Continuous Control of Tracheal Cuff Pressure and Microaspiration of Gastric Contents in Critically Ill Patients

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Rationale: **Underinflation of the tracheal cuff frequently occurs in critically ill patients and represents a risk factor for microaspiration of contaminated oropharyngeal secretions and gastric contents that plays a major role in the pathogenesis of ventilator-associated pneumonia (VAP).**

Objectives: **To determine the impact of continuous control of tracheal cuff pressure (P_{cuff}) on microaspiration of gastric contents.**

Methods: **Prospective randomized controlled trial performed in a single medical intensive care unit. A total of 122 patients expected to receive mechanical ventilation for at least 48 hours through a tracheal tube were randomized to receive continuous control of P_{cuff} using a pneumatic device (intervention group, n = 61) or routine care of P_{cuff} (control group, n = 61).**

Measurements and Main Results: **The primary outcome was microaspiration of gastric contents as defined by the presence of pepsin at a significant level in tracheal secretions collected during the 48 hours after randomization. Secondary outcomes included incidence of VAP, tracheobronchial bacterial concentration, and tracheal ischemic lesions. The pneumatic device was efficient in controlling P_{cuff}. Pepsin was measured in 1,205 tracheal aspirates. Percentage of patients with abundant microaspiration (18 vs. 46%; $P = 0.002$; OR [95% confidence interval], 0.25 [0.11–0.59]), bacterial concentration in tracheal aspirates (mean ± SD 1.6 ± 2.4 vs. 3.1 ± 3.7 $\log_{10}$ cfu/ml, $P = 0.014$), and VAP rate (9.8 vs. 26.2%; $P = 0.032$; 0.30 [0.11–0.84]) were significantly lower in the intervention group compared with the control group. However, no significant difference was found in tracheal ischemia score between the two groups.**

Conclusions: **Continuous control of P_{cuff} is associated with significantly decreased microaspiration of gastric contents in critically ill patients.**

Keywords: pneumonia; ventilator-associated; infection; intensive care; aspiration

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Microaspiration of gastric contents is a risk factor for ventilator-associated pneumonia. Underinflation of the tracheal cuff is common in intubated patients. The impact of continuous control of tracheal cuff pressure (P_{cuff}) on microaspiration of gastric contents is unknown

What This Study Adds to the Field

Continuous control of P_{cuff} is associated with significantly decreased microaspiration of gastric contents.

Microaspiration of contaminated oropharyngeal secretions and gastric contents is common in intubated critically ill patients and represents a key factor in the pathogenesis of ventilator-associated pneumonia (VAP) (1, 2). Risk factors for microaspiration include patient-related factors and invasive procedures, such as enteral nutrition through a nasogastric or an orogastric tube and mechanical ventilation through a tracheal tube (3). Supine position, sedation, coma, tracheal diameter, viscosity of secretions, and atmospheric pressure above the tracheal cuff are patient-related factors (4–8). Impossible closure of vocal cords, longitudinal folds in high-volume low-pressure polyvinylchloride (PVC) cuffed tracheal tubes, and underinflation of tracheal cuff are tracheal-tube related factors promoting microaspiration in intubated critically ill patients (9–12).

In spite of manual control of cuff pressure (P_{cuff}) using a manometer, underinflation (< 20 cm H_2O) and overinflation (> 30 cm H_2O) of the tracheal cuff frequently occurs in intensive care unit (ICU) patients (13, 14). Underinflation and overinflation of the tracheal cuff are well-known risk factors for VAP and tracheal ischemic lesions (15, 16), which are associated with important morbidity and mortality in ICU patients (17–19).

Recently, devices allowing efficient continuous regulation of P_{cuff} have been developed (13, 20, 21). *In vitro* (21), animal (22), and human (13, 20) studies have demonstrated that these devices are more efficient in controlling P_{cuff} than routine care using a manual manometer. To the best of our knowledge, no study has evaluated the impact of continuous control of P_{cuff} on microaspiration of gastric contents. In addition, recently published guidelines and recommendations did not discuss this issue (23–26). We hypothesized that continuous control of tracheal P_{cuff} using a pneumatic device would allow reduction of microaspiration of gastric contents. Therefore, we conducted this prospective randomized controlled study to determine the impact of continuous control of P_{cuff} on microaspiration of gastric contents. Secondary outcomes of this study included incidence of VAP, tracheobronchial bacterial concentration, and tracheal ischemic lesions.

Some of the results of this study have been reported in the form of abstracts (27, 28).

METHODS

This prospective randomized controlled study was conducted in a single 10-bed medical ICU during an 11-month period. The study was approved

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Author contributions: All authors contributed to study design. S.N., F.Z., C.F., R.L., P.R., and M.B. collected data. S.N. drafted the manuscript. All authors critically revised the manuscript and agreed on the submitted version.

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by the institutional review board of the Lille University Hospital. Written consent was obtained from the patients or their proxies.

Study Design

Patients older than 18 years who were intubated and expected to require mechanical ventilation for at least 48 hours were eligible for the study. Patients were excluded if they (*1*) were already enrolled in another trial, (*2*) had a contraindication for semirecumbent position, (*3*) had a contraindication for enteral nutrition, (*4*) had already undergone mechanical ventilation for more than 48 hours at the time of screening for eligibility, or (*5*) were admitted to the ICU with prior tracheostomy.

Patients were randomly assigned to receive continuous control of P_{cuff} (intervention group) or routine care (control group). In both groups, management of the P_{cuff} was continued until the end of mechanical ventilation or death; target P_{cuff} was 25 cm H_2O. In the intervention group, continuous control of cuff pressure was performed using a pneumatic device (Nosten; Leved, St-Maur, France). In the control group, routine care of the tracheal cuff was performed using a manual manometer (Ambu Cuff Pressure Gauge; Ambu A/S, Ballerup, Denmark) to check and adjust P_{cuff} three times a day.

Study patients received enteral nutrition according to a written protocol. Sucralfate was used to prevent stress ulcer. Proton pump inhibitors were used to treat documented esophagitis or gastric ulcer. Patients were kept in semirecumbent position. Tracheal tube size was 7.5 and 8 in women and men, respectively. All tracheal tubes used in this study were high-volume low-pressure PVC cuffed.

Pepsin was quantitatively measured in all tracheal aspirates during the 48 hours after randomization. Quantitative tracheal aspirate was performed after intubation, three times a week thereafter, and whenever VAP was suspected. Bronchoalveolar lavage was performed in immunosuppressed patients with suspected VAP and in patients with nonresolving VAP. Fiberoptic bronchoscopy was performed during the 24 hours after extubation to evaluate ischemic tracheal lesions.

The primary end point was the incidence of abundant microaspiration of gastric contents. Secondary outcomes included suspected and microbiologically confirmed (positive tracheal aspirate culture $\geq 10^6$ cfu/ml or bronchoalveolar lavage culture $\geq 10^4$ cfu/ml) VAP (29), bacterial concentration in tracheal aspirates, and tracheal ischemic lesions.

Patients with greater than 65% of tracheal aspirates pepsin positive (> 200 ng/ml) were considered as having abundant microaspiration. Tracheal ischemic lesions were defined based on the presence of hyperemia, ischemia, ulcer, and tracheal rupture (*see* Table E1 in the online supplement).

Statistical Analyses

Based on the incidence of microaspiration of gastric contents in our ICU, we estimated an incidence of abundant microaspiration of gastric contents of 70% in the control group and 45% in the intervention group. Randomly assigning 61 patients to each group would allow detection of this difference with 80% power and a two-tailed significance level of 0.05.

All *P* values were two-tailed. Categorical variables were described as frequencies (%). Normally distributed and skewed continuous variables were described as mean ± SD and median (interquartile range), respectively. χ^2 test or Fisher exact test were used to compare qualitative variables, as appropriate. Student *t* test or Mann-Whitney *U* test were used to compare normally distributed and skewed continuous variables, as appropriate.

The cumulative rates of remaining free of VAP in the two groups were examined by the Kaplan-Meier method and compared by log-rank test. All analyses were performed on an intention-to-treat basis.

Additional details on the methods are provided in the online supplement.

RESULTS

During the study period, 226 patients were admitted to the ICU. One hundred fifty-five (68%) consecutive patients received invasive mechanical ventilation and were screened for eligibility in the study. Twenty-six patients were not eligible because expected duration of mechanical ventilation was less than 48 hours. Among the 129 remaining patients, 4 patients refused to participate and 3 patients had exclusion criteria. One hundred

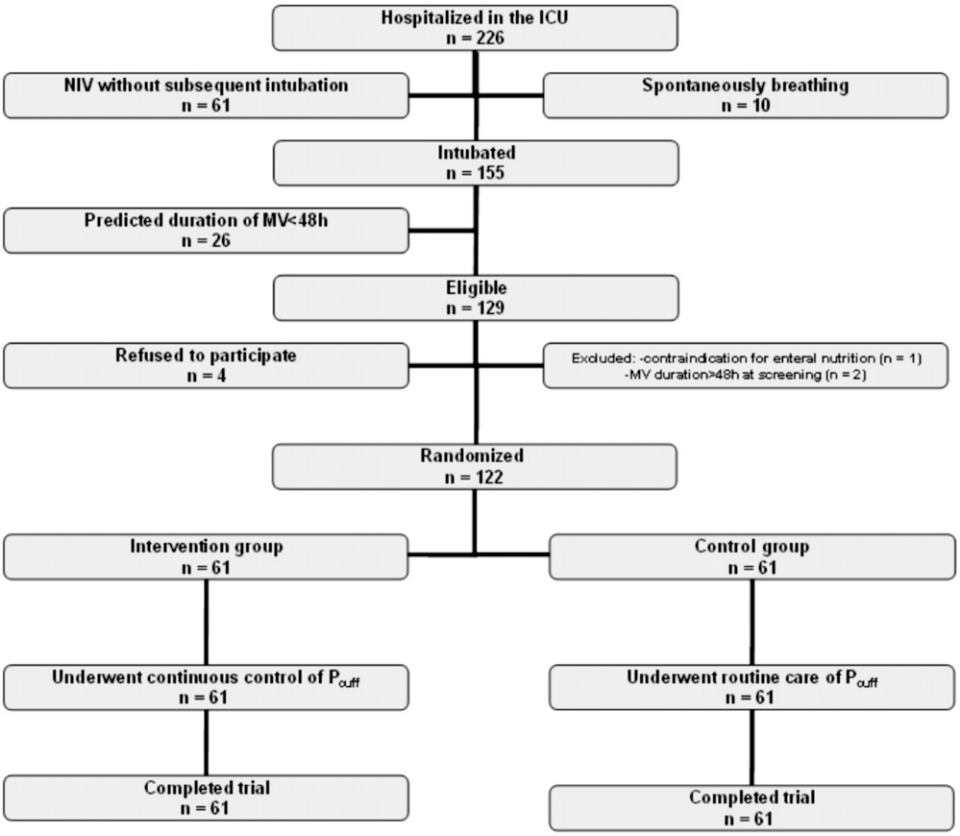

Figure 1. Study flow chart. ICU = intensive care unit; MV = mechanical ventilation; NIV = noninvasive ventilation; P_{cuff} = cuff pressure.

twenty-two patients were randomized (61 per group), 61 patients underwent continuous control of P_{cuff}, and 61 patients received routine care for P_{cuff}. All study patients were analyzed (Figure 1).

Patient characteristics at ICU admission and at randomization were similar in the two groups (Tables 1 and 2). Percentage of P_{cuff} determinations between 20 and 30 cm H_2O and P_{cuff} were significantly higher in the intervention compared with the control group. Percentage of patients with P_{cuff} less than 20 cm H_2O, percentage of patients with P_{cuff} greater than 30 cm H_2O, percentage of P_{cuff} determinations less than 20 cm H_2O, and percentage of P_{cuff} determinations greater than 30 cm H_2O were significantly lower in the intervention compared with the control group. No significant difference was found in patient characteristics during the 48 hours after randomization (Table 2). Percentage of days in the ICU with antibiotic treatment was significantly lower in the intervention compared with the control group. No significant difference was found in duration of mechanical ventilation between the two groups. Total mechanical ventilation days were 904 versus 822 in intervention and control groups, respectively. No significant difference was found in other patient characteristics during the ICU stay (Table 3).

Pepsin was measured in 1,205 tracheal aspirates (median [interquartile range], 11 [6–14] vs. 9 [6–13] per patient, $P = 0.131$, in intervention and control groups, respectively). Percentage of patients with abundant microaspiration was significantly lower in the intervention compared with the control group. In addition, pepsin level, rate of patients with suspected VAP, rate of patients with microbiologically confirmed VAP, and incidence rate of microbiologically confirmed VAP were significantly lower in the intervention compared with the control group. The probability of remaining free of VAP over the duration of mechanical ventilation was significantly higher in the intervention group compared with the control group (log-rank test, $P = 0.016$) (Figure 2). Bacterial concentration in tracheal aspirates was significantly lower in the intervention compared with the control group (mean ± SD, 1.6 ± 2.4 vs. 3.1 ± 3.7 $\log_{10}$ cfu/ml; $P = 0.014$) (Figure 3). At least one fiberoptic bronchoscopy was performed in 78% (96 of 122) of study patients during the 24 hours after extubation to determine tracheal ischemic lesions. No significant difference was found in tracheal ischemia score between the two groups (Table 4). Fiberoptic bronchoscopy was well tolerated in all patients, and no bronchoscopy-related complication occurred in study patients.

Gram-negative bacilli were the most frequently isolated microorganisms in patients with VAP and in those with tracheobronchial colonization. No significant difference was found between the intervention and control groups regarding percentage of patients with multidrug-resistant bacteria or percentage of patients with different microorganisms (Table E2). Time from starting mechanical ventilation to VAP occurrence (median [IQR], 7 [5–13] vs. 7 [4–9] d; $P = 0.4$) and time from starting mechanical ventilation to tracheobronchial colonization occurrence (5 [3–11] vs. 5 [3–8] d, $P = 0.5$) were similar in intervention and control groups, respectively. Most episodes of VAP were late onset (77% [17 of 22]); no significant difference was found in rate of patients with late-onset VAP between intervention and control group (83 vs. 75%, $P = 0.115$). Percentage of patient with VAP in whom the diagnosis was made using bronchoalveolar lavage was similar in the two groups (2 of 6 [33%] patients vs. 5 of 16 [31%], $P = 1$, in intervention and control groups, respectively).

TABLE 1. PATIENT CHARACTERISTICS AT ICU ADMISSION

	Continuous Control of P_{cuff}		
	Yes n = 61	No n = 61	*P* Value
Age, y, mean ± SD	59 ± 15	62 ± 16	1.0
Male sex	41 (67)	42 (68)	0.586
SAPS II, mean ± SD	41 ± 14	45 ± 16	0.184
LOD score, median (IQR)	5 (2.5–7)	5 (3–8)	0.424
Ultimately or rapidly fatal underlying disease*	26 (42)	27 (44)	1.0
Comorbidities			
Diabetes	4 (6)	12 (19)	0.058
COPD	17 (27)	17 (27)	1.0
Chronic heart failure	2 (3)	4 (6)	0.680
Cirrhosis	4 (6)	6 (9)	0.743
Chronic renal failure	1 (1)	1 (1)	1.0
Immunosuppression	10 (16)	12 (19)	0.814
Gastroesophageal reflux	3 (4)	2 (3)	1.0
Transfer from other wards	31 (50)	35 (57)	0.586
Infection	45 (73)	46 (75)	1.0
Prior antibiotic treatment	35 (57)	34 (55)	1.0
Causes for ICU admission†			
Shock	24 (39)	22 (36)	0.852
ARDS	9 (14)	16 (26)	0.178
Community-acquired pneumonia	15 (24)	16 (26)	1.0
Hospital-acquired pneumonia	13 (21)	9 (14)	0.481
Healthcare-associated pneumonia	4 (6)	6 (9)	0.743
Neurologic failure	10 (16)	9 (14)	1.0
Acute exacerbation of COPD	7 (11)	5 (8)	0.762
Congestive heart failure	0 (0)	2 (3)	0.496
Acute poisoning	3 (4)	4 (6)	1.0
Cardiac arrest	6 (9)	7 (11)	1.0

Definition of abbreviations: ARDS = acute respiratory distress syndrome; COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; IQR = interquartile range; LOD = Logistic Organ Dysfunction; P_{cuff} = cuff pressure; SAPS = Simplified Acute Physiology Score.

Data are presented as n (%) unless otherwise specified.

* According to McCabe classification (Reference E12).

† Several patients had more than one cause for ICU admission.

DISCUSSION

The results of our study suggest that continuous control of P_{cuff} is associated with reduced microaspiration of gastric contents, reduced tracheobronchial bacterial concentration, and reduced incidence of VAP. However, continuous control of P_{cuff} had no significant effect on the incidence of tracheal ischemic lesions.

To the best of our knowledge, our study is the first to evaluate the impact of continuous control of P_{cuff} on microaspiration of gastric contents. This result is plausible given that underinflation of the tracheal cuff is a recognized risk factor for microaspiration and that continuous control of P_{cuff} allowed significant reduction of underinflation of the tracheal cuff in the intervention group compared with the control group. The relatively small difference in pepsin level between the two groups could be explained by the fact that underinflation of the tracheal cuff is not the only risk factor for microaspiration. In addition, total suppression of microaspiration is probably impossible, especially during tracheal secretion suctioning and tracheal tube movements. Another explanation is the optimal tracheal cuff management in the control group as suggested by the relatively high percentage of P_{cuff} determinations between 20 and 30 cm H_2O (74%) compared with the results of a recent study (48.3%) (30).

An observational cohort study performed in 81 critically ill patients identified underinflation of the tracheal cuff as an independent risk factor for VAP in the subgroup of patients who did not receive antimicrobials (15). However, a recent randomized controlled study examined the effects of automatic control of P_{cuff} on the incidence of VAP (30). Patients were randomized to receive continuous regulation of P_{cuff} with an automatic device

TABLE 2. PATIENT CHARACTERISTICS AT RANDOMIZATION AND DURING THE 48 HOURS AFTER RANDOMIZATION

	Continuous Control of P_{cuff}		
	Yes n = 61	No n = 61	*P* Value
At randomization			
Duration of prior intubation, d	1 (0.25–2)	1 (0.5–2)	0.962
Size of tracheal tube	8 (7.5–8)	8 (7.5–8)	0.852
LOD score	4 (1–7)	4 (2–4)	0.538
During the 48 h after randomization			
P_{cuff} cm H_2O	26 (25–27)	22 (20–24)	<0.001
$P_{cuff} < 20$ cm H_2O	2 (3)	34 (55)	<0.001*
$P_{cuff} > 30$ cm H_2O	2 (3)	12 (19)	0.008*
Percentage of P_{cuff} determinations 20–30 cm H_2O, mean ± SD	98 ± 13	74 ± 26	<0.001
Percentage of P_{cuff} determinations < 20 cm H_2O, mean ± SD	0.1 ± 12	19 ± 23	<0.001
Percentage of P_{cuff} determinations > 30 cm H_2O, mean ± SD	0.7 ± 5	5 ± 18	0.003
Head of bed elevation, angle achieved, degrees	40 (36–45)	40 (37–45)	0.637
Quantity of enteral nutrition, ml/d	750 (750–1,000)	750 (750–1,000)	0.784
Vomiting	10 (16)	5 (8)	0.270
Prokinetic drugs	15 (24)	10 (16)	0.370
Proton pump inhibitor use	21 (34)	15 (24)	0.160
Residual gastric volume, ml/d	80 (30–120)	70 (25–110)	0.546
Sedation	39 (63)	37 (60)	0.853
Ramsay score	4 (2–4)	4 (2–4)	0.537
Paralytic agent use	3 (4)	8 (13)	0.205
Ventilatory mode			0.395
ACV	44 (72)	49 (80)	
PSV	17 (27)	12 (19)	
Positive end-expiratory pressure	5 (5–7.5)	6 (5–8)	0.257
Number of tracheal suctioning/24 h, mean ± SD	8 ± 1	8 ± 1	0.892
Death	2 (3)	1 (1)	>0.999
Unplanned extubation	5 (8)	2 (3)	0.439

Definition of abbreviations: ACV = assist control ventilation; LOD = logistic organ dysfunction; P_{cuff} = cuff pressure; PSV = pressure support ventilation.
Data are n (%) or median (interquartile range) unless otherwise specified.
*Odds ratio (95% confidence interval), 0.02 (0.01–0.12); 0.13 (0.03–0.64).

(n = 73) or routine care of P_{cuff} (control group, n = 69). No significant difference was found in VAP rate between the two groups. Although VAP was the primary outcome in the study by Valencia and colleagues (30), it was a secondary outcome in ours. In addition, the use of different devices to control P_{cuff} and the different incidence of VAP might explain the different results obtained in our study. A recent study demonstrated that automated P_{cuff} controllers with rapid pressure correction interfere with the self-sealing mechanism of high-volume low-pressure PVC-cuffed tracheal tubes and reduce their sealing characteristics (21). This interference is unlikely to be observed using a pneumatic device like the one used in our study.

TABLE 3. PATIENT CHARACTERISTICS DURING INTENSIVE CARE UNIT STAY

	Continuous Control of P_{cuff}		
	Yes n = 61	No n = 61	*P* Value
Sedation	52 (85)	52 (85)	>0.999
Red blood cell transfusion	23 (37)	21 (34)	0.851
Tracheostomy	3 (4)	5 (8)	0.717
Reintubation	17 (27)	9 (14)	0.121
Unplanned extubation	7 (11)	3 (4)	
Extubation failure	10 (16)	6 (9)	
Shock	29 (47)	28 (45)	>0.999
Transport outside the ICU	23 (37)	19 (31)	0.341
Head-of-bed elevation, angle achieved, degrees	40 (36–45)	41 (38–45)	0.526
Use of proton pump inhibitors	20 (32)	16 (26)	0.552
ICU-acquired infection other than VAP	6 (9)	6 (9)	>0.999
Ventilator-associated tracheobronchitis	2 (3)	5 (8)	0.436
Duration of antimicrobial treatment, d	9 (6–15)	10 (6–15)	0.778
% of Days in the ICU with antimicrobials	83 (56–100)	100 (75–100)	0.049
Duration of mechanical ventilation, d	8 (5–16)	8 (5–15)	0.867
Mechanical ventilation–free days	3 (1–4)	2 (1–3.5)	0.335
Length of ICU stay, d	12 (7–24)	10 (7–18)	0.476
ICU mortality	16 (26)	20 (32)	0.552

Definition of abbreviations: ICU = intensive care unit; P_{cuff} = cuff pressure; VAP = ventilator-associated pneumonia.
Data are n (%) or median (interquartile range).

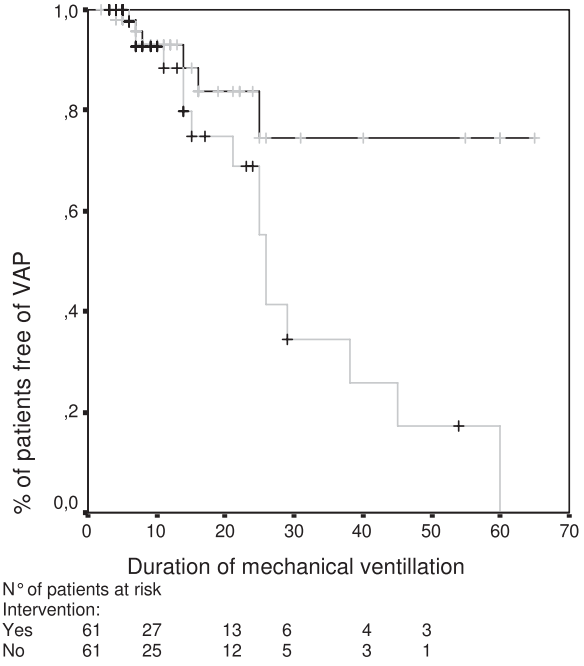

Figure 2. Cumulative rates of remaining free of ventilator-associated pneumonia (VAP) in the two groups examined by the Kaplan-Meier method; $P = 0.016$ by log-rank test. *Black line* and *gray line* indicate intervention and control groups, respectively. + indicates censored patients.

Our primary outcome was microaspiration of gastric contents and not VAP. Microaspiration is the first step in pathophysiology of VAP. Therefore, the aim of our study was to determine whether continuous control of P_{cuff} using a pneumatic device would be efficient in reducing microaspiration of gastric contents before conducting a large multicenter study to evaluate the impact of such a device on VAP prevention. Although our results suggest an important role of microaspiration of gastric contents, previous studies suggested a minor role for this mechanism in the pathogenesis of VAP (31, 32).

Incidence of VAP was high in the control group (26%). However, incidence rate of VAP (22 per 1,000 ventilator days) was in line with previous studies performed in French ICUs with similar severity scores (33, 34). This high rate of patients with VAP could be explained by the high Simplified Acute Physiology Score II at admission, the long duration of mechanical ventilation, and the high rate of patients with chronic obstructive pulmonary disease. These are well-known risk factors for VAP (35). The systematic use of sucralfate could have increased the rate of VAP in study patients (36). In addition, a recent observational study reported low incidence of bleeding from stress ulceration and raised concern about the benefit of stress ulcer prophylaxis (37). However, two metaanalyses of randomized controlled trials found stress ulcer prophylaxis to significantly reduce the incidence of bleeding (38, 39). In addition, a recent metaanalysis of randomized controlled trials reported significantly lower incidence of VAP in patients who received sucralfate compared with those who received histamine-2-receptor antagonists (40). Although VAP impact on ICU mortality is still a matter for debate, VAP is associated with significantly longer duration of mechanical ventilation (41). In spite of significant reduction in VAP rate, no significant impact of continuous control of P_{cuff} was found on duration of mechanical ventilation or ICU stay. Our study was probably underpowered to detect such an effect. Other recent randomized controlled trials on VAP prevention found similar results (42, 43).

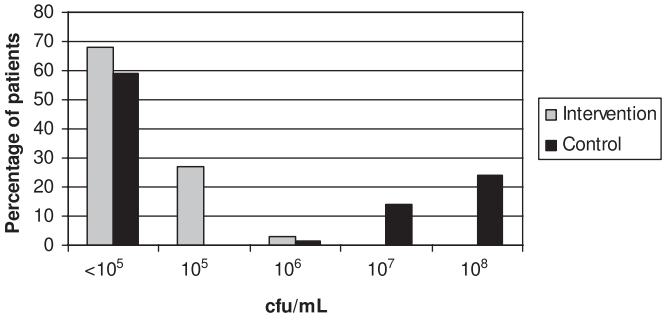

Figure 3. Tracheobronchial bacterial concentrations in intervention and control groups.

No significant effect of continuous control of P_{cuff} was found on tracheal ischemic lesions. To our knowledge, our study is the first human study to report data on tracheal ischemic lesions using fiberoptic bronchoscopy with a predefined score in a large number of patients (n = 96). Several potential explanations could be provided for this negative result. First, the impact of continuous control of P_{cuff} on tracheal ischemic lesions was a secondary outcome, and the study may have been underpowered to detect a beneficial effect. Second, the number of patients with prolonged mechanical ventilation (> 15 d) was small (n = 31). Prolonged mechanical ventilation through a tracheal tube is a major risk factor for tracheal ischemic lesions in critically ill patients (44). Third, routine care for P_{cuff} was probably optimal in the control group as suggested by the low percentage (5%) of P_{cuff} determinations greater than 30 cm H_2O compared with the rate reported by a recent study (20%) (30). Previous animal studies reported conflicting results on the impact of continuous control of ischemic tracheal lesions (22, 45). Our group performed a randomized unblinded animal study to determine the impact of continuous regulation of P_{cuff} on ischemic tracheal lesions (22). Twelve piglets were intubated and mechanically ventilated for 48 hours. Animals were randomized to manual control of P_{cuff} (n = 6) or to continuous control of P_{cuff} using a pneumatic device (n = 6). Hyperinflation of the tracheal cuff was performed to mimic high-pressure periods observed in intubated critically ill patients. Although the pneumatic device provided effective continuous control of P_{cuff}, no significant difference was found in tracheal mucosal lesions between the two groups. Another recent animal study examined the effects of dynamically modulating P_{cuff} by decreasing it during each ventilatory cycle instead of maintaining a constant level (45). The piglets were randomized to receive a novel device to modulate their P_{cuff} from 25 cm H_2O during inspiration to 7 cm H_2O during expiration (n = 5), or a constant P_{cuff} of 25 cm H_2O (n = 5). Both groups underwent ventilation under hypoxic conditions for 4 hours. Subglottic damage and tracheal damage were significantly less severe in the modulated-pressure group. However, the effect of a P_{cuff} at 7 cm H_2O during expiration on microaspiration of contaminated secretions was not evaluated in that study.

Our study has some limitations. First, we performed this study in a single center. Therefore, our results may not be extrapolated to all ICU patients, especially in ICUs with lower incidence of VAP or with surgical patients. Second, because of the nature of the intervention, physicians and nurses could not be blinded to the randomization arm. However, physicians who performed pepsin measurement and those who performed fiberoptic bronchoscopy were blinded to study group assignment. In addition, two investigators reviewed all chest X-rays and independently confirmed the presence of new pulmonary infiltrate. Third, an

TABLE 4. PRIMARY AND SECONDARY OUTCOMES

	Continuous Control of P_{cuff}			
	Yes n = 61	No n = 61	*P* Value	OR (95% CI)
Abundant microaspiration	11 (18)	28 (45)	0.002	0.25 (0.11–0.59)
Pepsin level in tracheal aspirates, ng/ml	195 (95–250)	251 (130–390)	0.043	—
VAP				
Suspected	10 (16)	24 (39)	0.008	0.3 (0.12–0.7)
Microbiologically confirmed	6 (9.8)	16 (26)	0.032	0.3 (0.11–0.84)
Incidence rate of microbiologically confirmed VAP	9.7 (7–14)	22 (17–26)	0.005	—
Bacterial concentration in tracheal aspirates, Log_{10} cfu/mL, mean ± SD	1.6 ± 2.4	3.1 ± 3.7	0.014	—
Tracheal ischemia score	4.5 (1–6)	4.5 (1–7)	0.924	—

Definition of abbreviations: CI = confidence interval; OR = odds ratio; P_{cuff} = cuff pressure; VAP = ventilator-associated pneumonia.
Data are n (%) or median (interquartile range) unless otherwise specified.

important proportion of patients had pneumonia at ICU admission. The diagnosis of VAP could be difficult in patients with abnormalities on chest X-ray before VAP. However, in all patients with VAP the initial episode of pneumonia was resolved, and antibiotic treatment was stopped before VAP diagnosis. Forth, pepsin was not measured during all mechanical ventilation periods. However, pepsin was measured during 48 hours of mechanical ventilation, representing 25% of median duration of mechanical ventilation in study patients. Risk factors for microaspiration of gastric contents have probably occurred in study patients during the 48-hour period of pepsin measurement, and thus such a period might reflect the routine care provided during the entire mechanical ventilation period. Fifth, the size of tracheal tubes used in our study (7.5–8) might have been smaller than tracheal tubes used in other ICUs (8–8.5 mm), which might have influenced our results on microaspiration. Furthermore, the proportion of reintubation was high in study patients (21%), especially in intervention group (27%). However, the difference between the two groups was not significant. In addition, other recent studies reported similar rates of reintubation related to self-extubation or respiratory failure (46, 47). Finally, we did not evaluate the effects of continuous control of P_{cuff} on microaspiration of oropharyngeal secretions or on the microbiology of these secretions. However, to our knowledge, there is no reason that continuous control of P_{cuff} could be efficient in reducing microaspiration of gastric contents without reducing microaspiration of oropharyngeal secretions. Furthermore, the microbiological assessment of oropharyngeal secretions was beyond the objectives of this study.

Conclusions

Continuous control of P_{cuff} is associated with reduced microaspiration of gastric contents, reduced tracheobronchial bacterial concentration, and reduced incidence of VAP. Implementation of this measure should now be considered in ICUs with high VAP rates even if randomized controlled multicenter studies are needed to confirm our results and to evaluate cost-effectiveness and long-term effect of continuous control of P_{cuff} on tracheal ischemic lesions before generalizing the use of this technique in every intubated patient requiring mechanical ventilation.

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