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Continuous assessment of gastric motility and its relation to gastric emptying in adult critically ill patients

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Abstract

Background: Critically ill patients frequently develop feeding intolerance, which is difficult to predict. In healthy subjects, gastric motility, assessed by nasogastric balloon tube, correlated with gastric emptying. We now investigated this correlation in critically ill patients, as well as the feasibility and safety of such application in a pilot study.

Methods: Endotracheally intubated adults, scheduled to receive enteral nutrition (EN), were included. After insertion of a double-lumen nasogastric balloon tube and radiographic confirmation of position, balloon pressure was recorded for 10h after inflation (4h fasted, 2h during administration of ^{13}C -labeled EN, and 4h postprandially). Gastric motility was expressed as Gastric-Balloon-Motility-Index (GBMI), reflecting the fraction of time in which phasic gastric contractions occurred. Gastric emptying was assessed by ^{13}C -octanoate breath test and expressed as gastric half-emptying time ($\text{GET}_{1/2}$). Correlation between GBMI (assessed in different time intervals) and $\text{GET}_{1/2}$ was investigated by Pearson/Spearman correlation. Feasibility was defined as the success of tube placement and pressure recording. Safety was assessed based on adverse device effects.

Results: Thirty patients were enrolled, of whom 19 had paired GBMI and $\text{GET}_{1/2}$ data. There was no correlation between GBMI and $\text{GET}_{1/2}$. The tube was successfully placed in 28/30 (93.3%) patients. In 3/28 (10.7%) patients, balloon leakage precluded analysis. Two safety events were directly linked to the device.

Conclusion: This pilot study showed no significant correlation between balloon-assessed gastric motility and emptying in critically ill patients. The feasibility/safety profile of the balloon tube appears similar to that of a standard nasogastric tube. NCT03512145

Clinical relevancy statement

Intolerance to enteral nutrition frequently occurs in critically ill patients and may induce potentially life-threatening complications. Yet, there is no validated tool to predict feeding

(in)tolerance. We previously developed a novel monitoring system, which continuously measures pressure variations in an inflated intragastric balloon that is mounted on a nasogastric feeding tube. The balloon-derived gastric motility index correlated well with gastric emptying in healthy subjects. In this pilot study, we aimed to evaluate this device in critically ill patients. We found no correlation between the motility index and gastric emptying. However, feasibility and safety appeared similar to that of a standard nasogastric tube. Future studies should investigate the clinical potential of the technique to predict and/or early detect feeding intolerance.

Introduction

Critically ill patients frequently develop feeding intolerance, characterized by nausea, vomiting, and abdominal discomfort following initiation of enteral nutrition (EN).^{1,2} In severe cases, potentially life-threatening complications may ensue, including aspiration pneumonia and associated acute respiratory distress syndrome and septic shock. Currently, no validated tool can predict and/or early detect feeding intolerance, whereby contemporary feeding guidelines recommend gradual EN initiation up to target.^{3,4} Measurement of gastric residual volumes (GRV) is frequently performed to monitor feeding (in)tolerance.⁵ However, this practice is debated, since a large randomized controlled trial found that omitting GRV measurement did not negatively affect the incidence of ventilator-associated pneumonia.^{5,6} Hence, an objective and more accurate tool to monitor gastrointestinal (dys)function might help to safely initiate EN.²

We recently developed and validated a tool that provides a continuous measurement of gastric motility by recording pressure fluctuations in an inflated intragastric balloon mounted on a nasogastric tube.⁷ We found the pressure recording was feasible and safe in healthy subjects, in whom the balloon-derived gastric balloon motility index (GBMI) correlated with gastric emptying.⁷ In this pilot study, we aimed to investigate the relationship between GBMI and gastric emptying, as well as feasibility and safety of the technique in critically ill patients.

Methods

The study was conducted in accordance with the principles of Good Clinical Practice, and was approved by the Ethical Committee Research UZ/KU Leuven. All participants or legal representatives provided written informed consent. ClinicalTrials.gov-identifier: NCT03512145.

Patients

Adult critically ill patients admitted to the surgical/trauma intensive care units (ICU) of the University Hospitals Leuven were eligible if they were deemed ready to receive EN and expected to remain intubated for the next 24 hours. Exclusion criteria were a contraindication for (re)placement of a nasogastric tube, history of gastric or esophageal surgery, receiving gastroprokinetics, moribund state, or pregnant/breastfeeding.

Study procedures

At day 0, a 12-French double-lumen nasogastric balloon tube was placed (VIPUN™ Gastric Monitoring System, developed at KU Leuven, Belgium) (Figure 1 and Figure 2). The tube has one lumen that connects an inflatable intragastric balloon to an external pressure sensor and data-recording unit, and a second lumen for nutrient and drug administration (Figure 2). The endings of the balloon are marked by radio-opaque bands, and the nutrient lumen contains a guidewire to facilitate tube insertion. After tube placement, patients remained fasted. Adequate tube position was confirmed radiographically on day 1 at 9:30±2h, after which the balloon was inflated (180 ml air), and pressure recording initiated, blinded to the patient and clinical staff. After 4 hours, at 13:30±2h, 150 ml EN (1 kcal.ml⁻¹, enriched with 0.5 mg.ml⁻¹ ¹³C-Na-octanoate) was administered over 2 hours. Upon EN initiation, exhaled breath samples were collected every 15 minutes for 6 hours, after which the balloon was deflated and pressure recording stopped. The exhaled ¹³C-content was analyzed by isotope-ratio-mass-spectrometry. Gastric emptying rate was expressed as gastric half-emptying time (GET_{1/2}).⁷

Assessment of gastric motility

Gastric motility was quantified by means of a previously described algorithm (MatLab® R2018a, The MathWorks®, Natick, MA, USA).⁷ In brief, the pressure signal was filtered to

exclude artifacts due to cardiac oscillations, breathing and muscle movements, after which data were smoothed and phasic gastric contractile waves were identified. GBMI was calculated as the fraction of time during which phasic gastric contractions were detected within predefined intervals –total study period (0-600 min), fasted (0-240 min), during EN administration (241-360 min), and during GET $\frac{1}{2}$ determination (241-600 min)–, ranging from 0 (no contractions) to 1 (continuous contractions).

Feasibility and safety

Feasibility was evaluated as the success of tube placement and pressure recording. Safety was recorded through device-related adverse effects. Patients in whom intragastric balloon was inflated were contacted 4-6 weeks after inclusion to detect potential late-onset complications (strictures, obstruction, reflux, dysmotility).

Statistical analysis

For this pilot study, we arbitrarily set the sample size at 20 subjects with paired GBMI and GET $\frac{1}{2}$ data. Subjects with incomplete data could be replaced, until a maximum of 30. Data were reported as median (interquartile range). Spearman/Pearson correlation coefficients were calculated to assess the correlation between GBMI and GET $\frac{1}{2}$. P values <0.05 were considered statistically significant.

Results

Thirty-three patients were potentially eligible, of whom 30 were enrolled (Figure 3). Nineteen patients had paired data available for analysis. Demographics and clinical outcomes are reported in table 1.

Correlation between balloon-assessed gastric motility and gastric emptying

Median GBMI, reflecting the fraction of time during which phasic gastric contractions were observed, was 0.42 (0.24-0.51) during the total study period, 0.47 (0.31-0.69) in fasted state, 0.32 (0.14-0.49) during EN infusion, and 0.34 (0.18-0.52) during GET $\frac{1}{2}$ determination. Median GET $\frac{1}{2}$ was 190 (177-208) min. There was no significant correlation between GBMI in the different time intervals and GET $\frac{1}{2}$ (all $p \geq 0.10$; Figure 4).

Feasibility and safety

The tube was successfully placed in 28/30 (93.3%) patients. In 3/28 (10.7%) patients, balloon leakage occurred, leading to incomplete (n=2) or absent (n=1) pressure recording. Two adverse device effects were directly attributed to the device. Epistaxis occurred during tube placement in one patient receiving therapeutic anticoagulation, whereby the procedure was aborted. In one patient, the guidewire protruded through the nutrient outlet, which could have posed a risk of trauma. This was noticed prior to tube placement, and shorter guidewires were delivered with subsequent tubes. At long-term follow-up, one prolonged critically ill patient requiring tracheostomy and prolonged mechanical ventilation had new-onset dysphagia. The responsible physician attributed this to prolonged intubation and generalized weakness rather than to tube placement. Nine patients died before clinical follow-up at 4-6 weeks could be performed, of whom 6 died within 28 days. Three patients who survived according to the medical file could not be reached during the 4-6 weeks follow-up period. Review of the

clinical files of these patients revealed no evidence for long-term complications related to tube placement.

Discussion

In this pilot study, we investigated the first application of a novel gastric motility monitoring system in critically ill patients. We found no significant correlation between the motility index GBMI, derived from pressure fluctuations in an inflated intragastric balloon attached to a nasogastric tube, and breath-test-assessed gastric emptying. Tube placement and pressure recording was feasible in the majority of patients. One device-related safety event occurred in a patient and a second was detected prior to patient contact.

The results contrast with a previous study in healthy subjects that found a significant inverse correlation between GBMI and $GET_{1/2}$.⁷ However, this does not refute the potential usefulness of the device. Indeed, the study may lack power due to the small and heterogeneous patient population. Second, there is no gold standard monitor of feeding intolerance in critically ill patients.^{2,5} We used $GET_{1/2}$ as comparator, which yields a quantifiable measure of gastric emptying, but is not validated as marker of feeding intolerance. Third, we only calculated one motility index, merely taking the frequency and not the amplitude of pressure fluctuations into account.⁷ Data mining might deliver a more accurate measure, which requires study in a larger dataset. Finally, no patient developed clinical signs of feeding intolerance during short-term EN, so we could not study any association of GBMI with feeding intolerance. Future studies should investigate the clinical value of the device in a larger population at risk of feeding intolerance.

The study suggested feasibility and safety of the technique. Only one adverse event in a patient –epistaxis– was directly linked to tube placement. Epistaxis is a known complication of nasogastric tube insertion, however, and therapeutic anticoagulation may have increased the risk thereof.⁸ One prolonged critically ill patient subsequently developed dysphagia,

which was attributed to the prolonged need for mechanical ventilation and associated weakness,⁹ although we cannot exclude a causal relationship with the device. We did not observe new-onset strictures, stenosis or reflux after 4-6 weeks. Since the study is small, however, we cannot exclude a higher risk of adverse events as compared to a standard nasogastric tube, which needs further investigation.

In conclusion, we confirmed feasibility of balloon-assisted gastric pressure monitoring in critically ill patients. Future studies should assess whether the monitoring system can predict and/or early detect feeding intolerance in a larger patient population.

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Conflict of interest

NG and PJ own shares in VIPUN Medical. MPC and JG report consultancy fees that were paid by VIPUN Medical to KU Leuven. All other authors have declared no potential conflicts of interest.

Statement of authorship

NG, PJ, JT, JG, MC contributed to the conception and design of the research; NG, PJ, TH, JG, MC contributed to the acquisition of the data; PJ, JM developed the MatLab motility algorithm; NG, PJ, JM contributed to the analysis of the data; NG, PJ, JT, GVdB, JG, MC contributed to the interpretation of the data; NG, PJ, JG and MC drafted the manuscript. All authors critically revised the manuscript, are agreeable to ensuring the work's integrity and accuracy, and have read and given final approval for the manuscript.

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Table 1: Demographics and clinical outcome of participants

	Total cohort (n=30)	Paired data cohort (n=19)
Baseline data		
Age (years)	63 (56-73)	59 (56-72)
Male gender	20/30 (66.7%)	13/19 (68.4%)
Body-mass-index (kg.m ⁻²)	28 (26-31)	28 (26-31)
APACHE-II	35 (28-39)	35 (27-39)
Emergency admission	29/30 (96.7%)	18/19 (94.7%)
Primary admission diagnosis		
- Trauma/burns	8/30 (26.7%)	4/19 (21.1%)
- Cardiac surgery	7/30 (23.3%)	4/19 (21.1%)
- Cardiac arrest/cardiogenic shock	4/30 (13.3%)	4/19 (21.1%)
- (Complicated) solid organ transplantation	4/30 (13.3%)	3/19 (15.8%)
- Neurological	4/30 (13.3%)	2/19 (10.5%)
- Pulmonary	2/30 (6.7%)	2/19 (10.5%)
- Skin and soft tissue infection	1/30 (3.3%)	
Days in ICU at inclusion	5 (5-8)	6 (5-9)
Clinical outcome		

28-day mortality*	6/29 (20.7%)	5/19 (26.3%)
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Data represent median (interquartile range) or n (%). APACHE-II, Acute Physiology and Chronic Health Evaluation II; ICU, intensive care unit.

*Mortality 28 days after inclusion in the study; 1 patient withdrew informed consent for further data collection.

Figure legends

Figure 1: Schematic representation of the gastric monitoring system.

Artist's impression of dimensions. Adapted with permission from Goelen et al.⁷

Figure 2: Schematic overview of study procedures on day 0 (gray) and day 1.

Figure 3: Patient diagram.

ICF, Informed consent form.

Figure 4: Correlation between Gastric Balloon Motility Index (GBMI) over different time intervals and gastric half-emptying time (GET_{1/2}).

GBMI reflects the fraction of time during which phasic gastric contractions were observed.