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

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EARLY ENTERAL NUTRITION IS THE standard of care in critically ill patients receiving invasive mechanical ventilation.1-3 However, numerous studies have shown that early enteral nutrition is frequently not used or associated with inadequate calorie delivery.4,6 The main reason for non-use is gastrointestinal intolerance to enteral nutrition,6,8 which has been ascribed to gastroparesis with increased gastric volume, gastroesophageal reflux, and regurgitation or vomiting carrying a risk of aspiration and ventilator-associated pneumonia (VAP).10-12 This theoretical sequence has prompted a recommendation13 to monitor the residual gastric volume of mechanically ventilated patients receiving early enteral nutrition. When the residual gastric volume exceeds a pre-determined cutoff, gastric prokinetic drugs are given and enteral nutrition is decreased or stopped to minimize the risk of aspiration and subsequent VAP.13,14

Importance Monitoring of residual gastric volume is recommended to prevent ventilator-associated pneumonia (VAP) in patients receiving early enteral nutrition. However, studies have challenged the reliability and effectiveness of this measure.

Objective To test the hypothesis that the risk of VAP is not increased when residual gastric volume is not monitored compared with routine residual gastric volume monitoring in patients receiving invasive mechanical ventilation and early enteral nutrition.

Design, Setting, and Patients Randomized, noninferiority, open-label, multicenter trial conducted from May 2010 through March 2011 in adults requiring invasive mechanical ventilation for more than 2 days and given enteral nutrition within 36 hours after intubation at 9 French intensive care units (ICUs); 452 patients were randomized and 449 included in the intention-to-treat analysis (3 withdrew initial consent).

Intervention Absence of residual gastric volume monitoring. Intolerance to enteral nutrition was based only on regurgitation and vomiting in the intervention group and based on residual gastric volume greater than 250 mL at any of the 6 hourly measurements and regurgitation or vomiting in the control group.

Main Outcome Measures Proportion of patients with at least 1 VAP episode within 90 days after randomization, as assessed by an adjudication committee blinded to patient group. The prestated noninferiority margin was 10%.

Results In the intention-to-treat population, VAP occurred in 38 of 227 patients (16.7%) in the intervention group and in 35 of 222 patients (15.8%) in the control group (difference, 0.9%; 90% CI, −4.8% to 6.7%). There were no significant between-group differences in other ICU-acquired infections, mechanical ventilation duration, ICU stay length, or mortality rates. The proportion of patients receiving 100% of their calorie goal was higher in the intervention group (odds ratio, 1.77; 90% CI, 1.25-2.51; P = .008). Similar results were obtained in the per-protocol population.

Conclusion and Relevance Among adults requiring mechanical ventilation and receiving early enteral nutrition, the absence of gastric volume monitoring was not inferior to routine residual gastric volume monitoring in terms of development of VAP.

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RESIDUAL GASTRIC VOLUME AND RISK OF VENTILATOR-ASSOCIATED PNEUMONIA

However, no studies have established that residual gastric volume monitoring decreases the VAP risk, and the measurement technique has never been validated. Moreover, the role for gastric content aspiration in VAP has been challenged. No clear relationship has been demonstrated between increased gastric volume, regurgitation, gastric content aspiration, and VAP. The results of a before-after study conducted in a single intensive care unit (ICU) in our study group suggested that absence of residual gastric volume monitoring might not be associated with an increased VAP rate compared with residual gastric volume monitoring. Furthermore, several studies suggest that residual gastric volume monitoring may be associated with decreased calorie delivery and therefore, with underfeeding and increased morbidity.

We designed a multicenter, randomized, noninferiority trial NUTRIREA1 to test the hypothesis that absence of residual gastric volume monitoring was not associated with an increased incidence of VAP compared with routine residual gastric volume monitoring in patients receiving invasive mechanical ventilation and early enteral nutrition. The secondary objectives of our trial included evaluations of whether absence of residual gastric volume monitoring affected enteral nutrition delivery and patient outcomes.

METHODS
Study Design and Setting
NUTRIREA1 was conducted in 9 intensive care units forming the Clinical Research in Intensive Care and Sepsis (CRICS) network (France). Of the 9 ICUs, 3 were medical and 6 were medical-surgical; 3 were in university hospitals and 6 in general university-affiliated hospitals. The study protocol was approved by the appropriate ethics committee (Comité de Protection des Personnes de Poitiers) on February 18, 2010. Because the strategies used in both study groups were considered standard care, there was no requirement for informed consent, although before study inclusion, all patients or next of kin were informed about the study and provided written confirmation.

Participants
Eligible patients were consecutive adults (aged ≥18 years) admitted to the study ICUs between May 2010 and March 2011, expected to require more than 48 hours of invasive mechanical ventilation, and started on enteral nutrition via a nasogastric tube within 36 hours after intubation. Exclusion criteria were abdominal surgery within the past month; history of esophageal, duodenal, pancreatic, or gastric surgery; bleeding from the esophagus, stomach, or bowel; contraindications to prokinetic agents; enteral nutrition via a jejunostomy or gastrostomy; pregnancy; treatment-limitation decisions; and current inclusion in a trial of VAP prevention, enteral nutrition tolerance, or both. Patients admitted to the study ICUs were screened for eligibility by the physicians and clinical research nurses, regardless of the day or time of day.

Randomization, Allocation Concealment, and Follow-up
After written confirmation of information about the study was obtained, eligible patients were randomly allocated in a 1:1 ratio to the intervention group or control group. Randomization and concealment were achieved using a secure, computer-generated, interactive, web-response system managed by the biometrical unit of the Tours University Hospital, which had no role in recruitment. Randomization was stratified by center using permutation blocks of variable sizes. Day 1 was the day of randomization. Included patients were observed until day 90.

Intervention and Enteral Nutrition Delivery
The intervention consisted in not monitoring residual gastric volume. In the intervention group, intolerance to enteral nutrition was diagnosed when vomiting occurred.

In the control group, the diagnosis of intolerance to enteral nutrition relied on the presence of vomiting, of residual gastric volume greater than 250 mL, or both. Residual gastric volume was measured every 6 hours by aspiration through the nasogastric tube using a 50-mL syringe. Aspirates smaller than 250 mL were returned to the patient.

In both groups, vomiting was defined as gastric contents detected in the oropharynx or outside the mouth. This definition included spontaneous regurgitation of enteral nutrition solution but not regurgitation during procedures associated with the vomiting reflex (eg, oral cavity care).

Enteral nutrition was initiated within 36 hours after intubation and delivered according to the same protocol in both groups (eMethods and eFigure 1 available at http://www.jama.com). All nurses and physicians were experienced in the use of this enteral nutrition protocol and in residual gastric volume monitoring and vomiting detection. Patients were in a semirecumbent position (30° to 45°) and received oral care every 6 to 8 hours with chlorhexidine solution. Subglottic secretions were not aspirated.

Blinding of group assignment to the physicians and nurses was not feasible. However, the primary end point was adjudicated by a blinded committee.

Diagnosis of VAP
VAP was suspected in patients who had new and persistent or progressive infiltrates on the chest radiograph with at least 2 of the following criteria: peripheral leukocytosis (>10,000/µL), leukopenia (4000/µL), body temperature of at least 38.5°C or of 35.5°C or less, and purulent tracheal aspirates. In the study ICUs, the criterion for confirming VAP was positive quantitative bacteriologic cultures of distal respiratory specimens obtained by bronchoalveolar lavage (significant bacterial count threshold of ≥10⁵ colony-forming units [cfu]/mL), protected specimen brush (significant threshold of ≥10⁴ cfu/mL), or tracheobronchial aspirate (significant threshold of ≥10⁴ cfu/mL). VAP episodes were recorded until day 2 after extubation. For the trial, all VAP diagnoses were adjudicated by an independent blinded committee based on all available clinical, radiological, and bacteriological data.
**Study Outcomes**

The primary outcome was the proportion of patients with at least 1 VAP episode. Secondary outcomes were the cumulative VAP incidence and total number of VAP episodes; microorganisms causing VAP; proportions of patients with at least 1 vomiting episode, enteral nutrition intolerance, prokinetic treatment, and diarrhea; score variations in SOFA (Sepsis-related Organ Failure Assessment); variations in serum albumin and C-reactive protein (CRP) levels during the first week of enteral nutrition; proportions of patients with ICU-acquired infections (bloodstream, urinary tract, catheter-related, and other infections); proportion of patients given 100% of the calorie target; cumulative calorie deficit from day 0 to day 7; mechanical ventilation duration; ICU and hospital lengths of stay; and ICU, day-28, and day-90 mortality rates.

**Sample Size**

A 10% noninferiority margin was predetermined in accordance with previous guidelines and reviews. Previous studies reported VAP in 9% to 27% of intubated patients. Given this broad range and the potential beneficial effects of the absence of residual gastric volume monitoring (ie, improved enteral nutrition delivery), we considered that a 10% margin was clinically acceptable.

We assumed a 19% rate of VAP with residual gastric volume monitoring, as reported in a previous study in a single center of our group. With a 10% noninferiority margin, we needed 191 patients in each group to establish noninferiority with 80% power and a 1-sided 5% type I error rate. To obtain this sample size in the per-protocol analysis, assuming that 10% of patients would finally receive invasive mechanical ventilation for fewer than 48 hours, at least of 420 patients were required.

**Statistical Analysis**

All analyses were conducted in both a modified intention-to-treat (ITT) population and a per-protocol population. The modified ITT population comprised all randomized patients except those who withdrew consent to study participation (as required by French legislation). For the per-protocol analysis, we excluded patients who did not meet inclusion or exclusion criteria, received invasive mechanical ventilation for fewer than 48 hours, or had medical reasons for study withdrawal.

The between-group difference in proportions of patients with at least 1 VAP episode was estimated based on the 2-sided 90% CI. The upper boundary of the 90% CI (corresponding with a 1-sided 95% CI) was then compared with the prestated noninferiority margin of 10%. Because death was a competing event, a sensitivity analysis was performed using competing risk models.

**RESULTS**

Of the 1984 mechanically ventilated patients assessed for eligibility, 452 were
allocated for randomization, 449 were included in the modified ITT (primary) analysis, and 423 were included in the per-protocol analysis (FIGURE 1). Baseline features were evenly balanced between the 2 study groups (TABLE 1).

### Table 1. Baseline Characteristics of the Modified Intention-to-Treat Populationa

<table>
<thead>
<tr>
<th></th>
<th>Intervention Group (n = 227)</th>
<th>Control Group (n = 222)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>61 (15)</td>
<td>62 (14)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>159</td>
<td>156</td>
</tr>
<tr>
<td>Women</td>
<td>68</td>
<td>66</td>
</tr>
<tr>
<td>Weight, mean (SD), kg</td>
<td>77.2 (19.7)</td>
<td>79.0 (21.7)</td>
</tr>
<tr>
<td>BMI, mean (SD)b</td>
<td>27.3 (6.5)</td>
<td>27.8 (7.1)</td>
</tr>
<tr>
<td>SAPS II, mean (SD)c</td>
<td>49 (17)</td>
<td>51 (16)</td>
</tr>
<tr>
<td>SOFA at baseline, mean (SD)d</td>
<td>8 (4)</td>
<td>8 (3)</td>
</tr>
</tbody>
</table>

*SI conversion factors: to convert serum albumin to g/L, multiply by 10; C-reactive protein values to nmol/L, multiply by 88.4.*

**Primary Outcome:**

**Ventilator-Associated Pneumonia**

In the modified ITT population, 38 of 227 patients (16.7%) in the intervention group and 35 of 222 patients (15.8%) in the control group had at least 1 VAP episode (difference, 0.9%; 90% CI, −4.8% to 6.7%). In the per-protocol population, 37 of 208 patients (17.8%) in the intervention group and 35 of 215 patients (16.3%) in the control group had at least 1 VAP episode (difference, 1.5%; 90% CI, −4.5% to 7.5%). In both populations, the upper limit of the 90% CI was within the prestated 10% noninferiority margin.

### Secondary Outcomes

The hazard ratio of the cumulative VAP incidence in the intervention groups vs the control group was 1.06 (90% CI, 0.72-1.55; P = .80) in the modified ITT population and 1.09 (90% CI, 0.74-1.60; P = .80) in the per-protocol population (FIGURE 2). For the total number of VAP episodes, the odds ratio in the intervention group was 0.98 (90% CI, 0.66-1.43) in the modified ITT analysis and 1.01 (90% CI, 0.68-1.49) in the per-protocol analysis (eTable 1). In each modified ITT group, 58 microorganisms causing 43 VAP episodes were identified. The proportions of *Staphylococcus aureus*, *Streptococcus* spp, *Enterobacteriaceae*, *Pseudomonas* spp, and other gram-negative bacteria did not differ between the 2 groups (eTable 2).

**TABLE 2** reports the results for the other secondary outcomes. Proportions of patients who vomited were significantly higher in the intervention group than in the control group, and more vomiting episodes were reported in the intervention group than in the control group (eTable 3; modified ITT: odds ratio [OR], 1.86; 90% CI, 1.32-2.61; P = .003; per-protocol OR, 1.93; 90% CI, 1.36-2.75; P = .002). However, the proportion of patients meeting the group-specific definition of enteral nutrition intolerance was higher in the control group, which also had a higher proportion of patients given the prokinetic agent erythromycin. The calorie target was achieved in a higher proportion of pa-
patients in the intervention group than in those in the control group (Figure 3; modified ITT OR, 4.13; 90% CI, 2.20-7.69; \( P < .001 \); per-protocol OR, 4.95; 90% CI, 2.59-9.12; \( P < .001 \)). Consequently, patients in the intervention group had a lower cumulative calorie deficit from day 0 to day 7 compared with patients in the control group (Table 2). The rates of diarrhea and ICU-acquired infections did not differ between groups (Table 2). Similar results were obtained in each infection subgroup (eTable 3).

Clostridium difficile diarrhea was diagnosed in 2 patients in each group. Variations in SOFA score, albumin, and CRP during the first week showed no significant between-group differences (eFigure 2, eFigure 3, and eFigure 4). The hazard ratio of the cumulative incidence of ICU death in the intervention group compared with the per-protocol control group was 1.10 (90% CI, 0.81-1.48; \( P = .62 \)) in the modified ITT population and 1.03 (90% CI, 0.75-1.42; \( P = .87 \)) in the per-protocol population (eFigure 5). The groups did not differ significantly for duration of invasive mechanical ventilation, ICU stay length, hospital stay length, day-28 mortality, or day-90 mortality (Table 2).

**COMMENT**

This multicenter, randomized, controlled, noninferiority trial shows that absence of residual gastric volume monitoring in patients receiving invasive mechanical ventilation and early enteral nutrition is not inferior to residual gastric volume monitoring in terms of VAP prevention. Despite a higher vomiting rate without residual gastric volume monitoring, prokinetic drug use was lower and the proportion of patients achieving calorie targets was higher in this group. Absence of residual gastric volume monitoring was not inferior to residual gastric volume monitoring regarding new infections, ICU and hospital stay lengths, organ failure scores, or mortality rates.

### Table 2. Secondary Outcomes

<table>
<thead>
<tr>
<th>Analysis of Gastric Volume Monitoring by Study Group</th>
<th>Modified ITT</th>
<th>Per Protocol</th>
</tr>
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<tbody>
<tr>
<td>Interven. (n = 227)</td>
<td>Control (n = 222)</td>
<td>Difference (90% CI)</td>
</tr>
<tr>
<td>Vomiting, No. (%)</td>
<td>90 (39.6)</td>
<td>60 (27.0)</td>
</tr>
<tr>
<td>Intolerance to enteral nutrition, No. (%)</td>
<td>90 (39.6)</td>
<td>141 (63.5)</td>
</tr>
<tr>
<td>Erythromycin as prokinetic treatment, No. (%)</td>
<td>89 (39.2)</td>
<td>139 (62.6)</td>
</tr>
<tr>
<td>Other prokinetic treatment, No. (%)</td>
<td>5 (2.2)</td>
<td>6 (2.7)</td>
</tr>
<tr>
<td>Cumulative calorie deficit from day 0 to day 7, median (IQR), kcal</td>
<td>319 (93-1012)</td>
<td>509 (185-1252)</td>
</tr>
<tr>
<td>Diarrhea, No. (%)</td>
<td>51 (22.5)</td>
<td>51 (23.0)</td>
</tr>
<tr>
<td>ICU-acquired infection, No. (%)</td>
<td>60 (26.4)</td>
<td>60 (27.0)</td>
</tr>
<tr>
<td>Duration of mechanical ventilation, median (IQR), d</td>
<td>7 (4-13)</td>
<td>7 (5-13)</td>
</tr>
<tr>
<td>ICU length of stay, median (IQR), d</td>
<td>10 (8-17)</td>
<td>10 (7-17)</td>
</tr>
<tr>
<td>Mortality</td>
<td>Day 28, No. (%)</td>
<td>63 (27.8)</td>
</tr>
<tr>
<td>Day 90, No. (%)</td>
<td>82 (36.3)</td>
<td>76 (34.2)</td>
</tr>
</tbody>
</table>

**Abbreviations:** ICU, intensive care unit; IQR, interquartile range; ITT, intention-to-treat.

\( a \) Data are reported as percentage difference (90% CI).

\( b \) In the intervention group, intolerance to enteral nutrition was defined as vomiting (no monitoring of residual gastric volume) and in the control group (group with monitoring of residual gastric volume) as vomiting and/or a residual gastric volume greater than 250 mL.

\( c \) Cumulative calorie deficit from day 0 to day 7 was the sum of the differences between calories required and the calories received by the patient each day from day 0 to day 7.

\( d \) Data are reported as Median difference (90% CI).

\( e \) ICU-acquired infections included ventilator-associated pneumonia, bacteremia, urinary tract infections, catheter-related infections, and other infections.
Several reasons may explain these results, which are consistent with findings from a single-center study conducted previously by our group. First, residual gastric volume measurement is not standardized or validated. Although residual gastric volume monitoring was more accurate than physical examination and radiography for detecting gastrointestinal intolerance to enteral nutrition, the accuracy of gastric aspiration for residual gastric volume measurement may vary according to tube position and diameter, number of tube openings, level of aspiration in the stomach, and experience of the evaluator. Measurement by refractometry or gastric content labeling is not feasible in everyday practice.

Second, no residual gastric volume cutoff value associated with significantly increased risks of vomiting or VAP has been identified. We used a 250-mL cutoff to define enteral nutrition intolerance in the control group, in keeping with current guidelines. However, in previous studies, residual gastric volume values lower than 250 mL were not associated with decreased complication rates and values as high as 500 mL were not associated with increased VAP rates. Moreover, residual gastric volume values failed to correlate with regurgitation or aspiration rates.

Third, the role for the gastropulmonary route in VAP development has been challenged by many studies. VAP is chiefly ascribable to leakage around the endotracheal tube cuff of subglottic secretions containing pathogenic microorganisms. The role for the stomach as a reservoir of VAP-causing microorganisms is controversial. In theory, gastric overdistension due to gastroparesis may lead to regurgitation and aspiration. However, there is no evidence of a sequence leading over time from gastric colonization to VAP. Data suggesting that the 45° semirecumbent position may decrease the risk of regurgitation and VAP have been challenged by recent studies. Studies involving bacterial DNA analysis strongly suggested that VAP was caused by oropharyngeal bacteria. Oral antiseptic use was effective in preventing VAP, whereas sucralfate therapy to modify the gastric flora by lowering the intragastric pH failed to influence VAP rates. Continuous enteral nutrition delivery in an attempt to restore intragastric acidity failed to affect gastric or oropharyngeal colonization rates or VAP rates. Interestingly, our group without residual gastric volume monitoring had a higher vomiting rate but no change in the VAP rate compared with the group with residual gastric volume monitoring. This finding constitutes an additional argument against a major role for the gastropulmonary route in the pathogenesis of VAP.

The main limitation of this study is that blinding of group assignment to clinicians and patients was not feasible. Therefore, we cannot completely exclude a change in nurse behavior related to knowledge of group assignment. Nurses may have responded to absence of residual gastric volume monitoring by overreporting vomiting and subsequently reducing enteral nutrition delivery. A strong argument against this hypothesis is the larger volume of enteral nutrition solution delivered in the group without residual gastric volume monitoring. This result suggests that the unblinded design had little or no effect on reported vomiting rates. Moreover, our use of end point adjudication by an independent blinded committee working with all available clinical, radiological, and bacteriological data probably substantially limited any influence of the unblinded design on VAP rates. Another limitation may be the predefined 10% noninferiority margin. Although determined according to previous guidelines and reviews, this margin may be considered large. However, the absolute between-group difference was less than 1% with an upper confidence bound of only 7%.

Strengths of our study include the multicenter randomized controlled design, large sample size, and reporting of results in accordance with CONSORT guidelines for noninferiority trials. This study was conducted in medical and surgical mechanically ventilated patients admitted to university and nonuniversity hospitals. Our study patients had SAPS II (Simplified Acute Physiology Score) and SOFA scores indicating severe acute illness. The beneficial effect of early enteral nutrition on survival may be most marked in the most severely ill patients. Rates of vomiting during early enteral nutrition were consistent with...
Residual gastric volume monitoring requires repeated gastric content aspiration and measurement and therefore adds to the nurse workload. Removing residual gastric volume monitoring from care bundles would allow an increased focus on interventions proven to decrease the VAP risk.36

In conclusion, the current study supports the hypothesis that a protocol of enteral nutrition management without residual gastric volume monitoring is not inferior to a similar protocol including residual gastric volume monitoring in terms of protection against VAP. Residual gastric volume monitoring leads to unnecessary interruptions of enteral nutrition delivery with subsequent inadequate feeding and should be removed from the standard care of critically ill patients receiving invasive mechanical ventilation and early enteral nutrition.

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Drafting of the manuscript: Reignier, Lascarrou, Le Gouge.

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REFERENCES


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