less extensively studied than PI, these results affirm the potential of RI as a secondary non-invasive marker for intracranial hypertension.

Regarding Marshall CT scale correlations, our results resonate with Goswami et al. [22], who reported that Marshall CT scores ≥ 4 significantly predicted mortality ($P = 0.0027$). Elkbuli et al. [23] also found higher mortality in TBI patients with Marshall scores ≥ 4 ($P < 0.05$). Furthermore, Mahmoud et al. [14] observed strong correlations between Marshall scale and GOS-E, reinforcing its role as an early radiological predictor of poor prognosis.

Regarding predictive accuracy of TCD indices, Dokponou et al. [24] showed that TCD-derived ICP had a sensitivity of 92.3% and specificity of 70% for TBI management, while Bouzat et al. [25] found TCD thresholds had 80% sensitivity and 79% specificity for predicting neurological worsening. These findings are in close agreement with our results where PI and eICP showed sensitivity $> 83\%$ and specificity ranging from 58% to 64%, reinforcing their utility as reliable non-invasive prognostic tools.

This study has several limitations. First, the sample size was relatively small and drawn from two centers, which may limit the generalizability of the findings. Second, although TCD was performed by experienced operators, its inherent operator-dependence may introduce variability. Third, we did not assess the inter-rater reliability of TCD-derived parameters or account for potential confounding factors such as sedation depth or cerebral autoregulation status. Finally, the follow-up period was limited to 28 days, precluding evaluation of long-term functional outcomes beyond that point.

CONCLUSIONS

TCD-derived PI is a valuable non-invasive marker that correlates with clinical outcomes in brain-injured patients. Its integration with standard monitoring may enhance prognostication, especially when invasive methods are contraindicated.

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