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Association between acute gastrointestinal injury grading system and disease severity and prognosis in critically ill patients: A multicenter, prospective, observational study in China

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ABSTRACT

Purpose: This prospective study investigated the association between disease severity and acute gastrointestinal injury (AGI) grade and between prognosis and AGI.
Methods: In 12 teaching hospitals in China, patients in intensive care units who had received a diagnosis of AGI were enrolled (N = 196). Their demographics, body mass index, Acute Physiology and Chronic Health Evaluation II score, Sepsis-related Organ Failure Assessment score, mechanical ventilation, acute kidney injury, intensive care unit stay, and 7-day and 28-day mortality were recorded.
Results: Of the 196 AGI patients, 90, 64, 29, and 13 were classified as grades I, II, III, and IV, respectively. Acute Physiology and Chronic Health Evaluation II scores independently predicted grades III and IV; acute kidney injury independently predicted grade III. The 28-day mortality rates of grades I and II were similar, as were those of grades III and IV. The mortality rate of patients with grades I + II (gastrointestinal dysfunction) was significantly lower than that of patients with grades III + IV (gastrointestinal failure).
Conclusion: Differentiating AGI as gastrointestinal dysfunction or gastrointestinal failure appears to be more valid for predicting prognosis than the AGI 4-grade system.

1. Introduction

In critically ill patients, the intestine is a vulnerable organ, and gastrointestinal dysfunction is common [1]. Conversely, gastrointestinal dysfunction can indicate a critical condition. It was reported that almost 50% of patients at admission to the intensive care unit (ICU) had enterocyte damage [2]. There is also strong evidence of intestinal epithelial hyperpermeability and bacterial translocation in ICU patients, supporting the concept that the gut can instigate multiple organ failure [3,4].

Patients with gastrointestinal failure have higher mortality rates [5,6]. It is therefore important to monitor the status of the gastrointestinal tract in critically ill patients. In 2012, The Working Group on Abdominal Problems (WGAP) of the European Society of Intensive Care Medicine (ESICM) proposed a definition for acute gastrointestinal injury (AGI) and recommended a 4-grade classification for AGI severity [7]. Although these recommendations were not based on strong evidence, they provide guidance in the clinical setting.

According to the WGAP-ESICM criteria, AGI patients with grades I or II can tolerate a certain amount of enteral nutrition, but the gastrointestinal tract is not able to adequately digest and absorb nutrients and water. AGI patients at grades III or IV are intolerant of enteral nutrition, and the gastrointestinal tract cannot digest or absorb nutrients or water in any significant way. Thus, AGI grades I and II can be grouped as gastrointestinal dysfunction, whereas grades III and IV represent gastrointestinal failure.

With appropriate management and interventions such as percutaneous drainage of intraabdominal fluid to decrease intra-abdominal hypertension [8,9], patients' gastrointestinal status can improve rapidly. Therefore, the AGI grade of patients may quickly change, and clear classification can be difficult. We hypothesized that the difference between gastrointestinal dysfunction (grades I and II) and gastrointestinal failure (grades III and IV) might differentiate non–life-threatening from life-threatening conditions.

To improve the ability of intensivists to recognize AGI in the ICU, herein we assessed the construct validity of a simplified 2-grade system (ie, gastrointestinal dysfunction and gastrointestinal failure) to define AGI in critically ill patients. Specifically, this study investigated the association between disease severity and AGI grade and between prognosis and AGI grade.

2. Methods

This is a prospective, observational, nationwide study involving 12 general ICUs in large teaching hospitals in China (Appendix A). These

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Table 1
Classification of AGI [7]

Grade	Definition
I	The function of the gastrointestinal tract is partially impaired, expressed as gastrointestinal symptoms related to a known cause, and perceived as transient. Examples: postoperative nausea and/or vomiting during the first days after abdominal surgery, postoperative absence of bowel sounds, diminished bowel motility in the early phase of shock.
II	The gastrointestinal tract is not able to perform digestion and absorption adequately to satisfy the nutrient and fluid requirements of the body. There are no changes in general condition of the patient related to gastrointestinal problems. Examples: gastroparesis with high gastric residuals or reflux, paralysis of the lower GI tract, diarrhea, intra-abdominal hypertension (IAH) grade I (intra-abdominal pressure [IAP] 12-15 mm Hg), visible blood in gastric content or stool. Feeding intolerance is present if at least 20 kcal/kg BW per day via enteral route cannot be reached within 72 h of feeding attempt.
III	Loss of gastrointestinal function, and restoration of gastrointestinal function is not achieved despite interventions, and the general condition is not improving. Examples: Despite treatment, feeding intolerance is persisting—high gastric residuals, persisting GI paralysis, occurrence or worsening of bowel dilatation, progression of IAH to grade II (IAP 15-20 mm Hg), low abdominal perfusion pressure (APP) (below 60 mm Hg). Feeding intolerance is present and possibly associated with persistence or worsening of multiple organ dysfunction syndrome.
IV	AGI has progressed to become directly and immediately life-threatening, with worsening of multiple organ dysfunction syndrome and shock. Examples: bowel ischemia with necrosis, GI bleeding leading to hemorrhagic shock, Ogilvie syndrome, abdominal compartment syndrome requiring decompression.

ICUs are members of the Chinese Society of Critical Care Medicine. Each of the hospitals has more than 1000 effective hospital beds and more than 10 ICU beds.

Before commencing the study, the authors conducted a training workshop focusing on the diagnosis of AGI. The diagnostic criteria (Table 1) were distributed to 1 staff member from each unit who was in charge of training his or her unit colleagues. The choice of these staff members was left to each participating ICU. The Ethics Committee of First Hospital of Jilin University and the other 11 hospitals' committees approved the study. Written informed consent was waived because of the study's observational nature. Patients or their legal representatives were verbally informed about the use of their data for this study. No specific protocols or recommendations for AGI management were imposed.

Patients were included if they received a diagnosis of AGI that was in accordance with the ESICM definition and grading system within 72 hours after admission [7]. Patients were enrolled from 1 January 2014 to 28 February 2014, and each was followed for 28 days. We did not determine sample size a priori.

Excluded from the study were patients younger than 18 years or with severe cardiovascular disease, chronic end-stage organ failure, malignancy, Crohn disease, ulcerative colitis, or short bowel syndrome, and patients who were hospitalized for less than 72 hours before the AGI diagnosis could be established. The patients were classified by AGI grade based on the ESICM recommendations. Nutritional support and other treatments were provided according to local practice guidelines and at the clinicians' discretion.

The following data were prospectively collected by the managing physicians of the patients: demographic data, AGI grade, body mass index (BMI), Acute Physiology and Chronic Health Evaluation (APACHE II) score (in the first 24 hours after ICU admission), Sepsis-related Organ Failure Assessment (SOFA) score (in the first 24 hours after ICU admission), days of mechanical ventilation, acute kidney injury, if the patient was admitted postoperatively or because of sepsis, ICU length of stay (LOS), and 7-day and 28-day mortality. Cases with insufficient or unclear information were excluded. Patients with missing data were excluded also. Data were entered into a Web-based system and stored centrally.

2.1. Statistical analyses

Categorical variables are presented as percentages, whereas continuous variables are presented as mean and standard deviation if normally distributed or as median and interquartile range (IQR) if not. Categorical variables were compared using the χ^2 test, and continuous variables were compared with the Kruskal-Wallis test for 4-grade AGI and Mann-Whitney *U* test for 2-grade AGI. All the variables at entry were compared using a univariate analysis with multinomial regression analysis for 4-grade AGI and binary regression analysis for 2-grade AGI.

Those variables that were statistically significant based on the univariate analysis ($P < .05$) were included in the multiple logistic regression analysis to identify the association between the AGI grade and disease severity. Kaplan-Meier curves were plotted for time to all-cause death from admission to day 28. A P value < .05 was considered statistically significant. All tests were 2-sided. Data analyses were performed using commercially available software (PASW Statistics, version 17.0; SPSS, Chicago, IL).

3. Results

3.1. Patient enrollment

Of the 245 patients initially enrolled in the study, 49 were excluded because of lack of complete information, loss to follow-up, or an unclear AGI classification.

3.2. Characteristics of the critically ill adult patient population with AGI

Among the 196 included patients, the numbers classified as grades I, II, III, and IV were 90, 64, 29, and 13, respectively (Table 2). Thus, 154 patients were grades I + II (acute gastrointestinal dysfunction), and 42 were grades III + IV (acute gastrointestinal failure). The median age

Table 2
Characteristics of the patients by AGI grade[a]

	I	II	III	IV	I + II[b]	III + IV[c]	Total
Sample size, n	90	64	29	13	154	42	196
Age, y	71.0 (55.2-80.0)	61.5 (45.5-80.8)	64.0 (46.0-79.0)	64.0 (52.5-82.0)	67.0 (47.0-80.0)	64.0 (46.0-80.5)	66.0(47.0-80.0)
Male	57 (63.3)	44 (68.8)	19 (65.5)	9 (69.2)	101 (65.6)	28 (66.7)	129 (65.8%)
BMI, kg/m^2	23.4 (22.0-25.2)	23.3 (21.1-24.7)	23.4 (20.2-26.2)	23.0 (21.0-25.5)	23.3 (21.8-25.0)	23.4 (20.8-26.1)	23.4 (21.3-25.4)
APACHE II score	14.0 (9.5-17.0)	15.0 (9.3-22.8)	23.0 (16.0-29.5)	26.0 (23-27.5)	14.0 (9.5-20.0)	24.0 (18.8-29.0)	16.0(10.0-23.0)
SOFA score	5.0 (4.0-7.0)	6.0 (4.0-10.0)	9.0 (5.0-14.0)	8.0 (5-12)	6.0 (4.0-8.0)	8.0 (5.0-13.0)	6.0 (4.0-9.0)
Surgery	48 (53.3)	27 (42.2)	11 (37.9)	5 (38.5)	75 (48.7)	16 (38.1)	91 (46.4%)
Sepsis	23 (25.5)	17 (26.5)	10 (34.5)	7 (53.8)	40 (26.0)	17 (40.5)	57 (29.1%)
Mechanical ventilation	60 (66.7)	45 (70.3)	22 (75.9)	12 (92.3)	105 (68.2)	34 (81.0)	139 (70.9%)
Acute kidney injury	13 (14.4)	15 (23.4)	14 (48.3)	4 (30.8)	28 (18.2)	18 (42.9)	46 (23.5%)

[a] Measurement values expressed as median (IQR, 25%-75%) categorical variables were reported as n (%).
[b] Acute gastrointestinal dysfunction.
[c] Acute gastrointestinal failure.