

Gastric Cross-Sectional Area to Predict Gastric Intolerance in Critically Ill Patients: The Sono-ICU Prospective Observational Bicenter Study

OBJECTIVES: To evaluate the correlation between gastric cross-sectional area (GCSA) and the occurrence of gastric intolerance in critically ill patients within 24 hours of the measurement.

DESIGN: Two-center prospective observational study.

SETTING: Two academic ICUs in France between June 2020 and August 2021.

PATIENTS: All surgical intubated ICU patients greater than or equal to 18 years old receiving enteral feeding for greater than 12 hours.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: Forty-four patients were included, 11 (25%) of whom presented digestive intolerance. Primary outcome was assessment of the association between GCSA and the occurrence of gastric intolerance within 24 hours of the measurement. GCSA value was significantly higher in patients with upper digestive intolerance compared to those without (553 mm² [interquartile range (IQR), 500–649 mm²] vs 970 mm² [IQR, 777–1,047]; $p < 0.001$, respectively). The optimal threshold for predicting upper digestive intolerance was 720 mm² (area under the receiver operating characteristic curve 0.86; positive predictive value 62.5%; negative predictive value 96.4%; sensibility 0.91; and specificity 0.81). Multivariate analysis (weighted by propensity score), including known risk factors, showed that GCSA above the 720 mm² threshold was independently associated with the occurrence of upper digestive intolerance (odds ratio, 1.85; 1.37–2.49; $p < 0.0002$). Measurement quality was “good” (i.e., liver, aorta, superior mesenteric vein, and pancreas were all visualized) in 81% of cases.

CONCLUSIONS: Measurement of GCSA by ultrasound would allow prediction of gastric intolerance in critically ill patients. This should be confirmed by a prospective score validation and interventional trials.

KEY WORDS: antral sonography; enteral feeding; gastric cross-sectional area; gastric intolerance; intensive care unit

Daniel El Khoury, MD¹

Emmanuel Pardo, MD¹

Amelie Cambriel, MD¹

Francis Bonnet, MD, PhD¹

Tai Pham, MD²

Bernard Cholley, MD, PhD³

Christophe Quesnel, MD, PhD¹

Franck Verdonk, MD, PhD¹

Enteral feeding (EF) is an important aspect of supportive care in patients hospitalized in an ICU reducing morbidity, occurrence of infectious complications, and length of stay (1–3). Occurrence of EF intolerance varies from 30% to 50% in critically ill patients, leading to regurgitation and vomiting (4). EF intolerance is associated with ventilator-associated pneumonia (VAP) (5) and prevents the recommended daily caloric intake (6). Some risk factors for poor tolerance of EF have been previously identified (7, 8) including diabetes, depth of sedation, and neuromuscular blocking agents (NMBAs) (9–11). The measurement of gastric residual volume (GRV) by aspiration, commonly used in ICUs, is no longer recommended because of its negative

Copyright © 2023 The Authors. Published by Wolters Kluwer Health, Inc. on behalf of the Society of Critical Care Medicine. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/CCE.0000000000000882



KEY POINTS

Question: Is sonographic measure of gastric cross-sectional area (GCSA) predictive of gastric intolerance (GCSA) in critically ill patients receiving enteral feeding?

Findings: In this prospective observational bicenter study that included 44 surgical critically ill patients receiving enteral feeding for greater than 12 hours, the value of GCSA measurement was significantly higher in patients with upper digestive intolerance compared with those without and the optimal threshold for predicting upper digestive intolerance was 720 mm² (area under the receiver operating characteristic [ROC] curve [AUC], 0.86; positive predictive value, 62.5%; negative predictive value, 96.4%; Se, 0.91; Sp, 0.81).

Meaning: A GCSA greater than 720 mm² measured by gastric ultrasound can predict the occurrence of gastric intolerance in critically ill patients requiring enteral feeding.

effect on the daily calorie intake target and because of its lack of impact on the occurrence of VAP (12, 13). Indeed, the measurement of GRV by aspiration involves multiple causes of inaccuracy and hence unreliability, such as the size of the gastric tube, its position in the stomach, the intra-abdominal pressure, as well as the type of aspiration used (14). Up to now, no other noninvasive tool, readily available in routine practice, has been reported to reliably predict EF tolerance, thus guiding EF and the prescription of treatments such as prokinetics (15).

Ultrasound measurement of the gastric cross-sectional area (GCSA), easily performed at the bedside, is a technique that has been developed in anesthesia, particularly in the preoperative period, to evaluate the gastric content before induction of an anesthetic (16). It has also been used in the ICU (17). The measurement of GCSA has been shown to correlate with the gastric volume whether measured by GRV (18) or by CT scan (19). It has been mainly validated for identifying a “full stomach” (>0.8 mL/kg or 340 mm² of GCSA) before anesthesia. Currently, there is little available data to correlate GCSA with the occurrence of gastric intolerance in the ICU.

The objective of this prospective observational bicenter study was, therefore, to determine a GCSA threshold, predictive of gastric intolerance in critically ill patients, and to evaluate risk factors for poor tolerance of EF.

MATERIAL AND METHODS

Study Design

SONO-ICU is a prospective, bicenter, observational study, evaluating the association between measured GCSA and gastric intolerance in critically ill patients.

Population

Eligible patients were greater than or equal to 18 years old, mechanically ventilated through an endotracheal tube and receiving continuous EF for more than 12 hours (Nutrition Protocol in **Supplemental Material**, <http://links.lww.com/CCX/B156>). Two French University teaching surgical ICUs (Saint-Antoine Hospital and Georges Pompidou European Hospital, Assistance Publique Hôpitaux de Paris [AP-HP], Paris) participated in the study.

Patients were not eligible if they were pregnant or presented with a history of upper digestive tract surgery, potentially altering or impeding the GCSA measurement, or if the investigator was not available to perform the ultrasound measurement.

Investigation Procedure

All patients who had been fed by EF for more than 12 hours and where a trained operator was available to perform a routine gastric ultrasound were included for the duration of the study period. EF protocol was the same for every patient. Continuous feeding with 2 kcal/mL Fresubin HP fiber free (Fresenius Kabi, Louviers, France) in the form of 16.7 g carbohydrates, 10 g fat, and 10 g protein per 100 mL was administered through a nasogastric tube, starting with a rate of 20 mL/hr; the feeding rate was increased by 25% every day until the target energy requirement was reached. According to the 2016 American Society for Parenteral and Enteral Nutrition (ASPEN)/Society of Critical Care Medicine (20) guidelines, based on actual body weight, the target energy requirement was calculated as 25 kcal/kg/d, and the protein requirement was 1.4 g/kg/d.

Following the methodology described by Van de Putte and Perlas (21) (see also [16] and [22]), ultrasound with GCSA measurement was performed by trained operators who were senior physicians with experience in more than 30 measurements of gastric content using ultrasonography. They had received specific training in gastric ultrasound, which included self-directed learning, conventional lecture programs, and hands-on practice. Each GCSA value was calculated as the mean of two measurements. Each measurement was performed with a low-frequency (2–5 Hz) abdominal ultrasound probe (General Electric Logiq-e or General Electric Voice, Video, and Data E90 ultrasound machines, GE HealthCare Technologies, Inc. Chicago, Illinois, U.S.). The probe was placed under the xiphoid process in order to visualize the left lobe of the liver and the inferior vena cava. The antrum is usually visualized in the vicinity of the superior mesenteric artery, the abdominal aorta, the pancreas, and the left lobe of the liver, which constitute the main anatomical landmarks. The antrum appears as a flattened ellipse or an anechoic black circle surrounded by a wall with several layers of variable echogenicity (**Supplementary Fig. 1**, <http://links.lww.com/CCX/B156>). The GCSA was measured with the patient half-seated (45°), with the aorta as an anatomical axial landmark, in the absence of gastric contraction, by contouring the antral serosa using the “free tracing” tool (**Supplemental Fig. 2**, <http://links.lww.com/CCX/B156>).

Gastric ultrasound measurements on the day of inclusion or on the day the patient presented with gastric intolerance were collected on a dedicated form. This measurement did not affect usual clinical management, which remained at the discretion of the physician in charge. Each measurement was qualitatively assessed and classified as “not feasible,” “difficult,” or “good.” We considered the GCSA measurement as “not feasible” if no anatomic structure was identified; “difficult” if only one or two structures were distinguished; and “good” if the liver, aorta, superior mesenteric vein, and pancreas were all visualized.

Demographic data, Simplified Acute Physiology Score 2 (SAPS2), medications, VAP (yes or no), duration of invasive ventilation, and the length of stay in the ICU were collected using patients’ medical charts.

Outcomes

Primary Outcome. The primary outcome was the occurrence of gastric intolerance within 24 hours after the measurement. “Gastric intolerance” was defined as a composite criterion including regurgitation, and/or discontinuation of EF, and/or nasogastric tube aspiration, and/or 24-hour caloric intake of less than 20% of the previous day’s intake (due to inability to receive EF).

Secondary Outcomes. The secondary outcomes were to define a GCSA threshold predictive of gastric intolerance and to identify risk factors of gastric intolerance using predefined clinical criteria (sedation, NMBA, diabetes mellitus, body mass index [BMI], vasopressors, and SAPS2 on admission). We also assessed the association between gastric intolerance and days of mechanical ventilation, VAP, and mortality. Furthermore, we assessed the feasibility of such measurements in critically ill patients.

Statistical Methodology

No sample size calculation was performed as no study has previously evaluated GCSA in this population of patients; this was an exploratory study.

Quantitative variables are shown as median (25–75th percentiles) or mean (SD) and qualitative variables as count (proportion). Categorical variables were compared using Fisher exact tests and chi-square tests, and numeric variables were compared by Mann-Whitney or Student *t* test according to the normality of quantitative variables assessed by a Shapiro-Wilk test. The tests were two-sided, with an alpha risk of 0.05. A *p* value of lower than 0.05 was considered significant.

If no gastric intolerance occurred during the ICU stay, we recorded the first GCSA measure during the ICU stay; otherwise, we used the GCSA assessed on the day gastric intolerance occurred.

A multivariate logistic regression analysis was performed with the factors already described in the literature as associated with gastric intolerance in critically ill patients and the variables significantly associated with gastric intolerance on the day of the study (9–11). Results are expressed as odds ratios (ORs) with their 95% CIs. Multivariate model selection was performed using a two-way stepwise procedure aiming to minimize the Akaike information criterion. The final model was adjusted for BMI, diabetes, opioid use, NMBA,

and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia. The goodness of fit was assessed using the Hosmer-Lemeshow test.

In order to be used in daily clinical practice, the variable "GCSA at study day" was dichotomized at the optimal threshold, determined by the highest Youden index (Sensitivity + Specificity - 1). Positive and negative predictive values (NPVs) and receiver operating characteristic (ROC) curves were calculated using the *Cutpoint* package (23).

To validate our hypothesis of an association between high GCSA and the occurrence of gastric intolerance, and to optimize the comparability of the groups in the absence of randomization, the multivariate analyses were repeated using a propensity score. The propensity was modeled using the "Gradient Boosting Machine," a nonparametric machine-learning algorithm included in the *Twang* package. Confounding factors included in the propensity score were diabetes, SARS-CoV-2, opioid use, and use of NMBA. The balance of the propensity model was analyzed by the standardized effect size of the variables. Generally, standardized effects of less than 0.20 were considered small (better balance), 0.40 as moderate, and 0.60 as large.

The weights calculated from the propensity score were used to perform a weighting on the multivariate logistic regression. Unlike propensity score matching, weighting keeps the sample complete by assigning each subject an individual weight. It is then possible to evaluate the association with the occurrence of gastric intolerance in a pseudopopulation, in which the characteristics of the subjects with or without a high GCSA are balanced.

Intraoperator reliability between the two area measurements was assessed by the intraclass correlation coefficient (ICC). The ICC was interpreted as follows (24): less than 0, poor agreement; 0.01–0.20, slight agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, substantial agreement; 0.81–1.00, almost perfect agreement.

The R software (version 4.1.2 Graphical User Interface (GUI) 1.77 for Macintosh, Licenses "Gnu's Not Unix!" (GNU) General Public Licence (GPL), The R foundation for statistical computing, Vienna, Austria) and the Rstudio interface Version 2022.02.0 (RStudio, Inc. Boston, Massachusetts, U.S) were used to perform the statistical analyses.

Ethics

This prospective observational study obtained the approval of the Research Ethics Committee of the Sorbonne University CER-2020-47 (May 28, 2020; Pr Chetouani), and procedures were performed in accordance with the Helsinki Declaration of 1975.

All patients were informed via the AP-HP website of the possible use of their medical data in the framework of research aiming to improve the quality of care, as well as of their rights and procedures for any dispute. In addition, the patient and/or relatives received confirmation of enrollment in the study at the time of inclusion.

To guarantee the security of personal data, the investigators collected and integrated information in an anonymized form in a secure database, in accordance with the Commission Nationale de l'Informatique et des Libertés (CNIL) MR-004 methodology and registered in the AP-HP data processing register 20220718171756.

The investigators who had direct access to the data took all necessary precautions to ensure the confidentiality of the information relating to this trial and to the persons who took part in it.

RESULTS

Patient Characteristics

Of the 285 patients screened between June 4, 2020, and August 4, 2021, 44 patients 18 years old or older were included (**Fig. 1**). Clinical and demographic data are listed in **Table 1**.

The median SAPS2 was 40 (interquartile range [IQR], 31–60). Twenty-three patients (52%) were managed in the ICU for acute respiratory failure associated with SARS-CoV-2.

Primary Outcome

Eleven patients (25%) had gastric intolerance. The clinical and gastric ultrasound data on the day of measurement were collected on day 8 (IQR, 5–24) following admission to the ICU. Comparative data, using univariate analysis for the groups with and without gastric intolerance, are shown in **Table 2**.

On univariate analysis, GCSA was significantly different between the two groups, with a median of 553 mm² (IQR, 500–649) in patients without

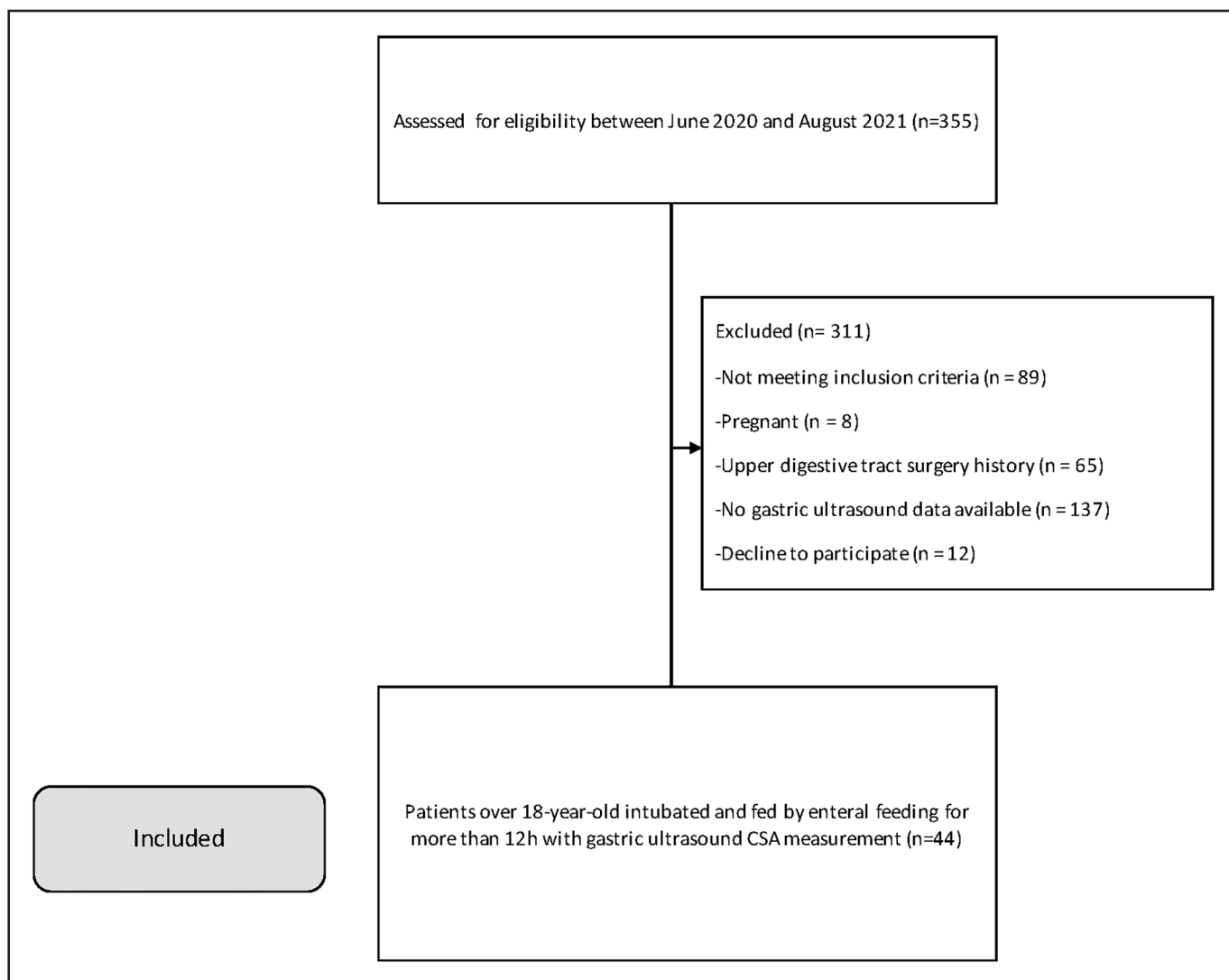


Figure 1. Flowchart. CSA = cross-sectional area.

intolerance versus 970 mm² (IQR, 777–1,047) in patients with gastric intolerance ($p < 0.001$).

Secondary Outcomes

GCSA Threshold Value

We used a receiver operating characteristic (ROC) curve to dichotomize the variable for a prediction of the event “gastric intolerance” (Fig. 2). Area under the ROC curve was 0.86 ($p = 0.000014$).

The threshold of 720 mm² was considered optimal because it had the highest Youden index (optimal Youden cutpoint: 720.5).

A threshold of 720 mm² yields a positive predictive value of 62.5% and an NPV of 96.4% (Supplemental Fig. 3, <http://links.lww.com/CCX/B156>). Using this threshold, sensitivity was 0.91, specificity was 0.81,

positive likelihood ratio was 5.00, and negative likelihood ratio was 0.11.

Multivariate Analysis

Multivariate analyses with and without propensity score weighting are shown in Table 3. A GCSA higher than 720 mm² was found to be the only risk factor independently associated with gastric intolerance.

A GCSA greater than 720 mm² was associated with the occurrence of the event of interest in both the unweighted (OR, 1.01; CI, 1.00–1.02) and the weighted population (OR, 1.85; CI, 1.37–2.49).

Other Outcomes

Patients with gastric intolerance did not differ from other patients for most parameters, including

TABLE 1.
Clinical and Demographic Characteristics

| Variables | <i>n</i> = 44 |
|--|------------------|
| Age (mean [sb]) | 62.1 (10.9) |
| Male, <i>n</i> (%) | 32 (72.7) |
| Weight (median [IQR]) | 80.5 (78.7–90.5) |
| Body mass index (median [IQR]) | 28.7 (24.8–31.4) |
| Simplified Acute Physiology Score 2 (median [IQR]) | 40.0 (31.0–60.0) |
| Ventilation days (before GCSA measurement, median [IQR]) | 20.0 (17.0–35.0) |
| Days in ICU (before GCSA measurement, median [IQR]) before GCSA measurement, median [IQR]) | 29.0 (15.0–58.5) |
| Reason for ICU admission, (%) | |
| Cardiac arrest | 3 (6.8) |
| Cardiogenic shock | 2 (4.5) |
| Septic shock | 2 (4.5) |
| Respiratory distress | 1 (2.3) |
| Endocarditis | 1 (2.3) |
| Pancreatitis | 3 (6.8) |
| Severe acute respiratory syndrome coronavirus 2 pneumopathy | 23 (52.3) |
| Cardiac surgery | 7 (15.9) |
| Digestive surgery | 1 (2.3) |
| Trauma | 1 (2.3) |
| Diabetes, <i>n</i> (%) | 13 (29.5) |
| Obesity, <i>n</i> (%) | 14 (31.8) |
| Hypothyroidism, <i>n</i> (%) | 4 (9.1) |
| Alcoholism, <i>n</i> (%) | 9 (20.5) |
| Smoking, <i>n</i> (%) | 8 (18.2) |
| Days in ICU before inclusion (median [IQR]) | 8.50 (5.00–24.0) |

GCSA = gastric cross-sectional area, IQR = interquartile range. Values are mean (sd), median (IQR), or effectiveness (%).

previously reported risk factors (sedation, NMBA, diabetes, and SARS-CoV-2). Patients with intolerance received opioids more frequently (60.6% vs 100%; $p = 0.015$) (Table 2).

The most common event found in the composite criterion “gastric intolerance” was regurgitation (100%).

The duration of mechanical ventilation, extubation rate, occurrence of VAP, and mortality did not differ between the two groups (Table 4).

Quality of Measurements and Intraoperator Reliability

In 81% of cases, the ultrasound was of good quality, whereas in 18% of cases, it was difficult. In 91% of cases, three out of four structures (liver, pancreas, superior mesenteric vein, and aorta) could be visualized. Ninety-three pairs of measurements were performed for each GCSA measurement; the ICC was 0.868 (95% CI, 0.804–0.911).

DISCUSSION

This prospective, bicenter, observational study documented an association between the size of the GCSA and the occurrence of gastric intolerance in 44 critically ill patients. The occurrence of the gastric intolerance event was significantly more frequent in patients with a GCSA higher than 720 mm². According to multivariate analysis, GCSA measurement was the only independent risk factor of gastric intolerance.

To our knowledge, this is the first study available in English to associate an ultrasonically measured GCSA with gastric intolerance in the ICU. Two other studies previously reported results in a similar setting but are not available in English (25, 26). These studies, involving 150 and 42 patients, 28% of whom presented gastric intolerance, reported GCSA gastric intolerance-associated thresholds of 710 and 711 mm², respectively. In addition, the present study confirmed the feasibility of gastric ultrasound in the ICU with a high rate (>80%) of good quality ultrasound, comparable with the feasibility observed in the study by Hamada et al (19). We also found good intraoperative reliability with ICCs considered as “almost perfect agreement” (24). A recent study by Jahreis et al (17) and one by Bouvet et al (27) support our data in terms of feasibility (100% feasible GCSA measurements in 217 patients and 75 patients in the two studies, respectively). Furthermore, this examination is simple and can be rapidly learned (95% success rate after 33 measurements) (28), so the process could be transferred to paramedical teams. GCSA has good inter- and intraoperator reproducibilities (29). Although training is necessary, this examination seems relevant to improve practice as well as EF prescription, with the objective of personalizing care.

Gastric intolerance is mainly associated with regurgitation, and VAP is the main complication. The

TABLE 2.
Univariate Analysis Depending on Enteral Feeding Tolerance

| Variables | No Gastric Intolerance (n = 33) | Gastric Intolerance (n = 11) | p |
|--|---------------------------------|------------------------------|---------|
| Age (mean [sd]) | 61.24 (11.44) | 64.73 (9.33) | 0.367 |
| Male, n (%) | 24 (72.7) | 8 (72.7) | 1.000 |
| Simplified Acute Physiology Score 2 (median [IQR]) | 41.00 (33.25–64.25) | 38.00 (26.50–51.00) | 0.227 |
| Type 1 diabetes, n (%) | 3 (9.1) | 0 (0.0) | 0.730 |
| Type 2 diabetes, n (%) | 6 (18.2) | 4 (36.4) | 0.406 |
| Severe acute respiratory syndrome coronavirus 2, n (%) | 14 (42.4) | 9 (81.8) | 0.055 |
| Obese, n (%) | 9 (27.3) | 5 (45.5) | 0.455 |
| Hypothyroidism, n (%) | 3 (9.1) | 1 (9.1) | 1.000 |
| Alcoholism, n (%) | 7 (21.2) | 2 (18.2) | 1.000 |
| Smoking, n (%) | 7 (21.2) | 1 (9.1) | 0.652 |
| On day of study, n (%) | | | |
| Ventilatory acquired pneumonia | 16 (48.5) | 7 (63.6) | 0.601 |
| Digestive transit | 10 (30.3) | 6 (54.5) | 0.278 |
| Neuromuscular blocking agents | 5 (15.2) | 2 (18.2) | 1.000 |
| Opioids | 20 (60.6) | 11 (100.0) | 0.015 |
| Sedation | 17 (51.5) | 8 (72.7) | 0.380 |
| Vasopressive drugs | 7 (21.2) | 3 (27.3) | 0.703 |
| Prokinetics | 2 (6.1) | 0 (0.0) | 0.705 |
| Gastric sonography | | | |
| Difficult sonography, n (%) | 6 (18.2) | 2 (18.2) | 1.000 |
| GCSA first measure (median [IQR]) | 553.00 (520.00–627.00) | 900.00 (758.50–1,000.00) | 0.001 |
| GCSA second measure (median [IQR]) | 560.00 (479.00–700.00) | 940.00 (765.00–1,020.00) | < 0.001 |
| Mean GCSA (median [IQR]) | 553.50 (500.00–649.00) | 970.00 (776.75–1,047.50) | < 0.001 |
| Days in ICU before inclusion (median [IQR]) | 9.00 (5.00–27.00) | 7.00 (5.00–16.50) | 0.249 |

Values are mean (sd), median (IQR), or effectiveness (%). *p* comes from Fisher exact test for qualitative variables and Mann-Whitney *U* test for quantitative variables with nonnormal distribution. A Bonferroni correction was used to assess the signification threshold. GCSA = gastric cross-sectional area, IQR = interquartile range.

occurrence of VAP is doubled in cases of regurgitation. A reduction in caloric intake of almost 25% over a complete stay in an ICU (5), an increase in mechanical ventilation duration (11.7 d vs 3.3 d; $p < 0.001$), and ICU length of stay (14.4 d vs 11.7 d; $p < 0.001$) (7) are also described in cases of gastric intolerance. Current practices to limit this intolerance consist of daily measurement of GRV by aspiration followed by

adaptation of EF flow rates or introduction of prokinetics (30). The use of GRV by aspiration has been justified by different teams, most notably by Montejo et al (31) and McClave et al (32), who used different thresholds to predict intolerance to EF and/or gastric emptying. These articles have been questioned with regard to clinical relevance and because they fail to show a reduction in occurrence of VAP. Furthermore,

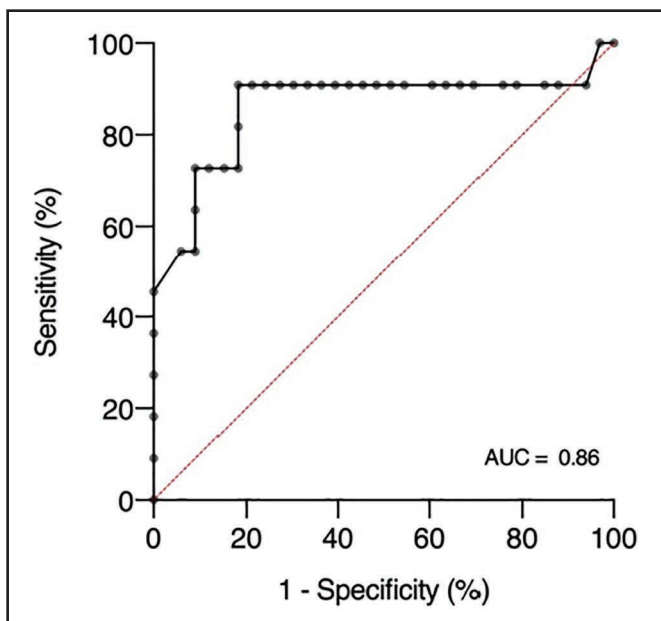


Figure 2. Receiver operating characteristic (ROC) curve. ROC curve for cross-sectional area greater than 720mm² predictive for gastric intolerance. Area under the ROC curve (AUC) = 0.8609; $p = 0.000014$.

TABLE 3.
Multivariate Analysis With and Without Propensity Score Weighting

| Variable | Without Propensity Score Weighting | | With Propensity Score Weighting | |
|-----------------------------------|------------------------------------|----------|---------------------------------|----------|
| | OR (95% CI) | <i>p</i> | OR (95% CI) | <i>p</i> |
| Mean gastric cross-sectional area | 1.01 (1–1.02) | 0.00287 | 1.85 (1.37–2.49) | 0.00017 |

OR = odds ratio.

Values are represented as OR (95% CIs). Propensity weighted model with adjustment for body mass index, diabetes, opioids use, neuromuscular blocking agents, and severe acute respiratory syndrome coronavirus 2 pneumonia.

TABLE 4.
Univariate Analysis on Days With Mechanical Ventilation, Ventilatory-Associated Pneumonia, Extubation Rate, and Mortality Depending on Enteral Feeding Tolerance

| Variables | No Gastric Intolerance (<i>n</i> = 33) | Gastric Intolerance, (<i>n</i> = 11) | <i>p</i> |
|---|---|---------------------------------------|----------|
| Days with mechanical ventilation (median [interquartile range]) | 23.00 (17.00–36.00) | 20.00 (14.00–31.00) | 0.757 |
| Ventilatory-associated pneumonia (%) | 16 (48.5) | 7 (63.6) | 0.601 |
| Death (%) | 10 (32.3) | 1 (9.1) | 0.270 |

Values are represented as median (interquartile range) or effectiveness (%). *p* comes from Fisher exact test for qualitative variables and Mann-Whitney *U* test for quantitative variables with nonnormal distribution. A Bonferroni correction was used to assess the signification threshold.

a prospective interventional trial by Reignier et al (13), which included 449 patients, and a meta-analysis (including 7 clinical trials) of 1,585 patients by Yasuda et al (33) showed that measurement of GRV led to a reduction in intake by stopping EF and that this practice had no impact on 30-day survival of critically ill patients, length of stay, or even on the occurrence of gastric intolerance (33). Measurement of GRV by aspiration is, therefore, no longer recommended or may not be required as part of routine care to monitor critically ill patients on EF, as stated by the ASPEN guidelines (34). However, the prediction of gastric intolerance remains a challenge to help reduce the occurrence of gastric complications and to improve EF flow adjustment or the introduction of prokinetics (35).

As already documented in the preoperative setting (21, 36), our results suggest that gastric ultrasonography, with GCSA measurement, could be used in the ICU, to help prevent intolerance to EF. The main advantages of this noninvasive examination are three-fold: 1) it does not require discontinuation of EF and, therefore, reduction of intake because of the measurement, 2) the results in our study achieved a predictive performance not reached by GRV (32), and 3) it allows quick and noninvasive evaluation of the effectiveness of therapeutic measures.

This study has some limitations. First, although data collection was prospective and bicentric, it presents limitations inherent to its observational design. The absence of randomization may be a source of both selection bias and confounding factors, necessitating caution when interpreting the results. The use of a propensity score after weighting for risk factors reduces these biases. In addition, risk factors of gastric intolerance found in previous studies, including diabetes, the level of sedation, and

NMBA (7–11), were not associated with a higher occurrence of gastric intolerance in our study. This may be explained by a lack of power due to a small sample size ($n = 44$). Another explanation could be that this measure has a high sensitivity compared with other risk factors.

Furthermore, despite a significant proportion of patients with severe SARS-CoV-2 pneumonia (53%) in our study, we did not find a higher occurrence of digestive intolerance when compared with other critically ill patients.

CONCLUSIONS

In conclusion, in critically ill patients requiring EF, a GCSA greater than 720 mm² measured by gastric ultrasound can predict the occurrence of gastric intolerance. Interventional trials involving pharmacological or nonpharmacological prevention are needed to confirm the utility of this measure in clinical practice.

- 1 Department of Anaesthesiology and Intensive Care, Hôpital Saint-Antoine Assistance Publique des Hôpitaux de Paris and Sorbonne University, GRC 29, DMU DREAM, Paris, France.
- 2 Department of Intensive Care Medicine, Hôpital Kremlin Bicêtre Hospital and Paris Saclay University, Assistance Publique des Hôpitaux de Paris, Paris, France.
- 3 Department of Anaesthesiology and Critical Care Medicine, Hôpital Européen Georges Pompidou—Assistance Publique Hôpitaux de Paris, and Université Paris Cité, INSERM, Innovative Therapies in Haemostasis, Paris, France.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (<http://journals.lww.com/ccejournal>).

Drs. El Khoury, Pardo, and Verdonk designed the study protocol. Drs. El Khoury and Verdonk led the study. Dr. Pardo performed the statistical analysis. Dr. El Khoury was responsible for writing the draft of the article with assistance from Drs. Pardo, Cambriel, Bonnet, Pham, Quesnel, and Verdonk. All authors read, provided input, and approved the final article. Drs. El Khoury and Verdonk accessed and verified the data.

For information regarding this article, E-mail: franck.verdonk@aphp.fr

REFERENCES

1. Hadfield RJ, Sinclair DG, Houldsworth PE, et al: Effects of enteral and parenteral nutrition on gut mucosal permeability in the critically ill. *Am J Respir Crit Care Med* 1995; 152:1545–1548
2. Li J, Kudsk KA, Gocinski B, et al: Effects of parenteral and enteral nutrition on gut-associated lymphoid tissue. *J Trauma* 1995; 39:44–52
3. Gianotti L, Alexander JW, Nelson JL, et al: Role of early enteral feeding and acute starvation on postburn bacterial translocation and host defense: Prospective, randomized trials. *Crit Care Med* 1994; 22:265–272
4. Reintam Blaser A, Starkopf L, Deane AM, et al: Comparison of different definitions of feeding intolerance: A retrospective observational study. *Clin Nutr* 2015; 34:956–961
5. Mentec H, Dupont H, Bocchetti M, et al: Upper digestive intolerance during enteral nutrition in critically ill patients: Frequency, risk factors, and complications. *Crit Care Med* 2001; 29:1955–1961
6. Kim H, Stotts NA, Froelicher ES, et al: Why patients in critical care do not receive adequate enteral nutrition? A review of the literature. *J Crit Care* 2012; 27:702–713
7. Gungabissoon U, Hacquoil K, Bains C, et al: Prevalence, risk factors, clinical consequences, and treatment of enteral feed intolerance during critical illness. *J Parenter Enteral Nutr* 2015; 39:441–448
8. Nguyen NO, Ng MP, Chapman M, et al: The impact of admission diagnosis on gastric emptying in critically ill patients. *Crit Care* 2007; 11:R16
9. Hsu C-W: Impact of disease severity on gastric residual volume in critical patients. *WJG* 2011; 17:2007
10. Reignier J, Thenoz-Jost N, Fiancette M, et al: Early enteral nutrition in mechanically ventilated patients in the prone position. *Crit Care Med* 2004; 32:94–99
11. van der Voort PH, Zandstra DF: Enteral feeding in the critically ill: Comparison between the supine and prone positions: A prospective crossover study in mechanically ventilated patients. *Crit Care* 2001; 5:216–220
12. Elke G, Felbinger TW, Heyland DK: Gastric residual volume in critically ill patients: A dead marker or still alive? *Nutr Clin Pract* 2015; 30:59–71
13. Reignier J, Mercier E, Le Gouge A, et al; Clinical Research in Intensive Care and Sepsis (CRICS) Group: Effect of not monitoring residual gastric volume on risk of ventilator-associated pneumonia in adults receiving mechanical ventilation and early enteral feeding: A randomized controlled trial. *JAMA* 2013; 309:249–256; 1–27
14. Diamond SJ, Medici V, Rice TW, et al: Should we stop using gastric residual volumes? *Curr Nutr Rep* 2015; 4:236–241
15. Lewis K, Alqahtani Z, McIntyre L, et al: The efficacy and safety of prokinetic agents in critically ill patients receiving enteral nutrition: A systematic review and meta-analysis of randomized trials. *Crit Care* 2016; 20:259
16. Bouvet L, Chassard D: Apport de l'échographie pour l'évaluation préopératoire du contenu gastrique. *Ann Françaises d'Anesthésie et de Réanimation* 2014; 33:240–247
17. Jahreis T, Kretschmann J, Weidner N, et al: Sonographic evaluation of gastric residual volume during enteral nutrition in critically ill patients using a miniaturized ultrasound device. *JCM* 2021; 10:4859
18. Sharma V, Gudivada D, Gueret R, et al: Ultrasound-assessed gastric antral area correlates with aspirated tube feed volume in enterally fed critically ill patients. *Nutr Clin Pract* 2017; 32:206–211

19. Hamada SR, Garcon P, Ronot M, et al: Ultrasound assessment of gastric volume in critically ill patients. *Intensive Care Med* 2014; 40:965–972
20. McClave SA, Taylor BE, Martindale RG, et al; Society of Critical Care Medicine: Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *JPEN J Parenter Enteral Nutr* 2016; 40:159–211
21. Van de Putte P, Perlas A: Ultrasound assessment of gastric content and volume. *Br J Anaesth* 2014; 113:12–22
22. Vernieuwe L, Wallyn A, Van Dyck L, et al: Gastric ultrasound for feeding intolerance in the ICU: Close but not quite right. *BMC Gastroenterol* 2022; 22:33
23. Thiele C, Hirschfeld G: Improved estimation and validation of optimal cutpoints in R [Internet]. *J Stat Soft* 2021; 98
24. Landis JR, Koch GG: The measurement of observer agreement for categorical data. *Biometrics* 1977; 33:159–174
25. Zou T-J, Ran Q-F, Yin W-H, et al: The value of gastric antrum cross-sectional area measured by bedside ultrasound predicted feeding intolerance in critically ill patients. *Sichuan Da Xue Xue Bao Yi Xue Ban* 2019; 50:815–820
26. Chuang Chen, Jiefeng Xu, Yuzhi Gao, et al: A study on the monitor of gastric residual volume by ultrasound and its prediction on feeding intolerance during enteral nutrition in critically ill patients in intensive care unit/中华急诊医学杂志. *Chin J Emerg Med* 2020;12:1291–1295
27. Bouvet L, Zieleskiewicz L, Loubradou E, et al; AzuRea CAR'Echo collaborative networks: Reliability of gastric suctioning compared with ultrasound assessment of residual gastric volume: A prospective multicentre cohort study. *Anaesthesia* 2020; 75:323–330
28. Arzola C, Carvalho JCA, Cubillos J, et al: Anesthesiologists' learning curves for bedside qualitative ultrasound assessment of gastric content: A cohort study. *Can J Anesth* 2013; 60:771–779
29. Ricci R, Bontempo I, Corazziari E, et al: Real time ultrasonography of the gastric antrum. *Gut* 1993; 34:173–176
30. Reintam Blaser A, Starkopf J, Alhazzani W, et al; ESICM Working Group on Gastrointestinal Function: Early enteral nutrition in critically ill patients: ESICM clinical practice guidelines. *Intensive Care Med* 2017; 43:380–398
31. Montejo JC, Miñambres E, Bordejé L, et al: Gastric residual volume during enteral nutrition in ICU patients: The REGANE study. *Intensive Care Med* 2010; 36:1386–1393
32. McClave SA, Snider HL, Lowen CC, et al: Use of residual volume as a marker for enteral feeding intolerance: Prospective blinded comparison with physical examination and radiographic findings. *JPEN J Parenter Enteral Nutr* 1992; 16:99–105
33. Yasuda H, Kondo N, Yamamoto R, et al: Monitoring of gastric residual volume during enteral nutrition [Internet]. *Cochrane Database Syst Rev* 2021; 9:9
34. Boullata JI, Carrera AL, Harvey L, et al; ASPEN Safe Practices for Enteral Nutrition Therapy Task Force, American Society for Parenteral and Enteral Nutrition: ASPEN safe practices for enteral nutrition therapy. *JPEN J Parenter Enteral Nutr* 2017; 41:15–103
35. Röhm KD, Schöllhorn T, Boldt J, et al: Nutrition support and treatment of motility disorders in critically ill patients - results of a survey on German intensive care units. *Eur J Anaesthesiol* 2008; 25:58–66
36. Perlas A, Mitsakakis N, Liu L, et al: Validation of a mathematical model for ultrasound assessment of gastric volume by gastroscopic examination. *Anesth Analg* 2013; 116:357–363