Upper digestive intolerance during enteral nutrition in critically ill patients: Frequency, risk factors, and complications

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Objective: **To study the frequency of and risk factors for increased gastric aspirate volume (GAV) and upper digestive intolerance and their complications during enteral nutrition (EN) in critically ill patients.**

Design: **Prospective observational study.**

Setting: **Intensive care unit (ICU) in a general hospital.**

Patients: **A total of 153 patients with nasogastric tube feeding.**

Interventions: **None.**

Measurements and Main Results: **Upper digestive intolerance was considered when GAV was between 150 and 500 mL at two consecutive measurements, when it was >500 mL, or when vomiting occurred. Forty-nine patients (32%; 95% confidence interval [CI], 25%–42%) presented increased GAV after a median EN duration of 2 days (range, 1–16 days), and 70 patients (46%; 95% CI, 38%–54%) presented upper digestive intolerance. Independent risk factors for high GAV were GAV >20 mL before the start of EN (odds ratio [OR], 2.16; 95% CI, 1.11–4.18; $p = .02$), GAV >100 mL during EN (OR, 1.49; 95% CI, 1.01–2.19; $p < .05$), sedation during EN (OR, 1.78; 95% CI, 1.17–2.71; $p = .007$), use of catecholamines during EN (OR, 1.81; 95% CI, 1.21–2.70; $p = .004$). Complications related to high GAV were a lower feed intake (15 ± 7 vs. 19 ± 8 kcal/kg/day; $p = .0004$) and vomiting (53% vs. 23%; $p = .0002$). Complications related to upper digestive intolerance were the development of pneumonia (43% vs. 24%; $p = .01$), a longer ICU stay (23 ± 21 vs. 15 ± 16 days; $p = .007$), and a higher ICU mortality (41% vs. 25%; $p = .03$), even after adjustment for Simplified Acute Physiology Score II (OR, 1.48; 95% CI, 1.04–2.10; $p = .028$).**

Conclusion: **In ICU patients receiving nasogastric tube feeding, high gastric aspirate volume was frequent, occurred early, and was more frequent in patients with sedation or catecholamines. High gastric aspirate volume was an early marker of upper digestive intolerance, which was associated with a higher incidence of nosocomial pneumonia, a longer ICU stay, and a higher ICU mortality. (Crit Care Med 2001; 29:1955–1961)**

KEY WORDS: critical illness; intensive care medicine; nutrition; enteral nutrition; gastric feeding tubes; gastric emptying; vomiting; hypnotics and sedatives; catecholamines; cross infections; pneumonia; length of stay; hospital mortality

Nutritional support is essential in critically ill patients. The enteral route presents a number of major advantages (1). However, upper digestive intolerance (UDI) caused by impaired gastric emptying (2, 3) and fear of complications of gastric reflux, such as inhalation pneumonia (4, 5), often prevent feeding goals from being achieved (6, 7). Estimation of the gastric residue has been recommended to monitor the tolerance of enteral nutrition and to guide nursing protocols (8–10). However, fearful management of enteral nutrition, based on avoidance of high gastric aspirate volumes, might expose intensive care unit (ICU) patients to unnecessary starvation (11–13). Moreover, before implementing routine gastric aspirate volume monitoring during enteral nutrition by already overworked ICU nurses, this new task needs to be evaluated. For this purpose, we conducted a prospective study to determine the frequency, risk factors and complications of UDI during enteral nutrition in ICU patients.

MATERIALS AND METHODS

From October 1997 to January 1999, all consecutive patients admitted to our medical and surgical ICU and placed on enteral nutrition (EN) via a nasogastric tube were enrolled in a prospective survey. According to the French law on biomedical research on human beings, as this was an observational study and because the unit's feeding protocol was not modified, ethics committee opinion was not sought and no informed consent was obtained. The feeding policy in our unit consists of starting EN via a nasogastric tube as soon as possible. When the physician in charge of the patient deemed EN possible, the nurse inserted a 14-Fr silicone nasogastric tube (Vygon, Ecouen, France). The correct position of the nasogastric tube was confirmed by injecting 50 mL of air with a syringe down the tube and auscultating the epigastric area or by radiography if necessary. Patients were fed at a constant rate using either a peristaltic pump or gravity over 20 hrs, except patients treated with insulin, who were fed over 24 hrs. The feeding goal was 25 kcal/kg/day. No starter regimen was used: the feed rate was immediately set to meet requirements from day 1. Patients were cared for in a semirecumbent position (angle of at least 30°) when allowed by the patient's hemodynamic status. Even when the patient was placed prone, a slightly elevated head position was recommended. Gastric aspirate volume (GAV) was measured by aspirating with a 50-mL syringe before starting EN, every 4 hrs from days 1 to 5 and then every 12 hrs from days 6 to 20 or until the end of EN. Aspirate was returned to the patient unless it exceeded 500 mL. EN was managed according to the unit's usual proto-

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col (Fig. 1). The presence of GAV between 150 and 500 mL on two occasions at two consecutive measurements justified the introduction of prokinetics. The presence of GAV >500 mL led to discontinuation of EN. UDI during EN was defined as a GAV between 150 and 500 mL on two occasions at two consecutive measurements, or a GAV >500 mL, or the presence of vomiting. During the study, sedation consisted of midazolam and fentanyl administered by continuous infusion. Sedation was only used in the case of fighting against invasive ventilation or hemodynamic instability and was titrated to a Ramsay score of 3 (14, 15). The Ramsay scale was evaluated every 4 hrs by a nurse.

Patients' characteristics were recorded at admission to the ICU and at the beginning of enteral nutrition, and severity indexes were calculated (Simplified Acute Physiology Score [SAPS] II, Sepsis-Related Organ Failure Assessment [SOFA] score). During enteral nutrition, patient and enteral nutrition characteristics were recorded daily. Complications of enteral nutrition were also recorded. Diarrhea was defined as more than three loose or liquid stools per day. Pneumonia was diagnosed as follows: 1) a chest radiograph demonstrated new infiltrates; 2) at least one of the following criteria was present: purulent tracheal aspirates, body temperature $\geq$38°C or $\leq$36.5°C, or a white blood count of $\geq$10,000/mm^3 or $\leq$4,000/mm^3; and 3) distal bronchial sampling yielded a bacteria at a significant concentration (i.e., $\geq 10^3$ colony-forming units [cfu]/mL for protected specimen brush and protected telescopic catheter, $\geq 10^4$ cfu/mL for bronchoalveolar lavage). Daily follow-up was performed until the onset of UDI, discontinuation of EN, or after 20 days, whichever occurred first. Patients were monitored for the development of vomiting and nosocomial pneumonia until ICU discharge. The patient's status (alive or dead) on ICU discharge and on hospital discharge was recorded.

Data are expressed as mean ± SD. Categorical data were compared by chi-square test, with Yates' correction or by Fisher's exact test, depending on sample sizes. Confidence intervals were determined by assuming a binomial distribution of the data. Continuous data were compared by Student's *t*-test. On univariate analysis for risk factors, to account for multiple comparisons, a p value $\leq$.01 was considered significant. Multivariate analysis consisted in forward logistic stepwise regression according to the Wald statistic. Continuous data, except SAPS II, were transformed into categorical data using a clinically relevant value whenever possible or the median as cutoff value. Data included in the logistic equation with a p value $\leq$.05 were considered to be independent risk factors. Survival curves were established according to the Kaplan-Meier method. A p value $\leq$.05 was considered significant on outcome analysis.

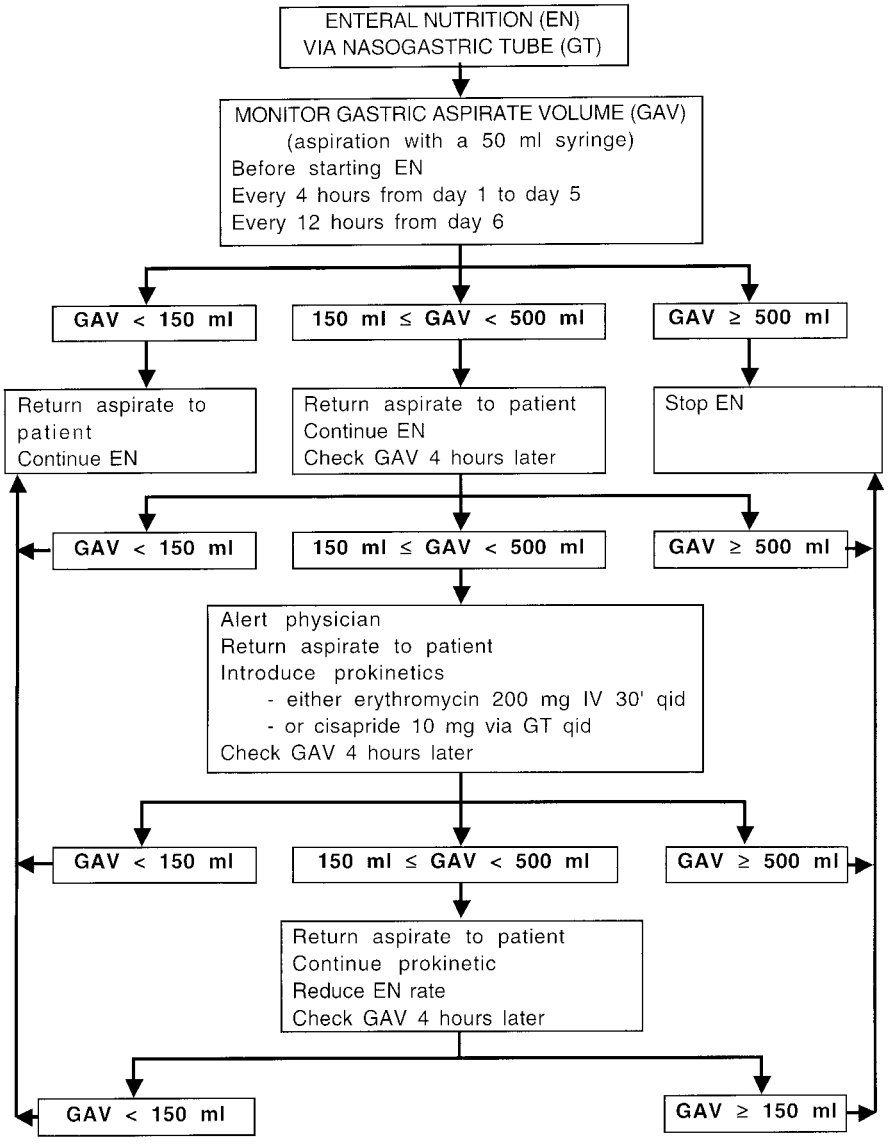

Figure 1. Enteral nutrition management protocol.

RESULTS

Study Population. During the study period, 153 consecutive patients were started on EN via a nasogastric tube and were enrolled in the prospective survey. There were 86 men and 67 women with a mean age of 65 ± 15 yrs, and a mean SAPS II on admission of 52 ± 17. The main diagnosis for ICU admission was medical in 142 patients (including digestive diseases in 5 cases), surgical in 5 patients (digestive diseases in every case), and multiple trauma in 6 patients. Forty-seven patients had undergone recent surgery (laparotomy in 18 patients, surgery for multiple trauma in 7 patients, miscellaneous in 22 patients). 830 days of enteral nutrition were monitored. Median length of survey per patient was 4 days (range, 1–20 days). The enteral feed administered was polymeric in 150 patients, a hydrolysed protein diet in 2 patients, and a supplemented nutrient in 1 patient. Most diets contained 1 kcal/mL.

Upper Digestive Tolerance of EN. Increased GAV was encountered in 49 patients (32%, 95% confidence interval [CI]: 25%–42%) after a median of 2 days (range, 1–16 days). In 20 cases, GAV was $\geq$500 mL; in 29 cases, GAV was between 150 and 500 mL on two consecutive aspirations. At least one episode of vomiting occurred in 40 patients (26%; 95% CI, 19%–33%) after a median of 2.5 days (range, 1–20 days). Nineteen of these patients also presented an increased GAV: vomiting occurred before increased GAV in 6 patients, and at the time of increased

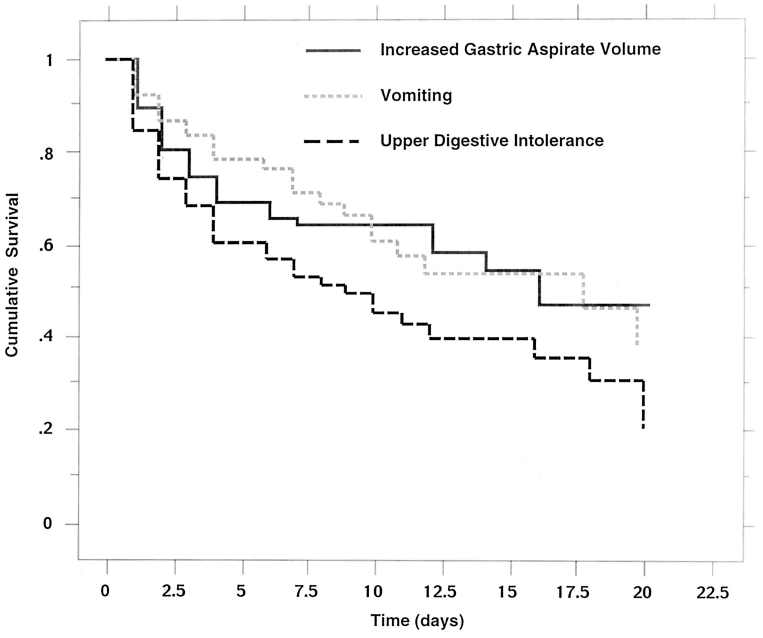

Figure 2. Cumulative survival without feeding intolerance during enteral nutrition in 153 intensive care unit patients.

GAV in 13 patients (11 of whom had GAV ≥500 mL). Twenty-one patients with normal GAV developed vomiting: 10 patients during EN, 11 patients after stopping EN. UDI during EN was encountered in 70 patients (46%; 95% CI, 38%–54%) after a median of 2 days (range, 1–20 days). In the 49 patients with increased GAV, EN was continued in 33 cases, restarted after stopping for at least 48 hrs in 9 cases, and permanently stopped in 7 cases. When the enteral route was not possible, patients received total parenteral nutrition with the same feeding goal.

Figure 2 displays Kaplan-Meier curves of enteral nutrition without increased GAV, vomiting, and UDI. After 20 days, 52% of patients presented increased GAV (95% CI, 35%–69%), 54% experienced vomiting (95% CI, 42%–85%), and 79% experienced UDI (95% CI, 64%–94%).

Risk Factors for Increased GAV and UDI. Comparison according to the patient characteristics at admission and at the beginning of enteral nutrition between patients who did and did not develop increased GAV during the survey is shown in Table 1. Patients with increased GAV were predominantly men, had higher GAV before starting EN, and were more likely to be sedated and to receive catecholamines at the beginning of EN. SOFA score at beginning of EN tended to be higher in patients who subsequently developed increased GAV.

Comparison of patients who did and did not develop increased GAV according to their characteristics during the survey is shown in Table 2. Before developing increased GAV according to the protocol definition, these patients had larger maximum GAV, lower maximum serum calcium, a higher maximum SOFA score, and a higher percentage of days with catecholamines, sedation, or in the prone position, among days of observation. Some comparisons were almost statistically significant: patients with increased GAV tended to have higher percentages of days with invasive ventilation and feeding without a peristaltic pump.

The following variables were entered into a logistic regression to determine independent risk factors for increased GAV during enteral nutrition:

At the beginning of enteral nutrition:
- SOFA score >6
- sedation
- use of catecholamines
- GAV before starting enteral nutrition >20 mL

During enteral nutrition:
- maximum GAV before meeting protocol definition >100 mL
- maximum SOFA score >7
- at least 1 day without peristaltic pump for feed administration
- at least 1 day with catecholamines
- at least 1 day with sedation
- at least 1 day with prone positioning

Independent risk factors for increased GAV during enteral nutrition were GAV before the start of enteral nutrition >20 mL, GAV during enteral nutrition >100 mL, sedation, and catecholamine use during enteral nutrition (Table 3).

When risk factors for vomiting and risk factors for UDI were studied in the same way, univariate analysis identified almost the same associations (data not shown). Multivariate analysis consistently identified sedation during EN as an independent risk factor for vomiting (data not shown) and for UDI as defined in our study. The use of sedation on at least 1 day during EN was the only independent risk factor for UDI (odds ratio [OR], 2.8; 95% CI, 1.9–4.0; $p < .0001$).

Outcome. Comparison according to outcome of patients who did and who did not develop increased GAV is shown in Table 4. Patients who developed increased GAV received a lower caloric intake. Vomiting during ICU stay after starting EN was more frequent in these patients.

The development of at least one episode of nosocomial pneumonia in ICU after starting EN showed a nonsignificant tendency to be associated with an increased GAV, whereas nosocomial pneumonia was significantly associated with sedation, vomiting, and UDI (Table 5).

Comparison according to outcome of patients who did and did not develop UDI is shown in Table 6. UDI was associated with a lower mean daily feed intake, a longer ICU stay, and a higher ICU mortality. In a logistic regression model for ICU mortality, UDI was a significant risk factor (OR, 1.48; 95% CI, 1.04–2.10; $p = .028$), even after adjustment for SAPS II at admission, but no longer after adjustment for SOFA score at the beginning of EN. Introduction of the development of pneumonia after starting EN did not modify the models.

DISCUSSION

In a prospective study in ICU patients, we found that UDI during enteral nutrition was frequent, occurred early, was more frequent in patients with sedation or catecholamines, and was associated with a higher incidence of nosocomial pneumonia, a longer ICU stay, and a higher ICU mortality.

Table 1. Comparison at admission and at the beginning of enteral nutrition according to measurement of gastric aspirate volume in 153 patients in the intensive care unit

	Normal GAV (n = 104)	Increased GAV (n = 49)	*p*
At admission			
Age, yrs	66 ± 15	62 ± 15	.19
Male gender (%)	50 (48)	36 (73)	.003
Weight, kg	70 ± 22	73 ± 26	.46
Height, cm	161 ± 10	164 ± 9	.10
SAPS II	53 ± 16	49 ± 19	.24
At the beginning of EN			
GAV (mL) before starting EN	6 ± 22	22 ± 55	.01
Abdominal perimeter, cm	96 ± 20	99 ± 17	.49
SAPS II	48 ± 15	49 ± 16	.53
SOFA score	6 ± 3	8 ± 4	.07
Glasgow Coma Scale score	12 ± 4	12 ± 5	.94
Serum potassium, mmol/L	3.9 ± 0.7	4.0 ± 0.9	.23
Serum glucose, mmol/L	9.5 ± 5.3	9.4 ± 4.2	.93
Serum calcium, mmol/L	2.08 ± 0.19	2.03 ± 0.21	.26
Feeding over 24 hrs (%)	32 (31)	11 (22)	.29
Peristaltic pump (%)	92 (88)	43 (88)	.90
SIRS (%)	86 (83)	38 (78)	.45
Ventilation			.56
Spontaneous without assistance (%)	4 (4)	1 (2)	
Mechanical through endotracheal tube (%)	99 (95)	48 (98)	
Mechanical through tracheostomy (%)	1 (1)	0 (0)	
Sedation (%)	39 (38)	33 (67)	.0006
Paralytic agent (%)	4 (4)	4 (8)	.47
Catecholamine (%)	22 (21)	20 (41)	.01
Recent surgery (%)	29 (28)	18 (37)	.27
Recent laparotomy (%)	11 (11)	7 (14)	.51
Digestive disease (%)	15 (14)	5 (10)	.47
Shock <7 days (%)	44 (42)	21 (43)	.95
Sepsis <7 days (%)	42 (40)	24 (49)	.32
Myocardial infarction <7 days (%)	9 (9)	4 (8)	.99
Hypothyroidism (%)	4 (4)	0 (0)	.31
Diabetes mellitus (%)	22 (21)	5 (10)	.10
Malnutrition (%)	39 (38)	20 (41)	.69
Ongoing peptic ulcer (%)	9 (9)	6 (12)	.68
Absence of bowel movements (%)	22 (21)	16 (32)	.12
Loperamide treatment (%)	3 (3)	0 (0)	.55

GAV, gastric aspirate volume; SAPS, simplified acute physiology score; EN, enteral nutrition; SOFA, sepsis-related organ failure assessment; SIRS, systemic inflammatory response syndrome.

Table 2. Comparison during enteral nutrition according to measurement of gastric aspirate volume in 153 patients in the intensive care unit

	Normal GAV (n = 104)	Increased GAV (n = 49)	*p*
% Days without peristaltic pump	5 ± 17	13 ± 32	.06
Maximum GAV, mL	87 ± 86	181 ± 147	<.0001
Maximum serum calcium, mmol/L	2.20 ± 0.23	2.08 ± 0.18	.003
Minimum serum calcium, mmol/L	2.01 ± 0.20	2.00 ± 0.16	.76
Maximum serum glucose, mmol/L	13.0 ± 5.5	11.8 ± 5.6	.18
Minimum serum glucose, mmol/L	7.1 ± 2.6	7.7 ± 2.8	.23
Maximum serum potassium, mmol/L	4.6 ± 0.7	4.6 ± 1.0	.46
Minimum serum potassium, mmol/L	3.5 ± 0.6	3.8 ± 0.6	.02
Minimum Glasgow Coma Scale score	12 ± 5	12 ± 5	.71
Maximum SOFA score	7 ± 3	8 ± 4	.009
% Days with SIRS	89 ± 24	87 ± 25	.64
% Days with a catecholamine	15 ± 33	47 ± 46	<.0001
% Days with sedation	24 ± 36	67 ± 43	<.0001
% Days with invasive ventilation	89 ± 24	96 ± 16	.06
% Days with prone position	2 ± 11	12 ± 26	.0009

GAV, gastric aspirate volume; SOFA, sepsis-related organ failure assessment; SIRS, systemic inflammatory response syndrome; % Days, number of days with risk factor/number of observation days.

We demonstrated that high gastric aspirate volume is an early marker of upper digestive intolerance (UDI) and that UDI is associated with nosocomial pneumonia and mortality in nasogastric tube-fed intensive care unit patients.

Our study focused on UDI that we defined as vomiting or increased GAV. McClave et al. (10) stated that intolerance was difficult to define and that none of the parameters they evaluated (radiography, physical examination, and GAV) emerged as an absolute gold standard. Many authors or expert panels recommend monitoring nasogastric feeding by GAV (6, 8, 10, 16, 17), which allows detection of intolerance before it becomes clinically obvious and dangerous, with vomiting and its complications. Our protocol to measure GAV was that described by McClave et al (10). The incidence of UDI is usually reported to be between 10% and 51% (6, 7, 18, 19). Our results in a large population of general hospital ICU patients compare well with those reported by Adam and Batson (6), who shown in 193 patients in five ICUs a 26% incidence of nausea and vomiting and a 29% incidence of high gastric aspirates. We observed a very short interval before the onset of manifestations of intolerance (2–2.5 days) as shown by others (6). Our estimates of incidence according to the Kaplan-Meier method showed that the risk did not decrease over time, which is consistent with the findings by Adam and Batson (6). As more energy is devoted to starting EN early in critically ill patients and to avoid untimely interruption of feeding, more patients will be fed for longer period of times. It might be anticipated that, with current feeding protocols, many patients may develop UDI. Our results justify continuous monitoring of EN tolerance until its withdrawal.

Numerous risk factors for UDI have been cited in the literature (9, 10, 19–

23). Only a few of the parameters we studied were associated with increased GAV. The significance of some of these factors in clinical practice, such as male sex and low maximum serum calcium level, is questionable. On the other hand, sedation and catecholamine use were found to be risk factors for increased GAV, both before and during EN. On multivariate analysis, high GAV was more frequent in patients with at least 1 day with sedation and in patients with at least 1 day with catecholamines. Sedation *per se* modifies digestive tract motility; in particular, opioids have been shown to affect antroduodenal motility in mechanically ventilated patients (24) and to impair gastric emptying in some studies (25), but not all (21). The magnitude of the role of sedation is stressed by its consistent identification as a risk factor in the various analyses performed in this study, not only for increased GAV but also for vomiting and UDI. Catecholamines might induce slowing of gastric emptying in decreasing digestive blood flow. They might also be markers of tissue hypoxia and metabolic acidosis that were not evaluated in this survey. Catecholamine use has already been identified as a risk factor for digestive intolerance during EN, but only on univariate analysis (7). Although sedation and catecholamines are frequently coadministered, they were independently associated with high GAV in our study. This link might be only an association and not causal, but these two items identify a frequent ICU population in which close monitoring of EN appears justified. Sedation and catecholamine use are frequently encountered in critically ill patients, but in our study, severity indexes, SAPS II, and SOFA score were not identified as risk factors for UDI. In our multivariate analysis, both a GAV >20 mL before the beginning of EN and a GAV >100 mL during EN were independently associated with a subsequent high GAV over the defined cut-off value. This means that even a minimal GAV before starting EN or a small increase in GAV during EN can identify patients at risk for intolerance.

The concern to screen and treat UDI during EN is justified to prevent its complications. Apart from the failure to reach nutritional goals because of suspension of feeding (6, 26), intolerance is considered to be a major cause of aspiration and pneumonia (8, 16, 17), especially among ventilated ICU patients (5). However, the link between intolerance or high GAV and aspiration is discussed (8, 12, 16, 27). In our study, UDI was statistically associated with the development of nosocomial pneumonia after starting EN, as was vomiting. Pneumonia was more frequent in patients with increased GAV but not significantly, possibly because of the small population. However, patients who developed increased GAV had more vomiting, not only during EN but also after stopping EN. A high GAV might therefore be useful as a warning sign of a more overt manifestation of intolerance. Our definition for nosocomial pneumonia, combining new radiographic infiltrates, signs of infection, and a quantitative culture of a distal bronchial sampling, was specific (28). Aspiration of pharyngeal secretions is one of the pathophysiological routes of bacterial seeding of the lung in ICU patients (28). No systematic detection of aspiration was planned in our survey. We chose to evaluate the frequency of all cases of bacterial pneumonia, regardless of the etiology (aspiration or hematogenous). Nevertheless, the frequency of pneumonia was higher in patients with UDI, emphasizing the strength of the association.

Because of the higher complication rate, patients with UDI had a longer ICU stay. A major finding of our study was the association between UDI and ICU mortality. This association was independent of SAPS II calculated at admission to the ICU or at the start of EN, but was not independent of the SOFA score calculated at the start of EN. UDI might therefore

Table 3. Multivariate analysis of risk factors for increased gastric aspirate volume during enteral nutrition in 153 patients in the intensive care unit

Variable	Wald	*p*	OR	95% CI
Catecholamines during EN	8.2	0.004	1.81	1.21–2.70
Sedation during EN	7.2	0.007	1.78	1.17–2.71
GAV before EN >20 mL	5.2	0.02	2.16	1.11–4.18
GAV during EN >100 mL	4.0	0.05	1.49	1.01–2.19
Constant	0.1	0.76		

OR, odds ratio; CI, confidence interval; EN, enteral nutrition; GAV, gastric aspirate volume.

Table 4. Comparison of outcome according to measurement of gastric aspirate volume during enteral nutrition in 153 patients in the intensive care unit (ICU)

	Normal GAV (n = 104)	Increased GAV (n = 49)	*p*
Mean caloric intake, kcal/kg/day	20 ± 8	15 ± 8	.0005
Diarrhea (%)	26 (25)	10 (20)	.53
Vomiting during survey (%)	21 (20)	19 (39)	.02
Vomiting after start of EN (%)	24 (23)	26 (53)	.0002
Pneumonia after start of EN (%)	30 (29)	20 (41)	.14
ICU length of stay, days	17 ± 20	22 ± 16	.09
ICU mortality (%)	30 (29)	20 (41)	.14
Hospital mortality (%)	44 (42)	27 (55)	.14

GAV, gastric aspirate volume; EN, enteral nutrition.

Table 5. Comparison of who did and who did not develop nosocomial pneumonia in 153 enterally fed patients in the intensive care unit

	No Pneumonia After Start of EN (n = 103)	Pneumonia After Start of EN (n = 50)	*p*
Maximum SOFA score	7 ± 4	8 ± 4	.07
% Days with sedation	33 ± 42	49 ± 43	.03
% Days with prone position	4 ± 17	7 ± 20	.46
Increased GAV during survey (%)	29 (28)	20 (40)	.14
Vomiting during survey (%)	22 (21)	18 (36)	.05
UDI during survey (%)	40 (39)	30 (60)	.01

EN, enteral nutrition; SOFA, sepsis-related organ failure assessment; % days, number of days with risk factor/number of observation days; GAV, gastric aspirate volume; UDI, upper digestive intolerance.

Table 6. Comparison of severity indexes and outcome according to upper digestive intolerance during enteral nutrition in 153 patients in the intensive care unit (ICU)

	Absence of UDI (n = 83)	Presence of UDI (n = 70)	*p*
SAPS II at admission	52 ± 16	51 ± 18	.70
SAPS II at beginning of EN	48 ± 15	48 ± 16	.99
SOFA score at beginning of EN	6 ± 3	8 ± 4	.001
Mean caloric intake, kcal/kg/day	20 ± 8	17 ± 8	.01
Diarrhea (%)	20 (24)	16 (23)	.86
Pneumonia after start of EN (%)	20 (24)	30 (43)	.01
ICU length of stay, days	15 ± 16	23 ± 21	.007
ICU mortality (%)	21 (25)	29 (41)	.03
Hospital mortality (%)	34 (41)	37 (53)	.14

UDI, upper digestive intolerance; SAPS, simplified acute physiology score; EN, enteral nutrition; SOFA, sepsis-related organ failure assessment.

represent a marker of patients with a poor prognosis. Gut failure has already been associated with mortality in mechanically ventilated blunt trauma patients (29). Nevertheless, UDI exposed patients to more complications that could explain the increased length of stay and death rate. Improvement of the upper digestive tolerance of EN therefore appears to be a major concern.

Our study has certain limitations. Our protocol did not plan to use jejunal feeding or partial parenteral nutrition. The outcomes described are therefore only relevant to gastric nutrition. When our study was designed and conducted, cisapride was still available as a prokinetic agent. When our protocol recommended administration of a prokinetic agent, cisapride was generally used. No death was attributed to cisapride-induced cardiac arrhythmia during the study (30). Since the end of the study, cisapride has been withdrawn from the market by the French Medicines Agency because of adverse events (30). We now use erythromycin as already defined in our feeding protocol (31).

The use of a protocol has been advocated to reach a compromise between nutritional goals and prevention of complications (6, 9). Our ICU's protocol was designed on the basis of published guidelines and recommendations (8, 9). We chose GAV to monitor upper digestive tolerance of enteral feeding, because it is a convenient tool for clinical practice (8–10). The choice of the cut-off point between tolerance and intolerance is a central issue when monitoring GAV. In the literature, a broad range of volumes are used to withhold enteral feeding: from 50 to 600 mL (6, 8–10, 13, 16, 18, 20, 22, 23, 27, 32). Only a few studies have provided scientific evidence for the choice of the appropriate level of GAV that should raise concern about impaired gastric emptying. We tried to reconcile both targets—efficacy and safety. We used a low cut-off (150 mL at two consecutive aspirations) for introduction of prokinetics and a high cut-off (500 mL at a single aspiration) for discontinuation of feeding delivery. McClave et al. (10) reported that a single high GAV does not justify automatic cessation of enteral nutrition inasmuch as it occurs in some patients with normal physical examination and radiographic results whose subsequent GAVs decrease. In keeping with this opinion, our protocol required two consecutive GAVs to exceed the lower cut-off before introduction of prokinetics. As previously shown (6), intolerance was associated with a lower mean daily feed intake in our study. We were also a long way from reaching our feeding goal in our study population, even in tolerant patients. This finding was somewhat disappointing, as the feeding protocol (Fig. 1) was designed to avoid unnecessary starvation (9, 26). Moreover, our protocol was associated with a high frequency of UDI, which, in turn, was associated with pneumonia and mortality, which we consider to be a strong argument in favor of modifying our current practice with evaluation of a lower GAV cut-off requiring intervention. On the basis of our data, intervention is mandatory as soon as GAV exceeds 20 mL before EN and 100 mL during EN. Rather than discontinuing feeding or slowing the delivery rate, we prefer to administer prokinetics to preserve the nutritional goals. This attitude needs to be evaluated by taking into account both the patient's nutritional needs and the risk of developing complications.

In summary, we demonstrated that high GAV is an early marker of UDI and that UDI is associated with nosocomial pneumonia and mortality in nasogastric tube-fed ICU patients. This justifies the use of GAV to monitor enteral feeding in this setting. It also warrants further evaluation of refinements of feeding protocols, such as a lowering of the GAV alert level.

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