Use of wireless motility capsule to determine gastric emptying and small intestinal transit times in critically ill trauma patients☆,☆☆,★

Stefan Rauch MDa,⁎, Kristine Krueger MDb, Alparslan Turan MDC, Jing You MSD, Norbert Roewer MDa, Daniel I. Sessler MDC

aDepartment of Anesthesiology, University of Würzburg, Germany
bDigestive Health Center, University of Louisville, Louisville, Kentucky
cDepartment of Outcomes Research, Cleveland Clinic, Cleveland, Ohio
dDepartments of Quantitative Health Sciences and Outcomes Research, Cleveland Clinic

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Abstract
Purpose: The purpose of this study is to use a novel wireless motility capsule to compare gastric emptying and small bowel transit times in critically ill trauma patients and healthy volunteers.

Materials and Methods: We evaluated gastric emptying, small bowel transit time, and total gastrointestinal transit time in 8 critically ill trauma patients. These data were compared with those obtained in 87 healthy volunteers from a separate trial. Data were obtained with a motility capsule that wirelessly transmitted pH, pressure, and temperature to a recorder attached to each subject’s abdomen.

Results: The gastric emptying time was significantly longer in critically ill patients (median, 13.9; interquartile range [IQR], 6.6-48.3 hours) than in healthy volunteers (median, 3.0; IQR, 2.5-3.9 hours), P < .001. The small bowel transit time in critically ill patients was significantly longer than in healthy volunteers (median, 6.7 hours; IQR, 4.4-8.5 hours vs median, 3.8 hours; IQR, 3.1-4.7 hours), P = .01. Furthermore, the capsules passed after 10 (IQR, 8.5-13) days in the critical care group and 1.2 (IQR, 0.9-1.9) days in healthy volunteers (P < .001).

Conclusions: Both gastric emptying and small bowel transit were delayed in critically ill trauma patients. © 2012 Elsevier Inc. All rights reserved.

1. Introduction

Delayed gastric emptying is a well-known problem in critically ill patients [1-7] and is associated with feeding disturbances and inadequate nutrition. However, evaluating gastrointestinal function remains challenging in critically ill patients who are mechanically ventilated. Many tests that are
practical and accurate under standardized, controlled conditions often fail in the critical care setting. For example, the consensus recommendations for gastric emptying scintigraphy that have been published recently [8] are impractical in intubated patients because they recommend low-fat, egg-white meal with imaging at 0, 1, 2, and 4 hours after meal ingestion. Another test, the lactulose hydrogen breath test, relies on prompt bacterial breakdown of lactulose in the colon; however, changes in bacterial flora—which are presumably common in critical care patients—can produce false transit times [9].

The $^{13}$C-octanoic acid breath test was reported by Ritz et al [4] as successful when used bedside to measure gastric emptying. However, manometry only assesses the upper gastrointestinal function, mainly esophagus, stomach, and proximal small bowel. Finally, video capsule technology has been used to determine small bowel transit time and pathomorphology in critically ill patients, although inadequate battery lifespan of the capsule (approximately 8-10 hours) could prevent complete examination in some cases [10].

An alternative technique, wireless capsule technology, may be useful for evaluating gastrointestinal motility in critical care patients. There are reports of using wireless capsule technology to measure intestinal temperature, pressure, and pH dating to the 1950s [11-13], but a brief communication in *Nature* in 2000 by Iddan launched the era of video capsule endoscopy in humans [14]. A newly developed motility capsule for assessing gastric emptying in patients with suspected gastroparesis has been available since 2006 [15-20]. It is a wireless capsule that transmits pH, pressure, and temperature (Fig. 1).

We describe the first use of a novel motility capsule to compare gastric emptying and small bowel transit times in critically ill trauma patients with intracranial hemorrhage with times recorded previously in healthy volunteers. Second, we compared critically ill patients and volunteers on whole-gut transit time.

### 2. Materials and methods

This prospective cohort study (NCT01159002) was approved by the Human Studies Committee of the University of Louisville, and authorized representatives of participating patients provided written informed consent.

All hospital intensive care units (ICUs) were screened for patients twice daily by the principal investigator. Patients were enrolled within 36 hours of ICU admission. Eligible patients were intubated, ventilated, and had an Acute Physiology, Age, Chronic Health Evaluation score of greater than 25. All had major trauma and had an intracranial hemorrhage. Patients were excluded if they were younger than 18 years, had open abdominal trauma or inflammatory bowel disease, had a history of complicated (eg, total or partial gastrectomy, colectomy) or unknown abdominal surgery, or presented with clinical evidence of ileus or suspected obstruction. Patients with a pacemaker were also excluded because the capsule we used is not recommended for use in these patients.

We enrolled 8 patients who were sedated with propofol (25-50 μg·kg$^{-1}$·min$^{-1}$) or midazolam and were given intravenous morphine/fentanyl intermittently. Patients were maintained supine, with the head of the bed elevated 30°.

Positioning of the motility capsule (SmartPill GI Monitoring Capsule; SmartPill, Inc, Buffalo, NY) was coupled with the medically necessary feeding tube placement 2 days after patients were admitted to an ICU. The capsule was inserted with a delivery device (AdvanCE, Mentor, Ohio) into the esophagus using a laryngoscope to overcome the narrowing of the hypopharynx caused by the endotracheal tube and then advanced blindly into the stomach. The capsule was deployed into the stomach, and its position was confirmed radiographically. Intestinal feeding was delayed for 12 hours after capsule insertion. Data were transmitted to a recorder attached to the patient over a 5-day period.

MotiliGI software (MotiliGI 1.3.1; SmartPill, Inc) (Fig. 2) was used to calculate gastric emptying. The transition from stomach to small bowel was marked by an abrupt pH rise (>3 pH units) from gastric baseline to a pH greater than 4 as well as a change in pressure patterns before emptying [21-23]. Pressure recordings showed high-amplitude phasic contractions just before the capsule’s emptying from the stomach. The pH change marked the end of the gastric pressure analysis window and the beginning of the small bowel pressure analysis window. Small bowel transit time was calculated from the time the capsule entered the duodenum until it reached the cecum characterized by a drop in pH and pressure changes. Pressure patterns are characterized as high-amplitude phasic gastric contractions, mean peak amplitude, and mean contractions per minute. Mean peak amplitude (between 10 and 300 mm Hg) is the sum of amplitudes/number of contractions.

The control group consisted of 87 healthy volunteers with no history of major abdominal surgery. They were studied in a separate, multicenter trial, NCT001282884, which was approved by the local institutional review board. Each subject gave informed consent before enrollment. After an overnight

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**Fig. 1** SmartPill GI Monitoring Capsule; SmartPill, Inc, Buffalo, NY.
fast, volunteers ingested a monitoring capsule with 50 mL of water and afterward drank 250 mL Ensure (Abbott Laboratories, Abbott Park, Ill) with an additional 120 mL water. They then fasted for approximately 8 hours after capsule ingestion. Volunteers were asked to remain seated for the first 8 hours but were then permitted nonstrenuous ambulatory activity.

Total gastrointestinal transit time was calculated from the time the capsule was placed until it passed from the body.

2.1. Statistical analysis

Demographics were summarized using means and standard deviations or frequencies and were compared for balance by Student t or Fisher exact test, as appropriate.

Primary outcomes of gastric emptying time and small bowel transit time were compared between the critically ill patients and the healthy volunteers with Wilcoxon rank sum tests. To account for simultaneous testing on 2 outcomes while maintaining a type 1 error of 0.05, we used a significance criterion of $P < .025$ for each of the 2 primary outcomes (Bonferroni adjustment). The corresponding median differences between critically ill patients and healthy volunteers were estimated with the corresponding 97.5% confidence interval (CI).

With 8 critically ill patients and 87 controls, the study had approximately 85% power at the .025 significance level to detect a difference of 2.5 or more hours in gastric emptying and small bowel transit times between critically ill patients and volunteers, assuming a standard deviation of 2 hours.

2.1.1. Secondary outcome

We also compared critically ill patients and healthy volunteers on the whole-gut transit time using the Wilcoxon rank sum test. In addition, the median difference and 95% CI were estimated.

SAS software version 9.2.2 for Windows (SAS Institute, Cary, NC) was used for the power analysis. R software version 2.12.0 for Windows (The R Foundation for Statistical Computing, Vienna, Austria) was used for all the other analyses. Values were expressed as median and interquartile range (IQR), unless otherwise specified.

3. Results

Demographic characteristics were well balanced between critically ill patients and healthy volunteers (Table 1). Analgesia, sedation, and vasopressor requirements were similar among the intensive care patients. None of the patients were given proton-pump inhibitor or prokinetic medication. They only received H2 blockers per hospital protocol.

<table>
<thead>
<tr>
<th>Table 1 Demographic and morphometric characteristics, and illness scores</th>
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<tr>
<td>Critical care</td>
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<td>Sex, male/female</td>
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<td>Age (y)</td>
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<td>APACHE III score</td>
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<td>Glasgow Coma Scale score</td>
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APACHE III, Acute Physiology, Age, Chronic Health Evaluation prognostic system; NA, not applicable. Data are presented as mean ± SD or frequency.

* Student t test, unless specified.
** Fisher exact test.
The gastric emptying time was significantly longer in critically ill patients (median, 13.9 hours; IQR, 6.6-48.3 hours; range, 4.3-74.3 hours) than in healthy volunteers (median, 3.0 hours; IQR, 2.5-3.9 hours; range, 1.7-17.1 hours), $P < .001$; the corresponding median difference was estimated as 10.9 hours (97.5% CI, 2.8-69.3). The small bowel transit time in critically ill patients (median, 6.7 hours; IQR, 4.4-8.6 hours; range, 3.4-13.8 hours) was significantly longer than in healthy volunteers (median, 3.8 hours; IQR, 3.1-4.7 hours; range, 1.8-13.5 hours), $P = .01$; the estimated median difference was 2.7 hours (97.5% CI, 0.2-5.1). Furthermore, the capsules passed after 10 (IQR, 8.5-13) days in the critical care group and 1.2 (IQR, 0.9-1.9) days in healthy volunteers (median difference, 8.8 days; 95% CI, 6.9-11.0; $P < .001$) (Table 2).

The mean high-amplitude phasic gastric pressure in critical care patients was 21.3 mm Hg (IQR, 19.4-23.0 mm Hg). The mean pressure in the small bowel (ileum) before entering the cecum was 17.5 mm Hg (IQR, 14.2-24.2 mm Hg). The mean pressure in the cecum was 19.1 mm Hg (IQR, 13.2-28 mm Hg). The mean peak amplitude was 8.0 mm Hg (IQR, 5.3-9.2 mm Hg) in the stomach, 14.6 mm Hg (IQR, 9.5-18.9 mm Hg) in the small bowel, and 11.8 mm Hg (IQR, 10.0-12.5 mm Hg) in the colon. The mean number of contractions per minute was 1.4 (IQR, 0.8-1.8) in the stomach, 3.2 (IQR, 2.5-3.5) in the small bowel, and 1.6 (IQR, 1.2-1.9) in the colon.

The mean high-amplitude phasic gastric pressure in the healthy volunteers was 30 mm Hg (IQR, 5.0-43.0 mm Hg). The mean pressure in the small bowel (ileum) before entering the cecum was 19.1 mm Hg (IQR, 16.0-23.1 mm Hg). The mean pressure in the cecum was 37.6 mm Hg (IQR, 30.4-44.8 mm Hg). The mean peak amplitude in the healthy volunteers was 21.3 mm Hg (IQR, 19.4-25.0 mm Hg) in the stomach, 18.3 mm Hg (IQR, 16.8-20.1 mm Hg) in the small bowel, and 41.1 mm Hg (IQR, 38.5-45.5 mm Hg) in the colon. The mean number of contractions per minute was 1.1 (IQR, 0.7-1.6) in the stomach, 3.4 (IQR, 2.4-4.3) in the small bowel, and 0.7 (IQR, 0.4-0.9) in the colon.

In the critical care patients, the average gastric pH before the capsule’s emptying was 2.9 (IQR, 2.1-3.9). The average pH in the small bowel after pyloric passage was 6.7 (IQR, 6.2-7.1). The pH at the end of the small bowel transition before entering the cecum was 7.7 (IQR, 7.5-8.2). Cecal pH was 6.6 (IQR, 6.3-7.0). The average pH over the entire recording time was 5.1 ± 1.7 in the stomach, 7.8 ± 0.5 in the small bowel, and 7.7 ± 0.5 in the colon.

In the volunteers, the average gastric pH before the capsule’s emptying was 1.61 ± 0.63. The pH in the small bowel (duodenum) was 6.6 ± 1.7. The pH in the ileum was 7.9 ± 2.2, and in the cecum, 6.8 ± 0.3. The average pH over the whole recording time was (mean ± SD) 3.0 ± 0.9 in the stomach, 7.0 ± 0.5 in the small bowel, and 6.9 ± 0.7 in the colon.

There were no complications associated with the insertion of the capsules or any other aspect of the study.

### 4. Discussion

Gastric emptying of the monitoring capsules took significantly longer in trauma patients than in the healthy volunteers. Our results are thus generally consistent with previous work suggesting that gastric emptying is delayed in ventilated critically ill patients. For example, Ritz et al [4] found that half-gastric emptying time was significantly delayed in 45% of unselected ICU patients (median, 155 minutes; IQR, 130-220) using the $^{13}$C-octanoic acid breath test. Nguyen et al [24] found that 78% of their study population had impaired gastric emptying (median, 102 minutes; IQR, 62-258) measured by scintigraphy. In a study of paracetamol absorption, 16 (59%) of 27 patients had prolonged gastric emptying [25]. Kao et al [2] reported an 80% incidence of abnormal gastric emptying half-time of a liquid meal (57 ± 21 minutes) in 35 patients with traumatic brain injury.

Unlike gastric emptying, which can be evaluated with various approaches, little is known about small intestinal motility in severely injured patients because the small bowel is relatively inaccessible to examination because of length, location, and tortuosity. Small bowel transit time was significantly prolonged in our critically ill patients: 6.7 vs 3.8 hours. Furthermore, the variability was greater in the ICU patients (IQR, 4.1 hours vs 1.6 hours), and 1 subject in each group had a small bowel transit time greater than 13 hours. The current results differ from those in our previous study in which small bowel transit time (median, 5.1 hours; IQR, 3.9-7.7 hours) was not significantly delayed in ventilated patients with isolated intracranial hemorrhage compared with healthy patients [10]. The difference could be explained by the fact that we did not include patients with severe brain injuries (Glasgow Coma Scale <6) or severe blunt abdominal injuries and shock. These are clinical situations that are associated with higher gastrointestinal complications (eg, ileus) and delayed transit times.

Motility capsule technology has been validated when comparing gastric emptying in gastroparetic and healthy subjects. Kuo et al [19] showed in their study that there is a correlation ($r = 0.73$) between the gastric emptying of the

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<th>Table 2</th>
<th>Gastric emptying time, small bowel and whole-gut transit time</th>
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<tbody>
<tr>
<td></td>
<td>Critical care (n = 8)</td>
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<tr>
<td>Gastric emptying time (h)</td>
<td>13.9 [6.6-48.3]</td>
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<tr>
<td>Small bowel transit time (h)</td>
<td>6.7 [4.4-8.6]</td>
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<tr>
<td>Whole-gut transit time (d)</td>
<td>10 [8.5-13]</td>
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Data presented as median [IQR].
capsule and transit of a radiolabeled meal (gastric scintigraphy). The study from Cassilly et al [16] compared the emptying of the capsule to the traditional measurements of gastric function assessed with gastric emptying scintigraphy and antroduodenal manometry. They demonstrated in healthy subjects that the emptying of the capsule correlated with scintigraphy \( r = 0.98 \). It emptied from the stomach with the occurrence of high-amplitude antral contractions. Antral phase III seems to be important for moving capsules from the stomach. It also depends on the size of the nondigestible solid (eg, capsule). Markers that are smaller than 4 mm are more likely independent from antral phase III motor activity [16,18].

The influence of food and nondigestible solids on gastric emptying has been evaluated in different studies. Studies in healthy subjects have shown that emptying of the capsule occurred faster while fasting, without meals [22]. Further studies have shown that gastric emptying is more delayed with a meal than with water [16,26]. In general, gastric emptying of the capsules remains physiologically despite the influence of different feeding regimens in healthy volunteers.

Our results are limited by the small number of critically ill patients, although the population was relatively homogeneous. Another limitation was that we excluded patients with increased intraabdominal pressure, open abdominal injury, and exploratory laparotomies. Although it would be interesting to study those pathologic entities that are associated with more gastrointestinal complications and disturbed motility, we did not because a lodged capsule—which is more likely in these patients—would have required surgical removal.

We measured gastric emptying and small bowel transit time only once during the ICU stay because it is not possible to start a new capsule examination until the previous one has passed from the body. Although delayed gastric emptying is most common in the first 3 days after ICU admission [27, 28], we cannot exclude disturbance of intestinal motility later in the critical care course. Of course, both enteral feeding and antacid therapies can alter intraluminal pH, complicating identification of the capsule’s transition from the stomach to small intestine. Despite the use of H2 blockers, all of our patients had a distinct pH pattern to identify the passage of the capsule. Nguyen et al [24] has shown in a retrospective study that morphine/midazolam and propofol can alter gastric emptying. It seems that patients under propofol-based sedation have a lower incidence of delayed gastric emptying. Although sedation and analgesia requirements were similar among the critically ill group, we cannot exclude that the pharmacologic effect of propofol/midazolam and fentanyl/ -morphine could have contributed to the prolonged gastric emptying time and small bowel transit time.

5. Conclusions

Gastric emptying and small bowel transit times were markedly prolonged in critically ill trauma patients with intracranial hemorrhage, compared with normal volunteers. Physicians caring for critically ill patients should consider small intestinal dysfunction, along with delayed gastric emptying.

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References


