A Simplified Approach to the Management of Gastric Residual Volumes in Critically Ill Mechanically Ventilated patients: A Pilot Prospective Cohort Study

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ABSTRACT: **Background:** Enteral nutrition in the critically ill patient is often complicated by gastrointestinal intolerance, manifested by a large gastric residual volume. The frequency of GRV assessment and the intolerant level above which feeding is stopped is controversial.

Objectives: To evaluate a novel approach to EN by allowing high GRV and once-daily assessment that was correlated with the paracetamol absorption test.

Methods: We conducted a pilot prospective study in an 18 bed general intensive care unit. The study group comprised 52 consecutive critically ill mechanically ventilated patients. Enteral nutrition was started at full delivery rate. Once-daily assessment of GRV with three consecutively repeated threshold volumes of 500 ml was performed before stopping EN. The paracetamol absorption test was performed and correlated to GRV. Patients were divided into two groups: low GRV (< 500 ml) and high GRV (at least one measurement of GRV > 500 ml). Clinical outcome included maximal calories delivered, incidence of pneumonia, ICU length of stay, and ICU and hospital mortality.

Results: There were 4 patients (9.5%) with ventilator-associated pneumonia in the low GRV group and 3 (30%) in the high GRV group ($P = 0.12$). GRV was inversely correlated to paracetamol absorption; however, neither GRV nor paracetamol absorption was associated with the development of pneumonia. Both groups had similar ICU length of stay (11.0 ± 8.2 vs. 13.8 ± 14.4 days, $P = 0.41$), and similar ICU (21% vs. 40%, $P = 0.24$) and hospital mortality (35% vs. 40%, $P = 1.0$).

Conclusions: In critically ill mechanically ventilated patients, allowing larger gastric residual volumes, measured once daily, enables enteral feeding with fewer interruptions which results in high calorie intake without significant complications or side effects.

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KEY WORDS: gastric residual volume, enteral nutrition, gastric emptying, critically ill, ventilator-associated pneumonia

GRV = gastric residual volume
EN = enteral nutrition
ICU = intensive care unit

Underfeeding in critically ill patients is associated with immunosuppression, increased risk of infection, and higher mortality [1]. Achieving nutritional goals via the enteral route in these patients, while avoiding total parenteral nutrition, has been shown to reduce infection rate, improve wound healing, and maintain gut mucosal integrity [2-4] Despite these major functions the delivery of EN is hampered by a myriad of complicated protocols and local practices that are diverse among different intensive care units. Critically ill patients often have gastrointestinal intolerance presumed to be manifested by an increased gastric residual volume [5]. Feeding protocols have tried to define the threshold volume above which feeding should be withheld as well as the frequency of GRV assessment [6]. Multiple interruptions in EN due to frequent daily assessments of GRV, discarding checked volumes, and withholding feeding or reducing the rate of feeding due to presumed high GRV may all contribute to low caloric intake and perhaps increased use of TPN, with effect on outcome [5,7]. Another common practice is the gradual step-up of feeding until the appropriate calculated energy goal is reached.

We developed a simple protocol, namely, initiating feeding at the maximal final delivery rate, allowing a larger GRV threshold of up to 500 ml before withholding feeding and decreasing the number of GRV assessments to once a day. We evaluated both the significance of GRV levels by concomitant paracetamol absorption and the safety of the protocol by outcome variables such as incidence of ventilator-associated pneumonia, intensive care unit length of stay, and ICU and hospital mortality.

PATIENTS AND METHODS

All intubated and mechanically ventilated medical and surgical patients admitted to the ICU for at least 24 hours and who needed EN were eligible to enter the study. Contraindications to EN were based on the American Society of Parenteral and Enteral Nutrition guidelines, and included severe diarrhea,

TPN = total parenteral nutrition

protracted nausea and vomiting, malabsorption, bowel resection, pancreatitis, bowel obstruction, perforation, or peritonitis. Patients were recruited to the study on commencing EN within 48 hours of admission. On recruitment the following data were obtained: age, gender, vital signs, diagnosis, and APACHE II score.

The study period was 5 days during which the following variables were recorded: liver function and coagulation tests, daily SOFA score, use of vasopressors and opioids, and daily total calories received expressed as a percentage of the daily planned calorie intake. Stopping EN and switching to TPN was recorded. Patients were followed for the development of VAP over a 30 day period. VAP was defined according to the U.S. Centers for Disease Control definition of nosocomial pneumonia [8]. Days on mechanical ventilation, ICU length of stay, and 30 day all-cause mortality were recorded. Patient consent was obtained from next of kin, according to the hospital's Helsinki Committee guidelines.

Nasogastric tube position was confirmed by auscultation and radiography. Enteral formulas were given as a 1 Kcal/1 ml strength solution using either full-strength feeds with isotonic formulas (Osmolite®, Abbott, USA), or half-strength feeds with hypertonic formulas (NephroCare®, Abbott). Gastric aspiration of less than 500 ml enabled the initiation of EN. The head of the patient's bed was elevated to 35º.

On the first study day, full caloric target delivery rate (in ml/hr) was initiated immediately, as determined by the Harris-Benedict equation [9], and continued for 4 hours [Figure 1] until the first GRV was checked (first GRV). A GRV < 500 ml allowed the resumption of full delivery rate without checking further gastric residue until the next day. Subsequently, GRV was assessed only once a day. Each morning a GRV < 500 ml permitted the continuation of feeding until the next assessment 24 hours later.

A first GRV > 500 ml either at the first 4 hour assessment or each morning during the 5 study days necessitated withholding feeding for 4 hours after which GRV was rechecked (second GRV). Metoclopramide 10 mg three times a day was initiated. At this second assessment, a gastric residue < 500 ml allowed the resumption of feeding, whereas a gastric residue > 500 ml necessitated the withholding of feeding until the next morning. On the next day, a third consecutive GRV (third GRV) > 500 ml culminated in stopping EN and commencing TPN.

GRV was assessed by connecting the nasogastric tube to a bag, thus allowing gastric residue to drain passively by gravity. At the end of the passive drainage, further gastric residue was checked by active suction of the nasogastric tube using a 50 ml syringe. Any additional volume obtained by the syringe was added to the passively drained volume. At each GRV assessment, a volume exceeding 500 ml was discarded, while a volume < 500 ml was returned back to the patient via the nasogastric tube.

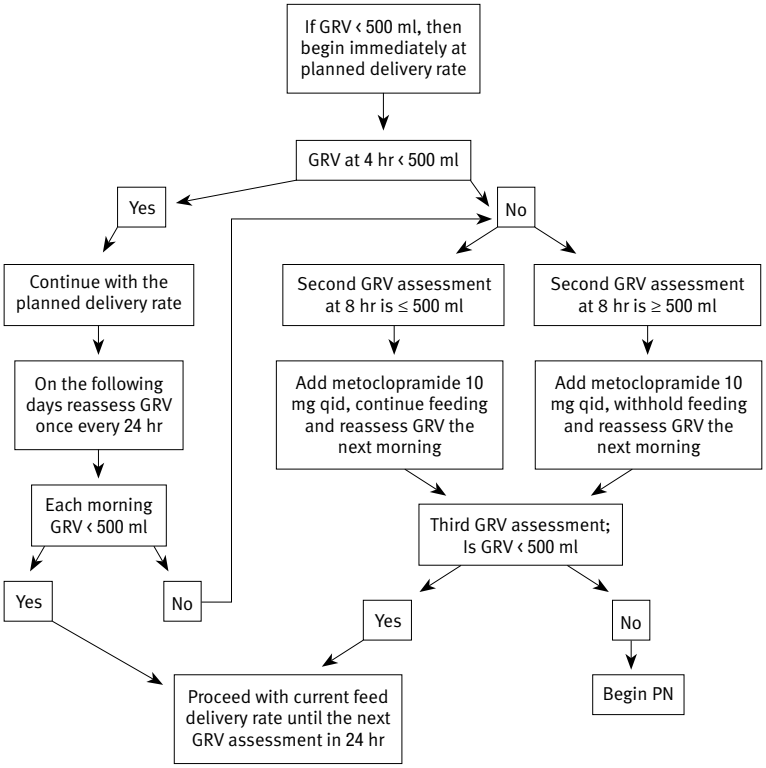
During the first 5 days a chest X-ray was performed daily to assess for new pulmonary infiltrates and to ensure correct nasogastric tube position. Two independent board-certified radiologists who were unaware of the study design reviewed all chest X-rays and assessed the appearance of new pulmonary infiltrates.

Each morning on the first 5 days of the study, 1 g of paracetamol was administered 1 hour prior to checking GRV. Paracetamol serum levels were obtained at time 0, 15, 30, 45, and 60 minutes after administration of paracetamol. The area under the paracetamol concentration-time curve from 0 to 60 minutes (AUC60) was calculated by the trapezoid rule. During the hour that it took to measure paracetamol blood levels, enteral feeding continued uninterrupted and the daily GRV assessment was performed during the next hour. Paracetamol absorption test was discontinued in the event of a twice normal rise in transaminase levels.

The presence of any enteral feed within the oral cavity was considered as a regurgitation/vomiting episode. Two consecutive such episodes within a period of 24 hours necessitated

APACHE = Acute Physiology and Chronic Health Evaluation
SOFA = Sequential Organ Failure Assessment
VAP = ventilator-associated pneumonia

Figure 1. Flowchart of enteral nutrition feeding study protocol in critically ill mechanically ventilated patients. PN = parenteral nutrition



stopping enteral nutrition and switching to TPN. Enteral nutrition continued until extubation or death.

Indications for withholding EN and initiating TPN were: three consecutive GRV measurements > 500 ml, two consecutive vomiting/regurgitation episodes within a period of 24 hours, upper gastrointestinal bleeding, or gastrointestinal surgery.

The patients were divided into two groups according to the GRV measurements. Patients with at least one GRV measurement > 500 ml over the 5 study days constituted the high GRV group and patients whose GRV never exceeded 500 ml constituted the low GRV group.

STATISTICAL ANALYSIS

The data were analyzed using BMDP Statistical software. Continuous variables were compared by groups, using Student's *t*-test. In those cases in which the variables did not have a Gaussian distribution we applied a square-route transformation in order to achieve "normality." Discrete variables were compared using Pearson's chi-square test or Fisher's exact test, as appropriate. Those comparisons having a small sample size were analyzed using non-parametric analysis. Spearman correlations were calculated between various parameters. A P value ≤ 0.05 was considered significant.

Table 1. Demographic data on admission

Parameter	Patients with GRV < 500 ml (N=42)	Patients with GRV ≥ 500 ml* (N=10)	*P* value**
Age (yrs, mean ± SD)	61.5 ± 20.6	52.9 ± 25.8	0.26
Male gender (%)	57%	80%	0.28
Body mass index (kg/m²)	29.0 ± 9.4	26.3 ± 4.8	0.40
APACHE II score	16.5 ± 8.9	18.1 ± 8.4	0.60
Diagnosis on admission (%)			
Septic shock	12 (28%)	4 (40%)	
COPD	8 (19%)	2 (20%)	
Head trauma	7 (17%)	4 (40%)	
Pneumonia	3 (7%)		
Meningitis	3 (7%)		
Drug overdose	2 (5%)		
Smoke inhalation	2 (5%)		
Miscellaneous	4 (9.5%)		*P* value§
Lab tests on admission (mean ± SD)			
Hemoglobin (g/dl)	11.0 ± 2.1	11.3 ± 1.4	0.64
WBC count (x 103/μL)	14.5 ± 9.5	20.6 ± 10.4	0.07
Creatinine (mg/dl)	1.5 ± 1.4	1.3 ± 1.1	0.63
Albumin (g/L)	28.6 ± 6.4	29.2 ± 10.2	0.81
Serum glucose (mg/dl)	179.6 ± 73.3	169 ± 92.0	0.70
Mechanical ventilation			
PEEP	6.2 ± 3.3	6.1 ± 3.8	0.96
PIP	23.8 ± 8.0	24.3 ± 6.6	0.85
PO_2/FiO_2 ratio	282 ± 117.1	325.1 ± 151.2	0.34

* No. of patients with at least one measurement of gastric residual volume › 500 ml during the study period

** P ‹ 0.05 was considered to be statistically significant.

§ Due to small number of patients in the subgroups, we could not calculate statistical significance for these parameters.

COPD = chronic obstructive pulmonary disease, PEEP = positive end-expiratory pressure, PIP = peak inspiratory pressure

RESULTS

Fifty-two consecutive critically ill mechanically ventilated patients were enrolled in the study: 42 had GRV < 500 ml (low GRV group) and 10 had at least one GRV measurement ≥ 500 ml (high GRV group).

Patient characteristics and laboratory results in both groups on admission were similar [Table 1]. SOFA score was also similar [Table 2]. Enteral nutrition was begun at 17.7 ± 12.0 hours from admission in the low GRV group, and 19.9 ± 8.5 hours in the high GRV group (P = 0.59) [Table 2].

Planned feed delivery rate in ml/hr and target Kcal/day to be delivered in both groups were similar. The percentage of daily calorie target achieved was similar on 3 of the 5 days of the study with more calories delivered on the 3rd and 4th day in the low GRV group, which was statistically significant

Table 2. Patient characteristics during 5 days of study

Parameter	Patients with GRV ‹ 500 ml (N=42)	Patients with GRV ≥ 500 ml (N=10)	*P* value
Hours from admission to start of enteral nutrition	17.7 ± 12.0	19.9 ± 8.5	0.59
Average planned feed delivery rate (ml/hr)	68.3 ± 14.8	67.6 ± 10.5	0.89
Average target kcal/day	1562 ± 356	1550 ± 230	0.92
Percentage of daily calorie target achieved			
Day 1	80.8 ± 10.3	77.6 ± 11.3	0.45*
Day 2	96.1 ± 9.8	93.6 ± 10.5	0.38*
Day 3	101.1 ± 6.9	91.3 ± 11.9	0.03*
Day 4	99.5 ± 9.1	83.2 ± 15.2	0.02*
Day 5	98.2 ± 6.6	87.4 ± 15.4	0.09*
Average daily GRV*			
Day 1	147.8 ± 130	264 ± 232.4	0.07*
Day 2	95.6 ± 110.7	330.0 ± 423.5	0.10*
Day 3	122.8 ± 133.4	352.8 ± 166.9	0.004*
Day 4	84.8 ± 100.3	554 ± 233.7	‹ 0.001*
Day 5	103.8 ± 123.6	140 ± 89.4	0.47*
Average paracetamol AUC60 (mg/min/L)			
Day 1	353.6 ± 268.7	261.1 ± 270.5	0.22 †
Day 2	432.7 ± 336.2	276.2 ± 299.5	0.17 †
Day 3	464.9 ± 446.1	262.1 ± 279.6	0.37 †
Day 4	491.0 ± 333.5	184.4 ± 209.0	0.03 †
Day 5	502.8 ± 367.0	409.4 ± 352.8	0.63 †
Daily SOFA score			
Day 1	4.9 ± 3.2	5.5 ± 3.6	0.65*
Day 2	4.9 ± 3.4	5.2 ± 3.1	0.85*
Day 3	5.2 ± 3.5	5.1 ± 2.8	0.87*
Day 4	4.4 ± 3.5	4.7 ± 3.6	1.00*
Day 5	4.8 ± 2.9	5.6 ± 4.0	0.70*
Vomiting during EN			
Day 1	5		
Day 2	2		
Day 3	1	2	
Day 4	2		
Day 5	0	1	*P* value§

* These *P* values were calculated using theMann-Whitney U-test

§ Due to the small number of patients we could not calculate statistical significance for these values.

[Table 2]. Concomitantly, the average daily GRV in both groups was similar except on the 3rd and 4th day, where GRV was significantly higher in the high GRV group.

There were 13 single regurgitation/vomiting episodes: 10 in the low GRV group and 3 in the high GRV group, and only one of these patients was switched to TPN due to concomitant intolerance [Table 2]. Thus there were more patients with vomiting in the low GRV group. However, the sample size was too small to calculate statistical significance.

When plotting GRV against paracetamol absorption (AUC60), we found a significant inverse correlation between the two parameters on the last 4 days of the study.

Table 3 presents a subgroup outcome analysis of patients who developed VAP as compared to those who did not. Of the 52 patients enrolled, 7 developed VAP (incidence of 13.5%) [Table 3]. Patients with and without VAP had similar GRVs during the study (except for day 1 when both volumes were clinically low). They also had similar paracetamol absorption test results (AUC60) [Table 3].

Of the 13 vomit/regurgitation episodes in 10 patients, only one patient developed VAP. ICU length of stay, days on mechanical ventilation, and ICU and hospital mortality were similar in patients with and without VAP. We compared the two groups with regard to actual feed intolerance. Three of the 10 high GRV group patients were switched to TPN, 1 patient due to gastrointestinal bleeding, 1 due to one episode of GRV > 500 ml followed by a vomiting episode, and only 1 patient due to 3 consecutive GRVs above 500 ml. One of the 42 patients in the low GVR group was switched to TPN because of gastrointestinal bleeding. Thus, in total, 4 of the 52 patients were switched to TPN, while only one of them actually exhibited full intolerance with three consecutive high GRV measurements above 500 ml.

When analyzing patient outcome in the high and low GRV groups, we found similar ICU length of stay, days on mechanical ventilation, and ICU and hospital mortality.

AUC60 = area under the curve from 0 to 60 minutes

Table 3. Patient outcome related to eventual development of pneumonia

Parameter	Patients without VAP (No = 45)	Patients with subsequent VAP* (N = 7)	*P* value
Time to appearance of pneumonia (days)**		2.7 (13.5%)	
No. of patients with at least one GRV measurement ≥ 500 ml	7 (15.6%)	3 (42.9%)	0.12‡
Average daily GRV			
Day 1	54.2 ± 68.0	10.7 ± 28.3	0.02§
Day 2	120.5 ± 157.1	328.3 ± 511	0.56§
Day 3	160.5 ± 163.3	270 ± 213.8	0.23§
Day 4	182.6 ± 256.4	300 ± 264.6	0.65§
Day 5	98.9 ± 102.4	200 ± 200	0.55§
Average paracetamol AUC60			
Day 1	346.5 ± 278.9	267.2 ± 177.7	0.72§
Day 2	434.5 ± 343.6	186.9 ± 97.8	0.15§
Day 3	457 ± 434.8	137.7 ± 52.5	0.19§
Day 4	431.7 ± 339.4	269.1 ± 268.4	0.39§
Day 5	505.6 ± 364.6	326.3 ± 327.3	0.41§
Daily SOFA score			
Day 1	5.4 ± 3.2	2.7 ± 2.6	0.03§
Day 2	5.3 ± 3.2	3.3 ± 3.4	0.14§
Day 3	5.4 ± 3.3	4.0 ± 3.9	0.45§
Day 4	4.4 ± 3.4	5.3 ± 4.2	0.53§
Day 5	4.8 ± 3.1	5.7 ± 3.8	0.64§
No. of patients with vomiting (%)	9 (20%)	1 (14%)	1.0‡
ICU length of stay (days)	11.8 ± 9.8	10.0 ± 8.4	0.60§
Days on mechanical ventilation	9.9 ± 8.4	8.4 ± 7.5	0.60§
No. of patients switched to parenteral nutrition (%)	2/45 (4.4%)	2/7 (28%)	0.08‡
ICU mortality at 30 days	10/45 (22.2%)	3/7 (42%)	0.35‡
Hospital mortality	16/45 (35.6%)	3/7 (42%)	0.70‡

* Patients enrolled in the study who subsequently developed ventilator-associated pneumonia
** Average time in days from start of study to appearance of pneumonia
‡ P value was calculated using Fisher's exact test (two-tailed).
§These P values were calculated using the Mann-Whitney U-test

DISCUSSION

GRV is frequently checked in critically ill patients fed by EN. However, there is no standard definition as to how frequently it should be checked and what constitutes a significant GRV above which feeding should be withheld.

In many intensive care units GRV is assessed three times a day, with no feeds delivered during the assessment. In addition, relatively low GRV thresholds of > 200 ml are commonly considered as EN intolerance, leading to a break in the feeding process. Furthermore, there is a tendency to discard all GRVs, even those below the high threshold. Added to these feed-withholding periods is the practice of gradually increasing the delivery of EN until the target dose is reached. The end result is a reduced caloric intake.

It is generally assumed that monitoring residual volumes and stopping EN above a certain threshold may reduce the risk of aspiration. However, keeping GRV below the presumed threshold has not been shown to protect patients from aspiration [10]. In their study Lukan and coworkers [11] added calorimetric microspheres to the EN in two patient groups with threshold GRV of 200 and 400 ml. Patients with threshold GRV of 400 ml did not have significantly higher aspirations than those in the 200 ml group. Choosing the threshold volume above which enteral tube feeding is withheld is therefore often arbitrary and not based on physiologic grounds or evidence-based clinical studies. Arbitrary threshold values for GRV above which EN is stopped range from as low as 30 to 200 ml in some reports, to as high as 400 to 500 ml in others [12].

Lin and Van Citters [13] described a mathematical model predicting that a normal gastric output would be between 232 and 464 ml/hr within 3 to 6 hours of initiation of EN

based on feeding levels and basal gastric secretion. Therefore, stopping EN for GRV less than 400 to 500 ml might not be physiologically appropriate.

The frequency of GRV assessments varies as well, ranging from 4 to 12 hours [14]. Various feeding protocols and recommendations have been reported in the literature [15,16], mostly with a threshold GRV of ≤ 200 ml. Yet, no one protocol has been reported to be superior to another. We therefore designed a simple feeding protocol with a single once-daily GRV assessment and a threshold of 500 ml that had to be repeated three consecutive times before switching to TPN [Figure 1].

GRVs below 500 ml were not discarded and were returned to the patients. Furthermore, we did not use a step-up approach and initiated feeding at the maximal delivery rate right from the start. This simple approach was intended to minimize feeding interruptions by ignoring insignificant GRVs < 500 ml.

The paracetamol absorption test is a simple, non-invasive technique for assessing gastric emptying. The test is supported by pharmacokinetic studies showing negligible paracetamol absorption in the stomach, while demonstrating rapid absorption from the small intestine [17,18]. When correlating paracetamol absorption to GRV we found, except for the first day, a significant inverse correlation between GRV values and paracetamol absorption. This indicates an association between high GRV and lower absorption of paracetamol. Despite this fact there was no difference in the AUC60 levels between the high and low GRV groups (except on day 4) [Table 2].

Furthermore, we found no correlation between GRV values and the rate of developed pneumonia or other outcome variables, thus supporting the notion that high GRV may be considered in critically ill patients.

In our study, new pneumonia developed in seven patients, an incidence of 13.5% which was consistent with most recent reports [19-22]. Patients who developed pneumonia had similar GRV values to those who did not [Table 3]. These results may indicate the lack of association between the magnitude of GRV and eventual development of pneumonia.

Previous studies report reaching an enteral feeding target range from as low as 51% of the prescribed calories [23,24] to as high as 76% [25]. In our study, patients in the low GRV group reached a calorie target of 80% on the first day, while patients in the high GRV group reached a similar high value of 77% ($P = 0.45$). However, over the next 4 days of the study patients in both groups reached higher target goals, ranging from 96% to 101% in the low GRV group and from 83% to 93% in the high GRV group. We presume that the somewhat lower percentage in the high GRV group was mostly due to high GRV measurements of > 500 ml that necessitated an occasional 4 hour break in feeding. Since we measured GVR only once daily we presume that our simple feeding protocol may not have detected, and consequently ignored, high GRV measurements that would have been detected with more frequent assessments. Furthermore, once-daily assessment could also have missed patients with vomiting due to high GRV. However, despite the fact that there were more vomiting episodes in the low GRV group, there were more cases of pneumonia in the high GRV group (not significant). Therefore, from the data available, and due to the small sample size, it is difficult if not impossible to determine an association between vomiting and development of pneumonia.

Length of ICU stay, duration of mechanical ventilation, and ICU and hospital mortality were similar in both groups, thus further supporting the clinical non-significance of high GRVs.

Our study had several limitations. First, since the current feeding protocol is commonly used in our ICU we did not have a control group. Second, the number of patients was small, thus precluding a definite conclusion. However, this was a feasibility trial, demonstrating that higher GRV values with less frequent assessment is safe and feasible, allowing more calories to be enterally delivered with no adverse outcome. No doubt, further studies with a larger number of patients are needed before this simple feeding protocol can be recommended. In conclusion, our results indicate that a higher GRV threshold and less frequent GRV assessments are feasible, result in high enteral caloric delivery, and may not be associated with a higher incidence of pneumonia or other adverse outcome.

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