ORIGINAL ARTICLE

Prognostic Value of Acute Gastrointestinal Injury Combined with Disease Severity Scores in Critically Ill Patients

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Abstract

Background: Critically ill patients are at high risk of multiple organ failure syndrome (MODS) and gastrointestinal (GI) injury and dysfunction, which are associated with increased mortality rates. The acute gastrointestinal injury (AGI) scale has shown promise in assessing GI dysfunction. However, the combined utility of AGI with established disease severity scores remains unclear. This study aimed to investigate the performance of AGI in conjunction with modified nutritional risk in critically ill (mNUTRIC), sequential organ failure assessment (SOFA), and acute physiology and chronic health evaluation II (APACHE II) scores for predicting mortality in critically ill patients.

Materials and methods: A retrospective cross-sectional study was conducted in the intensive care unit (ICU) from May 2021 to December 2021. Demographic and clinical data were collected, including AGI grade, mNUTRIC score, SOFA score, APACHE II score, and mortality.

Results: Among 93 critically ill patients, AGI was observed in 47.3% of cases, and the in-hospital mortality rate was 30.1%. The area under the curve (AUC) for AGI in predicting in-hospital mortality was 0.67 [95% confidence interval (CI), 0.56, 0.79; $p = 0.008$], similar to the AUCs of SOFA, APACHE II, and mNUTRIC scores. The combination of AGI with mNUTRIC, APACHE II, or SOFA scores improved the predictive performance compared with AGI alone.

Conclusion: The AGI grade, in conjunction with disease severity scores, such as mNUTRIC, SOFA, and APACHE II scores, shows promise in predicting mortality in critically ill patients. Integrating AGI into evaluating critically ill patients can enhance prognostic accuracy.

Keywords: Acute gastrointestinal injury, Critically ill patients, Disease severity scores, mNUTRIC score, Prognosis.

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Highlights

- Gastrointestinal (GI) dysfunction is a common and important complication in critically ill patients.
- Acute gastrointestinal injury (AGI) scale alongside modified nutritional risk in critically ill (mNUTRIC), sequential organ failure assessment (SOFA), and acute physiology and chronic health evaluation II (APACHE II) scores, improves predictive capabilities for in-hospital mortality among critically ill patients.
- Integrating AGI assessment into the evaluation of critically ill patients enhances prognostic accuracy and aids in clinical decision-making in the intensive care unit (ICU).

Introduction

Critical illness is a life-threatening condition that may lead to a high risk of mortality or morbidity without medical intervention. Critically ill patients are at risk of multiple organ failure syndrome (MODS) and require ICU admission or adequate management and intervention.[1]

The main functions of the GI tract include digestion, absorption, excretion, along with the others, such as endocrinologic, immunologic, and barrier functions. Gastrointestinal injury and dysfunction are widely recognized among critically ill patients and been linked to higher mortality rates.[2–4] Intestinal permeability alteration was observed prior to MODS onset in severely ill patients.[5] Among this group of patient, injury to the GI tract manifests as abnormal intestinal motility, delayed gastric emptying, and impaired intestinal barrier integrity.[6] A disruption of GI function results in altered nutritional status and poorer prognosis among patients in the ICU.

Studies have also shown the correlation of GI biomarkers to the prognosis among critically ill patients. Alteration of GI biomarkers such as D-lactate, heparin-binding protein, and citrulline was associated with the performance of severe patients in the ICU.[7–9] Due to the strong correlation between GI failure and critical illness, developing a grading scale to evaluate the GI function of ICU patients is vital.

In 2012, the AGI scale was proposed by the Working Group on Abdominal Problems (WGAP). According to this scale, GI injury was classified into four grades based on severity: grade I was defined as a self-resolving condition of GI injury with increased risk for GI dysfunction or failure in the future; grade II classified the injury as GI dysfunction, which required medical interventions to restore GI function; grade III is classified for patients with GI failure, in which interventions is not useful for GI function restoration; grade IV carried the worst prognosis, which defines patients with an immediate life-threatening GI failure.[10] A few limited studies

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have shown the benefits of the AGI grading scale in assessing GI malfunction and predicting the outcomes of patients in the ICU.[11,12]

Nutrition is an essential element for maintaining overall health and well-being, and it holds significant importance in the recuperation and survival of critically ill individuals. Studies have found a correlation between high nutritional risks, increased mortality, and poorer prognosis among patients in the ICU.[13,14] The modified nutrition risk in the critically ill (mNUTRIC) score is a nutritional assessment scale to assess nutritional-associated mortality risk in severely ill patients. It is an edited version of the NUTRIC grading scale by dropping the value of interleukin-6 because measuring the interleukin-6 concentration is not practical in general clinical settings.[15] Both NUTRIC and mNUTRIC scores have shown substantial benefits in evaluating nutritional risk and predicting the outcomes of critically ill patients.[16,17] The mNUTRIC score incorporates parameters such as the SOFA score, APACHE II score, age, hospital stay duration prior to entry to the ICU, and comorbidities. It has been established as a reliable and valuable tool for evaluating nutritional risk among ICU patients.

While the AGI grading system has emerged as a potential tool for evaluating gastrointestinal dysfunction and its impact on patient prognosis, its combined utility with established disease severity scores including mNUTRIC, SOFA, and APACHE II score remains uninvestigated. Our study aimed to discover the performance of AGI in conjunction with these scores for predicting mortality of patients in the ICU.

Materials and Methods

Study Design and Participants

A retrospective cross-sectional study was conducted in the Medical Intensive Care Unit of 108 Military Central Hospital in Vietnam from May 2021 to December 2021. Inclusion criteria were patients ≥18 years old with more than 24 hours of admission to the ICU. We exclude dead as well as discharged patients within the first 24 hours of admission. Participants are excluded if they were transferred from other ICUs. The research protocol was approved by the 108 Military Centra Hospital Institutional Review Board (No 6876/CN-HĐĐĐ BV). Informed consent was not necessary because of a retrospective study.

Data Collection

Data on the patients were gathered, covering demographic details, such as age and gender, as well as medical background, vital signs, duration of stay in the ICU, and use of mechanical ventilators, continuous renal replacement therapy (CRRT). Other variables include laboratory values, and the outcome of patients (mortality rate, duration of hospital stay, duration of ICU stay).

The AGI scale was assessed using the recommended criteria of the ESICM WGAP grading system.[10] The AGI grade was determined based on symptoms of the GI tract, intra-abdominal pressure, and ability to tolerate feeding. Acute gastrointestinal injury is classified into four grades, and AGI grade I was considered non-AGI in this study.

Acute physiology and chronic health evaluation II and SOFA score were assessed within 24 hours of ICU admission. The mNUTRIC score, ranging from 0 to 9 points, was determined using data gathered 24 hours following admission to the ICU. The mNUTRIC score is calculated by evaluating five criteria: the age of the patient, the number of previous health conditions they have, their SOFA score (which assesses organ dysfunction), their APACHE II score (which evaluates acute illness severity), and the duration of hospitalization before admission to the ICU.[15]

Statistical Analysis

Data analysis was performed using SPSS version 20.0 and Epi Info 2005 on Windows operating system. Variables of a categorical nature were presented as frequencies (percentages). Parametric continuous variables are described by mean values with or without standard deviation (SD), while nonparametric continuous variables were presented as median values with interquartile range (IQR). The analysis of categorical variables was done using either the Chi-square test or Fisher's exact test. The student's *t*-test was employed for quantitative data with normal distribution, whereas the Mann–Whitney test was utilized for data not following a normal distribution.

The ability of the AGI grade and disease severity scores to predict outcomes was assessed using the area under the curve (AUC) of the receiver operating characteristics (ROC) curve. To confirm factors associated with mortality, univariate analyses were performed. Multivariate logistic regressions were utilized to identify independent predictors of mortality. Logistic regression of multivariable were used to determine factors independently associated with mortality. The correlation between variables and the mortality risk were expressed using hazard ratios (HR). A *p*-value less than 0.05 was determined as significant statistically.

Results

Characteristics of the Patients

Among the 93 patients, the average age was 70 years, with males accounting for 73.1%. The prevalence of hypertension was 46.2%, while diabetes mellitus accounted for 38.7% of the cases. The leading cause of admission was pneumonia (44.1%), followed by septic shock (28%). Mechanical ventilation was required for 63.4% of the patients. Acute gastrointestinal injury was observed among 47.3% of cases. The death rate in the hospital was 30.1% (Table 1).

No notable discrepancy was noted in age gender, BMI, average heart rate, and mean blood pressure among those who survived and those who did not. Regarding comorbidities, we did not observe remarkable differences among survivors and nonsurvivors in the prevalence of hypertension, diabetes mellitus, heart failure, stroke, and cirrhosis.

The result of the study revealed a noteworthy disparity regarding the rate of pneumonia between the two groups, with a significantly higher proportion of pneumonia cases recognized in the nonsurvivors compared with the survivors (60.7 vs 36.9%, $p = 0.034$). Additionally, the creatinine clearance was notably higher in the survivors in comparison to the nonsurvivors' group (63.5 vs 47.6 mL/min, $p = 0.04$).

The SOFA, APACHE II, and mNUTRIC scores were significantly elevated in the nonsurvivors group in comparison with the survivors. Besides, a higher rate of AGI was observed among the nonsurvivors (71.4 vs 36.9%, $p = 0.002$).

The percentage of patients requiring CRRT was also more remarkable in the nonsurvivor group comparing to the survivors (35.7 vs 15.4%, $p = 0.028$).

Prognostic Value of AGI, SOFA, APACHE II, and mNUTRIC Score

The performance of AGI, SOFA, APACHE II, and mNUTRIC score in predicting mortality rate of severe patients in the hospital was assessed with ROC curves (Fig. 1). The AUC for AGI is 0.67

Table 1: Comparison of demographic and clinical characteristics between survivors and nonsurvivors

Characteristics	*All patients (n = 93)*	*Survivors (n = 65)*	*Nonsurvivors (n = 28)*	*p-value*
Male sex, *n* (%)	68 (73.1%)	46 (70.7%)	22 (78.6%)	0.436
Age, years	70 (58–79)	68 (55–79)	76.0 (65–79)	0.064
BMI, kg/m^2	21.3 (19.7–23.0)	21.3 (19.5–23.0)	21.2 (19.9–23.1)	0.836
HR, bpm	104 (87–120)	110 (85–120)	115 (91–130)	0.081
MAP, mm Hg	83 (76– 93)	83 (76–96)	83 (75–91)	0.372
Comorbidities				
Hypertension, *n* (%)	43 (46.2)	29 (44.6%)	14 (50.0%)	0.633
Type 2 DM, *n* (%)	36 (38.7)	27 (41.5)	9 (32.1)	0.393
Stroke, *n* (%)	19 (20.4%)	13 (20.0%)	6 (21.4%)	0.875
Heart failure, *n* (%)	9 (9.7%)	6 (9.2%)	3 (10.7%)	0.546
Acute pancreatitis, *n* (%)	8 (8.6)	6 (9.2)	2 (7.1)	0.547
Cirrhosis, *n* (%)	5 (5.4%)	3 (4.6%)	2 (7.1%)	0.635
Pneumonia, *n* (%)	41 (44.1%)	24 (36.9%)	17 (60.7%)	0.034
Abdominal surgery, *n* (%)	4 (4.3%)	3 (4.6%)	1 (3.6%)	0.650
Creatinine clearance	59.4 (34.7–76.8)	63.5 (41.3–109.3)	47.6 (25.8–85.8)	0.040
Septic shock, *n* (%)	26 (28.0%)	16 (24.6%)	10 (35.7%)	0.273
Severity of illness				
APACHE II score	19 (14–21)	17 (14–21)	20 (18–23)	0.011
SOFA score	7 (5–11)	7 (5–10)	8 (6–12)	0.018
mNUTRIC score	5 (3–6)	4 (2–6)	5 (4–6)	0.009
mNUTRIC score ≥5	47 (50.5%)	28 (43.1%)	19 (67.9%)	0.028
AGI score	1 (0–2)	1 (0–2)	2 (1–2)	0.004
AGI score ≥2	44 (47.3)	24 (36.9%)	20 (71.4%)	0.002
Outcomes				
MV, *n* (%)	59 (63.4%)	38 (58.5%)	21 (75.0%)	0.128
CRRT, *n* (%)	20 (21.5%)	10 (15.4%)	10 (35.7%)	0.028
Hospital LOS, days	18 (12–26)	18 (12–23)	18 (12–36)	0.441
ICU LOS, days	9 (5–15)	8 (5–13)	13 (6–17)	0.055

Measurement values expressed as median (25th percentile; 75th percentile) categorical variables were reported as *n* (%). AGI, acute gastrointestinal injury; AKI, acute kidney injury; APACHE II, acute physiology and chronic health evaluation II; CRRT, continuous renal replacement therapy; DM, diabetes mellitus; HR, heart rate; ICU, intensive care unit; LOS, length of stay; MAP, mean arterial pressure; MV, mechanical ventilation; SOFA, sequential organ failure assessment

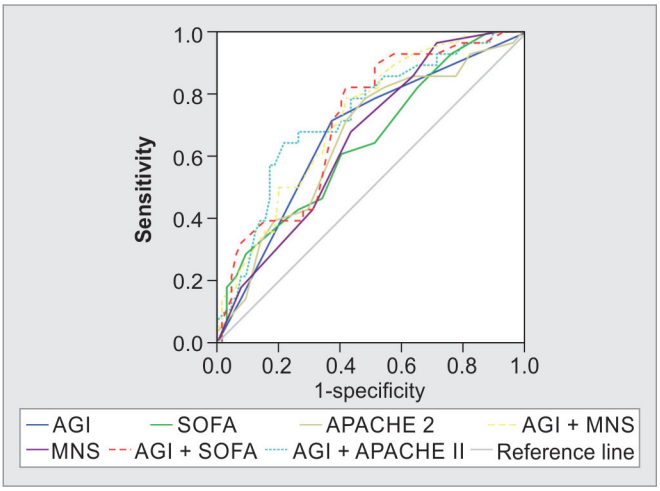

Fig. 1: Receiver operating characteristic curves of AGI, mNUTRIC, APACHE II, and SOFA score in predicting in-hospital mortality in critically ill patients

(95% CI, 0.56–0.79; $p = 0.008$). The same was observed regarding the AUC of SOFA, APACHE II, and mNUTRIC score.

Moreover, when combining AGI with mNUTRIC, the AUC representing the predictive power of mortality in the hospital significantly increased compared with AGI alone (AUC: 0.72 vs 0.67). Similarly, combining AGI with the APACHE II or SOFA scores also led to higher AUC values than AGI alone (0.73 vs 0.67), (0.71 vs 0.67), respectively (Table 2).

Univariate and Multivariate Analyses for In-hospital Mortality

Analyzing univariables showed remarkable associations ($p \leq 0.05$) between pneumonia, APACHE II, AGI, SOFA, mNUTRIC scores in predicting mortality.

Multivariate analysis, which included the variables pneumonia (HR 2.4, 95% CI, 0.88–6.52; $p = 0.085$), mNUTRIC (HR 1.28, 95% CI, 0.96–1.72; $p = 0.097$), and the presence of AGI (HR 3.93, 95% CI, 1.42–10.84; $p = 0.008$), only AGI was shown to have an independent predictive ability of motality in the hospital (Table 3).

Discussion

Gastrointestinal dysfunction is a frequently diagnosed condition among critically ill individuals.[2–4] The present study revealed that 47.3% of the cases exhibited acute injury gastrointestinal (AGI). Moreover, our study revealed that AGI, SOFA, APACHE II, and mNUTRIC scores exhibited predictive value for death rate among severely ill patients in the hospital. The AUC values for AGI, SOFA, APACHE II, and mNUTRIC scores were comparable, indicating similar predictive abilities. However, when AGI was combined with mNUTRIC, APACHE II, or SOFA, the AUC values increased significantly, suggesting improved predictive performance compared with AGI alone.

The gastrointestinal tract acts as the organ for absorption and digestion and works as a barrier to keep dangerous pathogens affecting other organs by the intestinal microflora.[18] Many factors can lead to AGI among severely ill patients, such as inadequate gut perfusion due to shock or hypovolemic status, parenteral nutrition, surgery, drugs or electrolyte disturbances.[19–22] Failure of gut homeostasis can lead to bacterial translocation and leakage of endotoxins directly into the blood, which may cause bacteremia or even sepsis in susceptible patients.[23]

The correlation of AGI and mortality of patients in the ICU highlights the importance of gastrointestinal dysfunction in determining patient outcomes. Acute gastrointestinal injury is a comprehensive grading system that assesses various aspects of GI injury, including symptoms, intra-abdominal pressure, and feeding tolerance. Acute gastrointestinal injury was notably more remarkable among those who did not survive, indicating its potential as an independent predictor of mortality.

In many previous studies, patients' outcomes were associated with GI function, in which a higher score of GI failure results in higher mortality in ICU patients.[18,20,24] In line with our findings, a multicenter study on 164 ICU patients by Li H et al. recognized the ability of AGI scale to reflect the severity of patients. Additionally, the study suggests that categorizing AGI to two groups, specifically AGI grade I + II vs grade III + IV, may have prognosis significance in terms of both 7-day and 28-day mortality.[25] In addition, other studies also demonstrated that critically ill patients with GI symptoms such as the absence of bowel sounds, GI bleeding, and the presence of more than two GI symptoms are associated with extended stays in the ICU and higher mortality rates. The presence of gastrointestinal symptoms within the first 7 days of ICU admission was found to correlate with a poor prognosis, particularly in patients experiencing three or more concurrent GI symptoms.[2] Chen et al. performed a retrospective study on 874 intensive care patients, showing that higher AGI grades could significantly worsen clinical outcomes and increase mortality rates, especially in secondary AGI.[26] A meta-analysis of 14 studies identified a high rate of acute GI injury among ICU patients (40%), and the prevalence of death doubled in patients with AGI.[4] With the consistent result from many different studies, the AGI grade is a trustworthy predictor for healthcare workers to assess the clinical condition of critically ill patients and the prognosis of their severity.

Although the impact of GI function on patients' outcomes, it is mainly assessed by clinical judgement. We lack the necessary tools or markers to measure GI function correctly, which is challenging

Table 2: Predictive value of APACHE II, SOFA, mNUTRIC score and AGI for in-hospital mortality in critically ill patients

Characteristics	*AUC*	*p-value*	*95% CI, lower bound*	*95% CI, upper bound*
AGI	0.67	0.008	0.56	0.79
APACHEII	0.66	0.015	0.54	0.78
SOFA	0.65	0.025	0.53	0.77
mNUTRIC	0.66	0.016	0.54	0.77
mNUTRIC + AGI	0.72	0.001	0.62	0.83
SOFA + AGI	0.71	0.001	0.60	0.82
APACHE II + AGI	0.73	<0.001	0.62	0.84

AGI, acute gastrointestinal injury; APACHE II, acute physiology and chronic health evaluation II; AUC, area under the curve; CI, confidence interval; SOFA, sequential organ failure assessment

Table 3: Univariable and multivariate analysis for predictors of in-hospital mortality in critically ill patients

	Univariable		*Multivariable*	
Dependent variables	*Hazard ratio (95% CI)*	*p*	*Hazard ratio (95% CI)*	*p*
Age	1.02 (0.99–1.02)	0.69	–	–
Male gender	1.51 (0.53–4.32)	0.438	–	–
Septic shock	1.70 (0.65–4.43)	0.276		
Cirrhosis	1.59 (0.25–10.07)	0.623		
Pneumonia	2.64 (1.06–6.56)	0.037	2.40 (0.88–6.52)	0.085
Heart failure	1.18 (0.27–5.09)	0.824		
MV	2.13 (0.79–5.72)	0.133		
APACHE II	1.14 (1.03–1.27)	0.015	–	–
AGI	1.87 (1.20–2.94)	0.006	–	–
AGI group	4.27 (1.63–11.1)	0.003	3.93 (1.42–10.84)	0.008
SOFA score	1.16 (1.02–1.32)	0.022	–	–
mNUTRIC	1.42 (1.08–1.87)	0.012	1.28 (0.96–1.72)	0.097
mNUTRIC ≥5	2.79 (1.10–7.09)	0.031	–	–

Data are expressed as hazard ratio and 95% CI. AGI, acute gastrointestinal injury; APACHE II, acute physiology and chronic health evaluation; CI, confidence interval; mNUTRIC, modified nutritional risk in critically ill; SOFA, sequential organ failure assessment

to evaluate accurately in acute situations. In the clinical setting, AGI grading depends mostly on symptoms related to digestion and absorption, skipping other significant roles GI tract, such as serving as a barrier against intraluminal bacteria and harmful substances.[27] A research project by Li et al. on 90 participants revealed that D-la levels in serum could reflect the functionality of the intestinal barrier and AGI severity.[8] Other studies also mentioned markers like i-FABP and LPS related to early intestinal ischemic, injury, or hyperpermeability of the GI barrier. However, their results are inconsistent, and those markers' clinical value remains unclear.[28–31]

The mNUTRIC score, which incorporates age, comorbidities, SOFA score, APACHE II score, and the length of hospital stay prior to ICU admission, has been established to be reliable scale for assessing nutritional risk of severely ill patients.[32] In this study, higher mNUTRIC scores were correlated with higher mortality rates, supporting the existing evidence linking nutritional risks to worse outcomes in the ICU setting.

Combining AGI with mNUTRIC, APACHE II, or SOFA scores demonstrated improved predictive performance compared with AGI alone. This suggests that integrating gastrointestinal dysfunction assessment with established disease severity scores can enhance the accuracy of mortality prediction in critically ill patients. The combined approach comprehensively evaluates patients' overall condition, considering the gastrointestinal function and disease severity.

Limitation

There are several limitations to our study. First, the relatively small sample size could limit the broader applicability of the results. Further studies with more participants are required to validate the findings. Besides, the study design was cross-sectional, limiting the recognition of the causality between the variables examined. Longitudinal studies or randomized controlled trials would reveal more findings for the predictive value of AGI in conjunction with other scoring systems. Additionally, the study focused on in-hospital mortality as the primary outcome and other critical clinical consequence, such as length of ICU stay or long-term survival, were not assessed.

Conclusion

Combining AGI with disease severity scores, including SOFA, APACHE II, and mNUTRIC, improves the predictive power for in-hospital mortality in critically ill patients. Incorporating AGI into existing scoring systems could enhance risk stratification and assist clinical decision-making. Further research is warranted to validate these findings and explore the potential benefits of this combined approach in critically ill patients.

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Statement of Ethics

This study protocol had been approved by the Ethics Committee of 108 Military Central Hospital (No. 6876/CN-HĐĐĐ BV), which stated that informed consent was not necessary because of a retrospective study.

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