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ORIGINAL RESEARCH

Aspartate aminotransferase to platelet ratio index as a predictor of mortality in traumatic brain injury

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Abstract

Background: The Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) is traditionally used to assess liver disease but may have prognostic value in other clinical contexts. This study evaluates APRI's ability to predict mortality in traumatic brain injury (TBI) patients. **Methods**: This retrospective cohort study included 6252 adult TBI patients (Head/Neck Abbreviated Injury Scale (AIS) $\geq$3) from the Trauma Registry System at Kaohsiung Chang Gung Memorial Hospital, covering admissions from 1998 to 2023. APRI was calculated at admission using aspartate aminotransferase (AST) levels and platelet counts. The area under the receiver operating characteristic curve (AUC) was used to evaluate APRI's predictive accuracy for mortality, and an optimal APRI cutoff was determined using Youden's index. Patients were divided into high and low APRI groups based on this threshold, with mortality and other clinical outcomes compared. **Results**: Among the cohort, 5658 patients survived, and 594 patients died. APRI demonstrated moderate predictive accuracy for mortality, with an AUC of 0.648. The optimal cutoff for APRI was 0.59, yielding a sensitivity of 63.6% and specificity of 60.3%. Patients with APRI $\geq$0.59 had significantly higher mortality (14.5% *vs.* 5.9%, $p < 0.001$) and longer hospital stays (15.9 *vs.* 12.0 days, $p < 0.001$). After adjusting for confounders, elevated APRI remained independently associated with increased mortality (Adjusted odds ratio (AOR) = 1.67, 95% Confidence interval (CI): 1.37–2.02, $p < 0.001$). This association was strongest in patients with severe injury, indicated as Injury Severity Score (ISS) $\geq$25), where APRI $\geq$0.59 yielded an AOR of 1.74 (95% CI: 1.36–2.22, $p < 0.001$). **Conclusions**: These results indicate that an elevated APRI is a significant predictor of in-hospital mortality in moderate and severe TBI cases even after adjustment for confounders, whereas its prognostic value is minimal in patients with minor injuries. However, its predictive power remains limited, and APRI should be used alongside existing trauma scoring systems for comprehensive risk assessment, with prospective validation recommended. Prospective studies are recommended to validate APRI's role in TBI and explore combined biomarker approaches to enhance predictive accuracy.

Keywords

Trauma; Traumatic brain injury (TBI); Aspartate aminotransferase-to-platelet ratio index (APRI); Prognosis; Mortality

1. Introduction

Traumatic Brain Injury (TBI) is a major cause of morbidity and mortality worldwide and accounts for approximately 30% of all injury-related deaths in the United States [1]. Outcomes after TBI are highly variable, ranging from complete recovery to fatality [2]. Established predictors of poor outcomes include advanced age, severe initial neurological impairment (*e.g.*, low Glasgow Coma Scale (GCS)), and markers of traumatic shock or coagulopathy. In particular, post-traumatic coagulopathy (such as thrombocytopenia) has been linked to worse prognosis in TBI patients [3]. Likewise, TBI can trigger systemic inflammatory responses that affect peripheral organs, as studies show that acute TBI is often accompanied by hepatic injury, evidenced by elevated liver enzymes within hours of injury [1]. These systemic effects of TBI suggest that laboratory biomarkers reflecting multi-organ stress may have prognostic value.

The Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) is a simple index originally developed to assess liver fibrosis in hepatitis patients. APRI is calculated from routine blood tests (aspartate aminotransferase (AST) level

and platelet count) and was initially validated for predicting hepatic fibrosis severity. Interestingly, recent evidence indicates that APRI may also reflect the severity of systemic illnesses. It has been identified as an independent risk factor for mortality in various critical conditions such as COVID-19, severe malaria, dengue fever, and sepsis [4]. APRI has been recognized for its potential to reduce reliance on invasive procedures like liver biopsy in staging liver fibrosis, especially in resource-limited settings [5]. In critical care settings, an elevated AST level often signals widespread tissue injury or shock, while a low platelet count can indicate consumption coagulopathy or severe inflammatory response. APRI combines these two parameters, potentially serving as a composite marker of systemic insult. Over the years, APRI's diagnostic and prognostic applications have expanded beyond its original scope, finding utility across diverse clinical scenarios [4, 6–10].

TBI presents unique pathophysiological challenges that induce systemic inflammatory responses, coagulopathy, and liver dysfunction, all of which may impact APRI values [11–13]. While APRI has been used to predict outcomes in liver diseases [14–16], inflammatory conditions like COVID-19 [7], and after total hip arthroplasty and arthroscopic rotator cuff repair [10, 17], its role in TBI outcomes has not been fully studied. To our knowledge, only limited data exist on liver-related indices in TBI prognosis. A recent study by Wang *et al.* [18] noted that TBI patients who did not survive had significantly higher APRI values and related liver fibrosis scores compared to survivors. The fibrosis-4 (FIB-4) index, which is based on AST and includes age and alanine transaminase (ALT), became a reliable predictor of death in that group [18]. However, APRI itself was not the primary focus, leaving a knowledge gap as to whether it independently predicted TBI mortality. Given AST's sensitivity to these systemic effects, it may serve as a valuable biomarker for early intervention in TBI, with further research needed to clarify its prognostic value in TBI and utility in early risk stratification.

The present study, therefore, aimed to determine whether APRI on admission is a significant predictor of mortality in patients with TBI. We conducted a retrospective cohort analysis to evaluate the association of APRI with in-hospital mortality after TBI while controlling for known risk factors. We hypothesized that elevated APRI at hospital admission would be associated with higher mortality, reflecting the burden of systemic injury in TBI.

2. Methods

2.1 Patient enrollment and study design

With approval number 202401700B0, the study protocal was authorized by Chang Gung Memorial Hospital's Institutional Review Board (IRB) before the research started. The need for informed consent was waived by the IRB due to the retrospective design of the study. Data from adult trauma patients aged 20 or older with severe head injuries (Head/Neck Abbreviated Injury Scale (AIS) $\geq$3) were analyzed using a retrospective cohort design. The data were gathered from the Trauma Registry System between 01 January 1998, and 31 December 2023. Patients with certain injury types (such as burns and hanging injuries) and those with insufficient information were excluded. Based on the initial laboratory tests performed upon hospital admission, laboratory data levels were evaluated. The calculation for APRI is as follows: divide the AST level by its upper limit of normal (34 IU/L), then divide by the platelet count (in units of 10^9/L), and finally multiply by 100. The research method involved a detailed recording of all retrieved cases' basic information (age, sex, past medical history, injury body region and mechanism, blood tests at admission, in-hospital mortality, Glasgow Coma Scale (GCS), and the Injury Severity Score (ISS).

2.2 Statistical analysis

The statistical analyses were performed by IBM's SPSS version 23 (Armonk, NY, USA). In order to evaluate categorical variables, chi-square tests for odds ratios (OR) and 95% confidence intervals, patients were first split into groups of deceased and survivors. The mean $\pm$ standard deviation (SD) was used to represent continuous variables. The study also determined the APRI's cut-off value for mortality prediction using the Receiver Operating Characteristic (ROC) curves and AUC values in patients of the study cohort and in the subgroups of patients with different injury severity (*e.g.*, ISS 1–15, ISS 16–24, and ISS $\geq$25). The mortality prediction performance of GCS in the study cohort was investigated for comparison. By optimizing the sum of sensitivity and specificity, the Youden Index determined the ideal cutoff point of the APRI for mortality prediction. The risks of mortality and adjusted odds ratios (AOR) for patients were then determined by classifying them according to this threshold, taking into account variables such as age, sex, pre-existing diseases, and the severity of the injury. It was deemed statistically significant when the p-value was less than 0.05.

3. Results

3.1 Patient enrollment

The study evaluated trauma patients from the Trauma Registry System between 1998 and 2023, focusing on those aged 20 years and older with a head or neck injury severity score (AIS) of $\geq$3. From an initial registry of 54,313 patients, 47,922 met the age criteria. Among these, 7657 patients presented with head or neck injuries classified as AIS $\geq$3. Further exclusions were applied, removing cases with hanging injuries (n = 5), burn injuries (n = 1), and instances of missing laboratory data (n = 1399). These exclusions led to a final cohort of 6252 patients. Within this cohort, 594 cases resulted in fatalities, while 5658 patients survived, as illustrated in Fig. 1.

3.2 Patient demographics

Table 1 demonstrates significant differences in demographics and clinical characteristics between deceased and surviving patients. Deceased patients were predominantly male (68.5% *vs.* 61.5%, p = 0.001) and slightly older, with an average age of 61.6 years compared to 58.1 years among survivors ($p <$ 0.001). The APRI was notably higher in deceased patients (1.9

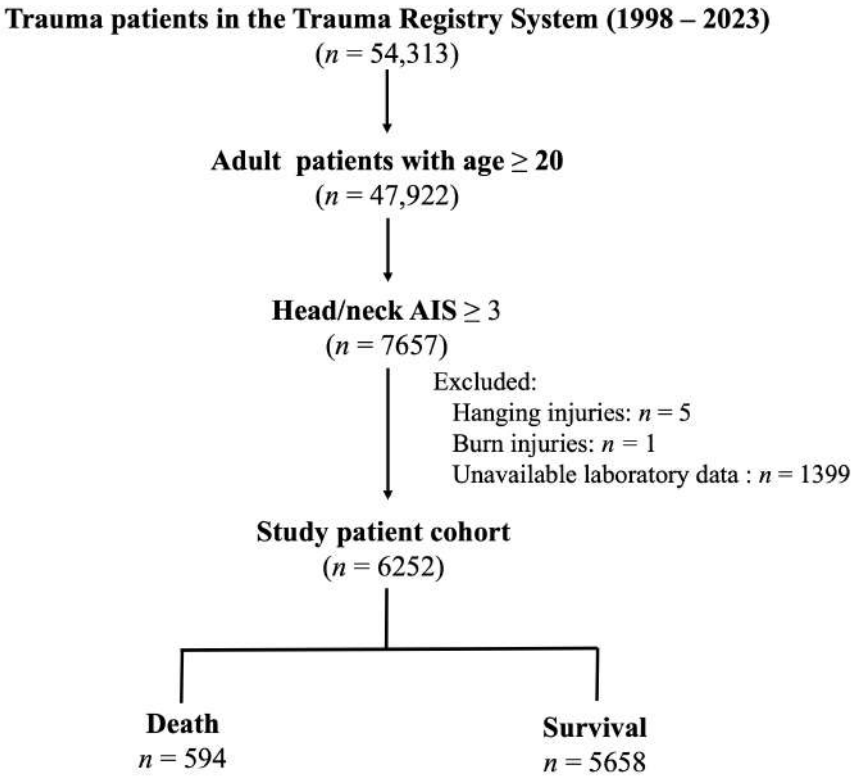

FIGURE 1. Patient enrollment flowchart for the traumatic brain injury cohort study. AIS: Abbreviated Injury Scale.

TABLE 1. Study participants baseline characteristics by survival outcome.

Variables	Death n = 594	Survival n = 5658	OR (95% CI)	*p*
Sex				
Male, n (%)	407 (68.5)	3477 (61.5)	1.37 (1.14–1.64)	0.001
Female, n (%)	187 (31.5)	2181 (38.5)	0.73 (0.61–0.88)	
Age (yr), mean ± SD	61.6 ± 18.9	58.1 ± 19.0	-	<0.001
APRI	1.9 ± 8.7	0.9 ± 2.4	-	<0.001
AST (IU/L), mean ± SD	123.9 ± 656.8	58.3 ± 109.9	-	<0.001
Platelet counts (10^9/L), mean ± SD	214.4 ± 74.7	221.8 ± 70.6	-	0.016
Comorbidities				
CVA, n (%)	31 (5.2)	308 (5.4)	0.96 (0.65–1.40)	0.818
HTN, n (%)	233 (39.2)	2082 (36.8)	1.11 (0.93–1.32)	0.244
CAD, n (%)	64 (10.8)	258 (6.3)	1.79 (1.35–2.37)	<0.001
CHF, n (%)	8 (1.3)	44 (0.8)	1.74 (0.82–3.72)	0.146
DM, n (%)	116 (19.5)	1161 (20.5)	0.94 (0.76–1.16)	0.569
ESRD, n (%)	47 (7.9)	131 (2.3)	3.63 (2.57–5.12)	<0.001
GCS, median (IQR)	4 (3–9)	15 (12–15)	-	<0.001
3–8, n (%)	425 (71.5)	871 (15.4)	13.82 (11.40–16.75)	<0.001
9–12, n (%)	58 (9.8)	651 (11.5)	0.83 (0.63–1.10)	0.203
13–15, n (%)	111 (18.7)	4136 (73.1)	0.09 (0.07–0.11)	<0.001
ISS, median (IQR)	25 (24–30)	16 (14–22)	-	<0.001
1–15, n (%)	24 (4.0)	1442 (25.5)	0.12 (0.08–0.19)	<0.001
16–24, n (%)	128 (21.5)	3108 (54.9)	0.23 (0.18–0.28)	<0.001
≥25, n (%)	442 (74.4)	1108 (19.6)	11.94 (9.82–14.52)	<0.001
Hospital stay (d)	9.4 ± 14.7	14.1 ± 14.1	-	<0.001

APRI: Aspartate Aminotransferase-to-Platelet Ratio Index; CAD: coronary artery disease; CHF: congestive heart failure; CI: confidence interval; CVA: cerebral vascular accident; DM: diabetes mellitus; ESRD: end-stage renal disease; GCS: Glasgow Coma Scale; HTN: hypertension; IQR: interquartile range; ISS: injury severity score; OR: odds ratio; SD: standard deviation; AST: aspartate aminotransferase.

vs. 0.9, $p < 0.001$), as were AST levels (123.9 IU/L *vs.* 58.3 IU/L, $p < 0.001$). Additionally, deceased patients had lower platelet counts (214.4 *vs.* 221.8, $p = 0.016$).

In terms of comorbidities, coronary artery disease (CAD) and end-stage renal disease (ESRD) were significantly more common in deceased patients (CAD: 10.8% *vs.* 6.3%, $p < 0.001$; ESRD: 7.9% *vs.* 2.3%, $p < 0.001$). Neurological status, as reflected by the GCS, was considerably worse in deceased patients, with a median GCS of 4 (IQR 3–9) versus 15 (IQR 12–15) for survivors ($p < 0.001$). Injury severity was also higher, with deceased patients showing a median ISS of 25 (IQR 24–30) compared to 16 (IQR 14–22) in survivors ($p < 0.001$). Hospital stays were shorter for deceased patients, averaging 9.4 days compared to 14.1 days for survivors ($p < 0.001$).

3.3 The mortality predictive performance of APRI

The effectiveness of the APRI as a tool for predicting death outcomes among the research cohort is shown in Fig. 2. In the overall cohort, APRI demonstrated only moderate discrimination for mortality (AUC = 0.648 with an optimal cutoff of 0.59, yielding 63.6% sensitivity and 60.3% specificity), whereas the GCS showed a substantially higher predictive accuracy (AUC = 0.835 at a cutoff of 9.5) (Fig. 2B). When stratified by injury severity, the predictive performance of APRI declined with increasing ISS. The AUC for APRI was 0.590 in the mild injury subgroup (ISS 1–15), 0.567 in the moderate ISS group (16–24), and 0.552 in the severe ISS category (ISS ≥25) (Fig. 2C–E), indicating only poor to fair discrimination within these strata.

3.4 Comparative analysis based on optimal cutoff value of APRI

Table 2 presents a comparative analysis of trauma patients divided by an APRI cutoff value of 0.59. Males were more prevalent in the higher APRI group (66.5% *vs.* 59.0%, $p < 0.001$), while females were more common in the lower APRI group. Patients with APRI ≥0.59 were slightly younger on average (56.5 *vs.* 59.8 years, $p < 0.001$). In terms of comorbidities, higher APRI was associated with significantly lower incidences of hypertension (HTN) and diabetes mellitus (DM) compared to those with APRI <0.59 (HTN: 33.8% *vs.* 39.3%, $p < 0.001$; DM: 17.4% *vs.* 22.6%, $p < 0.001$). However, patients in the higher APRI group had more severe clinical presentations, with a lower GCS score (14 (IQR 7–15) *vs.* 15 (IQR 13–15), $p < 0.001$) and a higher median ISS (20 (IQR 16–25) *vs.* 16 (IQR 13–20), $p < 0.001$). Patients with APRI ≥0.59 had longer hospital stays (15.9 *vs.* 12.0 days, $p < 0.001$) and higher mortality rates (14.5% *vs.* 5.9%, $p < 0.001$). After adjusting for sex, age, and relevant comorbidities, the adjusted odds ratio (AOR) for mortality in patients with APRI ≥0.59 was significantly higher (AOR 1.67, 95% CI: 1.37–2.02, $p < 0.001$). Correspondingly, using the identified APRI cutoff of 0.59 to dichotomize patients, high APRI patients (APRI ≥0.59) showed progressively stronger associations with mortality in higher ISS strata (Table 3). In the ISS 1–15 subgroup, mortality was low and did not differ significantly between high *vs.* low APRI groups (2.3% *vs.* 1.3%; OR = 1.77, 95% CI 0.79–3.99, $p = 0.161$). By contrast, for ISS 16–24 patients, an APRI ≥0.59 was associated with a significantly higher mortality rate (5.2% *vs.* 3.3%), with an unadjusted odds ratio of 1.60 (95% CI 1.12–2.28, $p = 0.009$). This association persisted after controlling for age, sex, and comorbidities, as reflected by an adjusted OR of 1.75 (95% CI 1.22–2.53, $p = 0.003$). Similarly, in the ISS

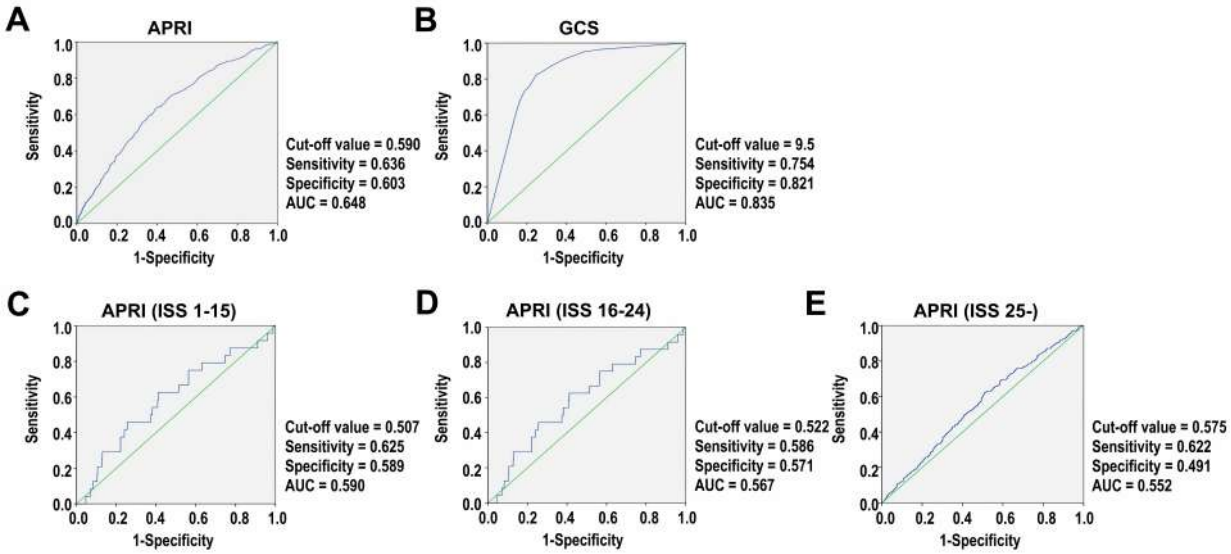

FIGURE 2. Receiver Operating Characteristic (ROC) curve analysis showing the mortality predictive performance of (A) Aspartate Aminotransferase-to-Platelet Ratio Index (APRI) and (B) Glasgow Coma Scale (GCS) in the overall traumatic brain injury cohort and APRI in patient subgroups stratified by injury severity: mild (ISS 1–15, C) moderate (ISS 16–24, D), and severe (ISS ≥25, E). For each analysis, the optimal cutoff value, sensitivity, specificity, and area under the curve (AUC) are displayed. ISS: Injury Severity Score.

TABLE 2. Receiver Operating Characteristic (ROC) curve analysis of APRI for mortality prediction in traumatic brain injury patients.

Variables	APRI		OR (95% CI)	*p*
	≥0.59 n = 2604	<0.59 n = 3648		
Sex				
Male, n (%)	1732 (66.5)	2152 (59.0)	1.38 (1.24–1.5)	<0.001
Female, n (%)	872 (33.5)	1496 (41.0)	0.72 (0.65–0.80)	
Age (yr), mean ± SD	56.5 ± 18.7	59.8 ± 19.1	-	<0.001
Comorbidities				
CVA, n (%)	109 (4.2)	230 (6.3)	0.65 (0.51–0.82)	<0.001
HTN, n (%)	880 (33.8)	1435 (39.3)	0.79 (0.71–0.87)	<0.001
CAD, n (%)	168 (6.5)	254 (7.0)	0.92 (0.75–1.13)	0.427
CHF, n (%)	21 (0.8)	31 (0.8)	0.95 (0.54–1.65)	0.852
DM, n (%)	454 (17.4)	823 (22.6)	0.73 (0.64–0.82)	<0.001
ESRD, n (%)	56 (2.2)	122 (3.3)	0.64 (0.46–0.88)	0.005
GCS, median (IQR)	14 (7–15)	15 (3–15)	-	<0.001
3–8, n (%)	791 (30.4)	505 (13.8)	2.72 (2.40–3.08)	<0.001
9–12, n (%)	340 (13.1)	369 (10.1)	1.33 (1.14–1.56)	<0.001
13–15, n (%)	1473 (56.6)	2774 (76.0)	0.41 (0.37–0.46)	<0.001
ISS, median (IQR)	20 (16–25)	16 (13–20)	-	<0.001
1–15, n (%)	477 (18.3)	989 (27.1)	0.60 (0.53–0.68)	<0.001
16–24, n (%)	1165 (44.7)	2071 (56.8)	0.62 (0.56–0.68)	<0.001
≥25, n (%)	962 (36.9)	588 (16.1)	3.05 (2.71–3.43)	<0.001
Hospital stay (d)	15.9 ± 15.9	12.0 ± 12.7	-	<0.001
Mortality, n (%)	377 (14.5)	217 (5.9)	2.68 (2.25–3.19)	<0.001
AOR of mortality*	-	-	1.67 (1.37–2.02)	<0.001

*APRI: Aspartate Aminotransferase-to-Platelet Ratio Index; AOR: Adjusted odds ratio; CAD: coronary artery disease; CHF: congestive heart failure; CI: confidence interval; CVA: cerebral vascular accident; DM: diabetes mellitus; ESRD: end-stage renal disease; GCS: Glasgow Coma Scale; HTN: hypertension; IQR: interquartile range; ISS: injury severity score; OR: odds ratio; SD: standard deviation. *Mortality adjusted by sex, age, CVA, HTN, DM, ESRD and ISS.*

TABLE 3. The odds of mortality in traumatic brain injury patients stratified by injury severity between the patients with APRI ≥0.59 *vs.* those with APRI<0.59.

Variables	APRI		OR (95% CI)	*p*
	≥0.59	<0.59		
ISS (1–15)	n = 477	n = 989		
Mortality, n (%)	11 (2.3)	13 (1.3)	1.77 (0.79–3.99)	0.161
AOR of mortality	-	-	1.86 (0.82–4.23)	0.139
ISS (16–24)	n = 1165	n = 2071		
Mortality, n (%)	60 (5.2)	68 (3.3)	1.60 (1.12–2.28)	0.009
AOR of mortality	-	-	1.75 (1.22–2.53)	0.003
ISS (≥25)	n = 962	n = 588		
Mortality, n (%)	306 (31.8)	136 (23.1)	1.55 (1.23–1.96)	<0.001
AOR of mortality*	-	-	1.74 (1.36–2.22)	<0.001

*APRI: Aspartate Aminotransferase-to-Platelet Ratio Index; AOR: Adjusted odds ratio; CI: confidence interval; ISS: injury severity score; OR: odds ratio. *Mortality adjusted by sex, age, CVA, HTN, DM, and ESRD.*

≥25 group, high APRI patients had a mortality of 31.8% compared to 23.1% in the low APRI group, corresponding to a significant unadjusted OR of 1.55 (95% CI 1.23–1.96, $p < 0.001$). After adjustment, APRI remained a significant independent predictor in this severe injury stratum (AOR = 1.74, 95% CI 1.36–2.22, $p < 0.001$). In summary, these results indicate that an elevated APRI is a significant predictor of in-hospital mortality in moderate and severe TBI cases even after adjustment for confounders, whereas its prognostic value is minimal in patients with minor injuries.

4. Discussion

Our study assessed the prognostic value of the APRI in predicting mortality among patients with TBI, with results indicating a moderate predictive performance. We identified an optimal cutoff of 0.59 for APRI, yielding an AUC of 0.648, with a sensitivity of 63.6%, and specificity of 60.3%. When comparing these findings with APRI's application in other clinical scenarios, APRI demonstrates variability in diagnostic and prognostic efficacy, likely influenced by the distinct pathophysiological processes across diseases.

TBI has a significant impact on systemic physiology, including liver function, due to complex neuro-inflammatory and systemic inflammatory responses. Studies have demonstrated that liver function test abnormalities are common in TBI patients, even in the absence of pre-existing liver conditions. Among these abnormalities, AST levels tend to rise due to hepatic ischemia, oxidative stress, and inflammatory responses triggered by brain injury [19]. The systemic inflammatory response following TBI involves cytokine release (Interleukin-1 beta, Interleukin-6, and Tumor Necrosis Factor alpha), which induces hepatocellular damage, leading to increased AST levels [20]. Histological analysis from experimental models suggests that TBI induces hepatocyte dystrophy, sinusoidal congestion, and hepatocellular necrosis, contributing to AST elevation [21]. The APRI score, is widely used as a non-invasive marker of liver fibrosis and function. In TBI patients, an elevated APRI score may serve as an indicator of multi-organ dysfunction and a predictor of mortality. Since platelet count is often reduced due to systemic inflammatory responses and disseminated intravascular coagulation post-TBI, and AST levels are elevated due to hepatocellular damage, a higher APRI score may reflect the severity of both hepatic injury and systemic complications. Previous studies in intensive care unit (ICU) populations have demonstrated an association between deranged liver function tests and poor prognosis, supporting the hypothesis that a high APRI score in TBI patients correlates with increased mortality risk [19].

In chronic liver diseases, APRI has shown significant diagnostic value in staging fibrosis and cirrhosis, especially in hepatitis B and C contexts. For instance, Jin *et al.* [15] observed an AUC of 0.79 for predicting significant fibrosis in hepatitis B, with sensitivities reaching 84% at a lower cutoff of 0.5, though specificity was moderate (41%). A systematic review showed moderate accuracy with AUC values of 0.74 for significant fibrosis, 0.73 for advanced fibrosis, and 0.73 for cirrhosis [14]. In hepatitis C, Lin *et al.* [5] reported an AUC of up to 0.83 for APRI in cirrhosis prediction, demonstrating APRI's robust application within liver disease. These AUC values exceed our findings in TBI, possibly due to APRI's closer association with chronic liver dysfunction rather than acute trauma-related responses. In hepatocellular carcinoma (HCC), APRI has shown prognostic significance, with elevated values correlating with poorer overall survival and recurrence-free survival. Zhang *et al.* [16] reported hazard ratios of 1.62 for overall mortality and 1.83 for recurrence in HCC patients with higher APRI levels, underscoring APRI's role in identifying high-risk HCC patients. In contrast, our study in a TBI population observed an AOR of 1.67 for mortality in patients with APRI values ≥0.59, indicating a significant association between elevated APRI and increased mortality risk in TBI. This AOR is similar to the hazard ratios reported in HCC studies, suggesting that APRI may serve as a marker of poor prognosis across diverse conditions.

Beyond liver-related conditions, APRI has been applied in COVID-19 and dengue fever. In COVID-19 patients, Çopur *et al.* [7] reported an AUC of 0.648 for APRI's mortality prediction, closely mirroring our study's findings in TBI. Their cutoff of 0.58 produced a sensitivity of 56.4% and specificity of 63.6%, indicating APRI's moderate predictive power for systemic inflammatory conditions. This result aligns with our findings in TBI, where we observed an AUC of 0.648, sensitivity of 63.6%, and specificity of 60.3% at a similar cutoff value of 0.59. These comparable results between COVID-19 and TBI underscore APRI's moderate yet consistent performance across diverse inflammatory and injury-related conditions. In contrast, our study's findings diverge from those of Jamil *et al.* [8] in complicated dengue fever, where APRI demonstrated a high predictive accuracy for severe complications, with an AUC of 0.93, sensitivity of 84.9%, and specificity of 89.0% at a cutoff of 9.04. This stark contrast may stem from the acute inflammatory and hematological changes in severe dengue, which directly impact platelet counts and liver function, thereby enhancing APRI's diagnostic relevance. In TBI, however, APRI's moderate sensitivity and specificity suggest a weaker correlation between liver enzyme and platelet changes and mortality outcomes.

In this study, GCS remains a substantially stronger predictor of TBI mortality than APRI, as evidenced by GCS's higher discriminative ability (AUC ~0.84 *vs.* ~0.65 for APRI). APRI's prognostic performance was only moderate overall, and its utility appeared to depend on injury severity. In stratified analyses, an elevated APRI (≥0.59) did not significantly predict death in patients with mild injuries (ISS 1–15), whereas it was associated with markedly higher mortality risk in moderate (ISS 16–24) and severe (ISS ≥25) trauma. This pattern suggests that APRI's prognostic signal emerges primarily when the overall injury burden is substantial—consistent with the notion that trauma-induced systemic insult (*e.g.*, coagulopathy from thrombocytopenia) contributes to worse outcomes in more severe TBI [3]. Clinically, while APRI can serve as an adjunct prognostic marker (especially in moderately to severely injured patients), its moderate accuracy and dependency on injury severity warrant a cautious application alongside established indices like GCS, rather than as a standalone predictor.

The variability in APRI's performance across studies can

be attributed to multiple factors. Differences in underlying disease mechanisms likely play a significant role; APRI was initially developed as a liver fibrosis marker, making it directly applicable to liver diseases. In contrast, TBI and other inflammatory conditions may only indirectly influence APRI through systemic inflammation, which limits its predictive strength. Additionally, variations in study populations, APRI cutoff values, and the presence of comorbidities can significantly impact its performance. Moreover, differences in measurement timing (*e.g.*, preoperative, at admission, or longitudinal) and study designs across settings add to the discrepancies in APRI's predictive capacity. Clinically, APRI can serve as a valuable supplementary tool for predicting mortality in TBI patients, helping to identify those at higher risk early on. Its non-invasive nature and ease of calculation make it particularly useful for rapid assessment in emergency settings. However, due to its moderate sensitivity and specificity, APRI should be interpreted in conjunction with other validated trauma scores, such as the GCS or ISS, to provide a more comprehensive risk evaluation. Rather than relying on a single measurement, tracking APRI trends over time may offer deeper insight into the progression or resolution of liver dysfunction. By incorporating serial APRI assessments into clinical practice, healthcare providers can better detect patients at risk of worsening hepatic dysfunction or coagulopathy, enabling timely intervention with supportive therapies, hemodynamic stabilization, and liver-protective strategies.

This study has several limitations. First, its retrospective design introduces selection bias, particularly due to the exclusion of patients with incomplete data, and limits causal inferences regarding APRI's role in TBI prognosis. Second, APRI's predictive performance may be confounded by pre-existing liver conditions or systemic inflammation unrelated to TBI, affecting its reliability. In addition, although APRI has been proven to be a valuable predictive tool in both liver-related trauma/surgical cases and non-liver surgical settings, the incidence and extent of liver injury could be accurately estimated or eliminated from its effect on the APRI expression, thus leading to a limitation in the interpretation of the results. Third, as a single-center study, the findings may not be generalizable to other populations, necessitating external validation in multi-center cohorts. Fourth, while APRI showed moderate predictive accuracy, it was not compared with established critical illness scores and trauma scores such as Acute Physiology and Chronic Health Evaluation (APACHE), or the Sequential organ failure assessment (SOFA) due to data limitations; future studies should integrate these scores for a more comprehensive evaluation. Finally, the lack of longitudinal APRI measurements prevents analysis of its dynamic changes over time, which could provide further insights into its role in monitoring patient recovery and deterioration. Future prospective, multi-center studies with repeated biomarker assessments are warranted to validate APRI's prognostic value and its integration into clinical decision-making.

5. Conclusions

In conclusion, while APRI demonstrated moderate predictive utility in TBI for mortality risk assessment, it is less effective than in chronic liver disease and other systemic conditions, highlighting the need for further investigation in trauma-specific applications.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

CYH and CHT—wrote the manuscript. WTS—performed the research and validate the data from database. SYH—analyzed the data. CHH—designed the research study.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

With approval number 202401700B0, the procedure was authorized by Chang Gung Memorial Hospital's Institutional Review Board (IRB) before the research started. The need of informed consent was waived by IRB due to the retrospective design on registered database.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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