Feasibility and effects of the semirecumbent position to prevent ventilator-associated pneumonia: A randomized study*

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Context: **Reducing aspiration of gastric contents by placing mechanically ventilated patients in a semirecumbent position has been associated with lower incidences of ventilator-associated pneumonia (VAP). The feasibility and efficacy of this intervention in a larger patient population, however, are unknown.**

Objective: **Assessment of the feasibility of the semirecumbent position for intensive care unit patients and its influence on development of VAP.**

Design: **In a prospective multicentered trial, critically ill patients undergoing mechanical ventilation were randomly assigned to the semirecumbent position, with a target backrest elevation of 45°, or standard care (i.e., supine position) with a backrest elevation of 10°.**

Main Outcome Measures: **Backrest elevation was measured continuously during the first week of ventilation with a monitor-linked device. A deviation of position was defined as a change of the randomized position >5°. Diagnosis of VAP was made by quantitative cultures of samples obtained by bronchoscopic techniques.**

Results: **One hundred nine patients were assigned to the supine group and 112 to the semirecumbent group. Baseline characteristics were comparable for both groups. Average elevations were 9.8° and 16.1° at day 1 and day 7, respectively, for the supine group and 28.1° and 22.6° at day 1 and day 7, respectively, for the semirecumbent group ($p < .001$). The target semirecumbent position of 45° was not achieved for 85% of the study time, and these patients more frequently changed position than supine-positioned patients. VAP was diagnosed in eight patients (6.5%) in the supine group and in 13 (10.7%) in the semirecumbent group (NS), after a mean of 6 (range, 3–9) and 7 (range, 3–12) days, respectively. There were no differences in numbers of patients undergoing enteral feeding, receiving stress ulcer prophylaxis, or developing pressure sores or in mortality rates or duration of ventilation and intensive care unit stay between the groups.**

Conclusions: **The targeted backrest elevation of 45° for semirecumbent positioning was not reached in the conditions of the present randomized study. The achieved difference in treatment position (28° vs. 10°) did not prevent the development of VAP. (Crit Care Med 2006; 34:396–402)**

Ventilator-associated pneumonia (VAP) accounts for almost half of all infections in critically ill patients and has been associated with prolonged duration of mechanical ventilation and the intensive care unit (ICU) stay, increased morbidity and mortality, and higher healthcare costs (1). Prevention of VAP therefore remains important in intensive care medicine.

In the pathogenesis of VAP, bacterial colonization of the oral cavity and subsequent aspiration of oropharyngeal fluids along the endotracheal tube are pivotal (2, 3). Controversy exists on the relevance of bacterial colonization of the stomach and gastroesophageal aspiration in the pathogenesis of VAP (4). Gastroesophageal aspiration is facilitated by the presence of a nasogastric tube and a supine body position (5). Experimental studies with radioactive-labeled enteral feeding indeed suggested that endotracheal aspiration of gastric contents occurred more frequently when patients were placed in supine rather than semirecumbent position (6). On the basis of these findings, the Centers for Disease Control and Prevention advised treatment of mechanically ventilated patients in a semirecumbent position as a VAP-preventive measure (7), although the intervention has not been widely used as default clinical policy (8).

The effects of the semirecumbent position on the development of VAP, however, have been assessed in only one study (9). Although the semirecumbent position was associated with a 75% reduction in incidence of VAP, some important questions emerged from this study.

***See also p. 559.**

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First and most important, control patients were treated in complete horizontal position (0°), which is not the standard of care in most ICUs. Generally, patients are positioned in a backrest elevation of approximately 10°, which increases when they are no longer sedated or weaned from ventilation and which should increase when patients receive enteral nutrition. The overall benefit of the intervention in that study was to a large extent created by a 50% incidence of clinically suspected VAP among patients treated in a horizontal position while receiving enteral nutrition through a nasogastric tube. Furthermore, the intervention of placing patients in upright position was not rigorously controlled (i.e., measured only once daily), and its practical feasibility was not analyzed.

Therefore, we aimed to determine the preventive effects and feasibility of the semirecumbent patient position on the incidence of VAP in mechanically ventilated patients. The semirecumbent position with an aimed elevation of 45° was compared to standard practice in a prospective, randomized, multicentered trial and was controlled by continuous computerized monitoring of patient positions.

METHODS

From January 1999 until December 2000, adult patients admitted to four ICUs in three university hospitals in the Netherlands (Vrije Universiteit Medical Center Amsterdam, University Medical Center Utrecht, and University Hospital Maastricht) were eligible for study inclusion if they were intubated within 24 hrs of ICU admission and had an expected duration of ventilation of at least 48 hrs. Patients were not eligible if they were undergoing selective decontamination of the digestive tract or if they could not be randomized to one of the two positions (e.g., patients with trauma of the pelvic region, extensive abdominal surgery, cared for in beds without the possibility of altering backrest elevation, and neurosurgical patients treated with 30° head elevation).

All patients received sucralfate or H_2 antagonists for stress ulcer prophylaxis. Prophylaxis was discontinued when enteral feeding was started. H^+K^+ATPase inhibitors were prescribed when evidence or history of gastrointestinal bleeding was present. Decisions on the formula, administration route, and composition of enteral feeding were left to the attending intensivists. Enteral feeding was given continuously via a nasogastric tube (16-French Tubaflex, Vygon, Ecouen, France; 4-mm Levin Stomach Tube, Sherwood Medical, Tullamore, Ireland), with an aimed maximum of 1500 to 2000 mL per 24 hrs. When cumulative residue measurements exceeded 500 mL/day, enteral feeding was stopped.

Randomization. Patients were randomly assigned, on a one-to-one allocation basis per hospital, to the semirecumbent position (i.e., an aimed 45° position of the head and back) or standard care (i.e., the supine position) by means of closed, nontransparent, numbered envelopes. An independent person who mixed the envelopes before numbering generated the allocations. The institutional review boards of all participating hospitals had approved the protocol, and written informed consent was obtained for all patients.

Intervention. Backrest elevation was defined as the angle of the head of the bed and was expressed in degrees of elevation above horizontal. This level was measured every 60 secs during the first week of ventilation by means of a transducer with pendulum, which was placed on the bed frame. Data were stored in a computer. Devices were calibrated before patients were placed in the randomized position and measurements commenced. Positions were expressed as mean degrees of elevation per day. Adherence to the randomized position was analyzed by determining the number of episodes and percentage of time with deviations from the randomized position. A deviation was defined as a change in the randomized treatment position of more than 5°. Patients' own wish to be placed in a more comfortable position was always respected. Disease-related treatment could lead to changes in patient position. If possible, all patients, regardless of the randomized position, were cared for in a semirecumbent position during weaning. In each ICU, one dedicated research nurse controlled patient position 2–3 times daily and restored backrest elevation to the randomized position when possible. Moreover, to continuously inform nurses, labels indicating the randomized position were present at each bedside monitor.

Data Collection. Demographic patient data were recorded on admission to the ICU: gender, age, medical history, Acute Physiology and Chronic Health Evaluation (APACHE) II score, reason for ICU admission, and length of hospital stay before ICU admission. In addition, number of ventilator days, length of ICU stay, use of stress ulcer prophylaxis, nutrition, parameters of infection (temperature, leukocyte count), presence of systemic inflammatory response syndrome (SIRS), antibiotic use, and sedative treatment were recorded daily during the period of study. Pressure sore development was staged daily by research nurses according to the four stages described by the National Pressure Ulcer Advisory Panel system (10): stage I, enclosing nonblanchable erythema of the intact skin; stage II, skin loss involving epidermis and/or dermis; stage III, enclosing full-thickness skin lesions as deep as the fascia; and stage IV, same as III but as deep as muscle, tendon, and bone. The study was discontinued when VAP was diagnosed, when patients were placed in a bed without the possibility to alter backrest elevation, and in the case of extubation or death.

Ventilator-Associated Pneumonia. A clinical suspicion of VAP was based on the criteria for nosocomial infections, as defined by the Centers of Disease Control and Prevention (CDC) (7): a new, persistent, or progressive radiographic infiltrate with at least two of the following: a temperature $>38°C$ or $<35°C$; number of leukocytes, $>10 \times 10^9$/L or $<3 \times 10^9$/L; and a positive culture of tracheal aspirate. Patients with clinically suspected VAP underwent fiberoptic bronchoscopic examination and bronchoalveolar lavage as previously described (11). The clinical suspicion of VAP was considered microbiologically confirmed if quantitative cultures of bronchoalveolar lavage fluid yielded $\geq 10^4$ colony-forming units (cfu)/mL or if blood cultures were positive for a microorganism colonizing the respiratory tract. Three investigators, blinded for randomization codes, independently evaluated all relevant data related to the diagnosis of VAP. All patients were classified for VAP according to the CDC criteria and microbiological confirmation (7, 12). In cases of disagreement, consensus on whether a patient had VAP was obtained by discussion. The occurrence of microbiologically confirmed VAP was the primary end point of the study.

Statistical Analysis. The primary objective of this study was to determine the effectiveness of semirecumbent positioning in the prevention of VAP in an intention-to-treat analysis. On the basis of a group sequential analysis presuming a 25% incidence of VAP among supine-positioned patients and a 40% reduction in the risk of VAP to 15% among semirecumbent-positioned patients, an expected total of 252 patients would be needed ($1 - \beta = 0.80$ and a one-sided α of 0.05) to reject the null hypothesis, and an expected total sample size of 176 patients would be needed to accept the null hypothesis of no risk reduction. Stopping rules based on sequential interim analysis were prospectively defined. After each group of ten patients, a sequential analysis was performed on the cumulative data by an independent statistician, evaluating whether or not the study could be discontinued (13). Investigators remained blinded for the results of interim analysis. Chi-square tests were used to compare differences in proportions between groups. Group mean or median values were compared by Student's *t*-test or Mann-Whitney *U* test.

Patient positioning during the first week was analyzed with use of a linear mixed-effects model, with the angle in which the patients were positioned serving as dependent variable and the group in which the patients were randomized the day after study entry and their interaction as independent variables. Analyses of patient position were based on including all participants and their follow-up results in the

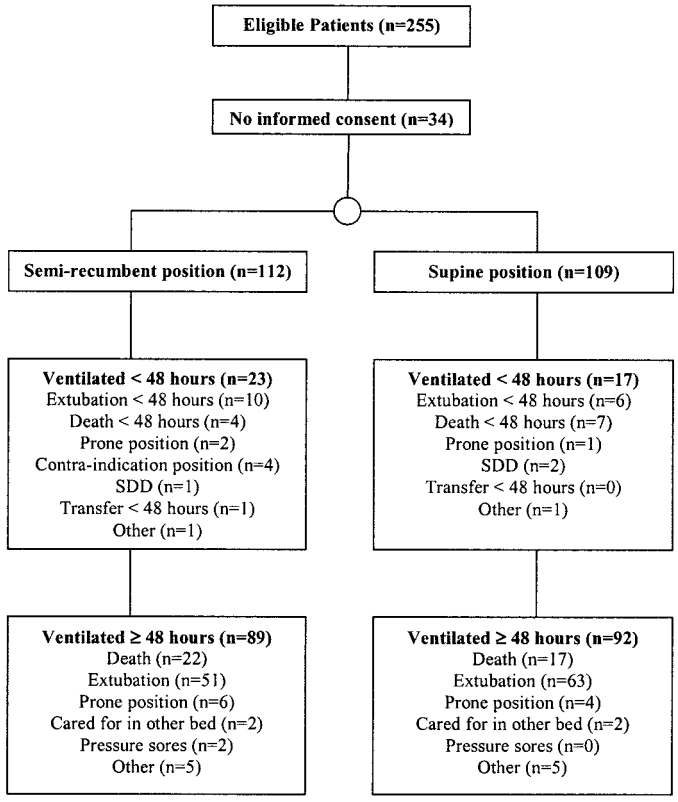

Figure 1. Stages of trial (*SDD*, selective decontamination of the digestive tract).

intervention group as initially assigned (intention-to-treat). A linear trend with time was modeled with random intercepts and random slopes for the patients (14).

RESULTS

Patient Inclusion. Of 255 eligible patients, 221 were included: 112 patients were assigned to the semirecumbent position and 109 to the supine position (Fig. 1). Thirty-four patients (or their relatives) refused to participate. In the semirecumbent group 23 patients (21%) were ventilated <48 hrs, as were 17 patients (16%) in the supine group. Main reasons for study termination in <48 hrs were extubation (n = 16), death (n = 11), prone positioning due to respiratory problems (n = 3), a contraindication for semirecumbent positioning after abdominal surgery (n = 4), administration of selective digestive decontamination (n = 3), and transfer to another hospital (n = 1). Demographic and baseline physiologic characteristics on admission were comparable for both groups (Table 1), and these remained comparable when only patients ventilated for >48 hrs were evaluated.

Enteral Feeding and Stress Ulcer Prophylaxis. The proportion of patients undergoing enteral feeding was comparable in both groups (87% and 82% for supine and semirecumbent patients, respectively), as was the median number of days at which enteral feeding was started: day 2 (range, day 1–16) in the semirecumbent group and day 2 (range, day 1–24) in the supine group. The distal tip of the feeding tube was positioned in the stomach in all patients. The mean amounts of gastric retention of enteral nutrition were 95 mL (0–742) per day in the semirecumbent group and 81 mL (0–1033) per day in the supine group (NS). Five patients had residues >500 mL/day in the semirecumbent position, vs. 7 mL/day in the supine group (NS). H_2 antagonists and/or H^+K^+ATPase inhibitors were administered to 65 patients in the semirecumbent group and 64 patients in the supine group (NS). One and three patients received sucralfate in the supine group and semirecumbent group, respectively (NS). Furthermore, mean duration of use of H_2 antagonists, H^+K^+ATPase inhibitors, and sucralfate was comparable in the two study groups (Table 2).

Patient Positioning. Backrest elevation was measured for 174 patients (90 patients randomized to supine position and 84 to semirecumbent position) for a mean of 6 days (range, 2–7 days in both groups). The mean daily backrest elevations during the first 7 days ranged from 29.3 ± 10.3° at day 1 to 23.1 ± 8.3° at day 5 for semirecumbent patients and from 9.8 ± 3.9° at day 1 to 14.8 ± 7.1° at day 7 for supine patients (Table 3). The mean number per day of deviations from the randomized position during the first 7 days ranged from 5.6 ± 3.6 at day 1 to 7.1 ± 3.7 at day 7 for semirecumbent patients and from 1.9 ± 2.6 at day 1 to 3.5 ± 4.3 at day 5 for supine patients (Table 3). For both groups backrest elevation was expressed as a linear function of day of the week, which was 8.72 + 1.06*day for patients in supine position and 29.06 − 0.92*day for patients in semirecumbent position, with significantly different slopes ($p < .001$). This resulted in an average elevation of 9.8° at day 1 and 16.1° at day 7 for the supine group and of 28.1° and 22.6° for days 1 and 7, respectively, in the semirecumbent group.

Since the aimed backrest elevation of 45° was not achieved, mean elevations for different subpopulations were further analyzed (Table 4). Medical specialty; severity of illness on admission (i.e., APACHE II score); age; gender; presence of infection, SIRS, or sepsis; and duration of sedation were not associated with different levels of backrest elevations. However, significant differences between the three participating centers were found: the mean semirecumbent position for patients admitted to the University Medical Center Utrecht was 32.0° ± 7.6°, compared with an average of 23.6° ± 7.6° for patients at the Vrije Universiteit Medical Center Amsterdam and the University Hospital Maastricht ($p < .0001$; mean difference, 8.4; 95% confidence interval [CI], 4.9–12.0). No reason for this difference was found.

Ventilator-Associated Pneumonia. A clinical suspicion of VAP did arise in 20 patients (14.3%) in the supine position and in 16 (18.3%) in the semirecumbent position (NS). Microbiologically confirmed VAP was diagnosed in 8 of 109 patients (7.3%) in the supine group (incidence rate, 7.8/1000 days) and in 13 of 112 patients (11.6%) in the semirecumbent group (incidence rate, 10.2/1000 ventilator days). According to the sequential interim analysis, the lower boundary was crossed after inclusion of 210 patients, implicating that the null hypothesis was accepted and that the pursued risk reduction was not demonstrated. Further inclusion of patients was at that point terminated (Fig. 2). The proportion of patients

Table 1. Demographic characteristics and baseline measurements

Characteristic	Supine (n = 109)	Semirecumbent (n = 112)
Mean age ± SD	63.0 ± 16.0	64.8 ± 13.8
Males, %/no.	67/73	60/67
APACHE II	24.8 ± 7.6	25.6 ± 7.7
Underlying disease: % of patients (no.)		
Cardiovascular disease	38 (41)	33 (37)
Chronic obstructive pulmonary disease	23 (25)	32 (36)
Gastrointestinal disease	18 (20)	15 (17)
Neoplastic disease	10 (11)	10 (11)
Neurologic disease	9 (10)	10 (11)
Diabetes mellitus	7 (8)	9 (10)
Chronic renal insufficiency	4 (4)	5 (6)
Acute renal insufficiency	1 (1)	2 (2)
Chronic dialysis	8 (9)	6 (7)
Malignant hematologic disease	0 (0)	3 (3)
Cirrhosis	6 (6)	4 (4)
Immunodeficiency	4 (4)	7 (8)
Alcohol and/or drug abuse	9 (10)	5 (6)
AIDS	7 (8)	4 (5)
Reason for admission ICU: % of patients (no.)		
Cardiovascular disease	12 (13)	13 (15)
Acute respiratory failure	51 (55)	54 (60)
Gastrointestinal disease	8 (9)	8 (9)
Neurologic disease	10 (11)	8 (9)
Sepsis	7 (8)	10 (11)
Trauma	8 (9)	1 (1)
Metabolic disorders	2 (2)	3 (4)
Other	2 (2)	3 (3)
Infection at admission: % of patients (no.)		
Respiratory tract, clinically suspected	39 (42)	38 (42)
Other	4 (4)	4 (4)

APACHE, Acute Physiologic and Chronic Health Evaluation; AIDS, acquired immunodeficiency syndrome; ICU, intensive care unit.

Table 2. Outcome data for the semirecumbent and supine patients

Variable	Median (Range) or Indicated Value	
	Supine n = 109	Semirecumbent n = 112
Days in study	5 (0–64)	6 (2–7)
Days ventilated	6 (0–64)	6 (0–281)
ICU stay, days	10 (0–91)	9 (0–281)
Hospital stay, days	24 (0–186)	27 (2–301)
Ventilator-associated pneumonia: % of patients (no.)		
Clinically suspected	18.3 (20)	14.3 (16)
Microbiologically confirmed	7.3 (8)	11.6 (13)
Antibiotics		
Courses	2 (0–5)	2 (0–6)
Antibiotic days	4 (0–45)	4 (0–25)
Enteral feeding		
% of patients	87	82
Number of days	2 (0–24)	2 (0–16)
Retention in mL	81 (0–1033)	95 (0–742)
Ulcer prophylaxis use, days		
H_2 antagonist	1 (0–31)	1 (0–24)
H^+K^+ ATPase inhibitors	0 (0–51)	0 (0–18)
Sucralfate	0 (0–16)	0 (0–26)
Days of sedation	3 (0–48)	3 (0–26)
Mortality: % of patients (no.)		
ICU	30 (33)	29 (33)
Hospital	38 (41)	39 (44)

ICU, intensive care unit.

with microbiologically confirmed VAP, adjusted for the sequential monitoring of the data, was 10.7% (95% CI, 7.0%–16.4%) and 6.5% (95% CI, 3.8%–9.4%) for the semirecumbent and supine positions, respectively. Incidences of VAP in the different study centers were comparable. Median number of days of ventilation before diagnosis of VAP was 7 (range, 3–12) in the semirecumbent group and 6 (range, 3–9) in the supine group. For patients developing VAP vs. those not developing VAP, backrest elevations during the first 7 days of study were comparable, both in the supine group (10.7 ± 2.7° vs. 12.7 ± 1.8°, respectively) and in the semirecumbent group (23.9 ± 3.6° vs. 25.0 ± 1.7°, respectively). In addition, percentages of time with deviation from the semirecumbent position (i.e., ≤40°) were comparable for patients developing VAP (89.4% ± 9.4) and patients not developing VAP (82.9% ± 8.2). All patients developing VAP underwent enteral feeding. Only 27 patients (12 in the supine and 15 in the semirecumbent group) did not undergo enteral feeding during the study, and none of them developed VAP. The distribution of etiological pathogens was similar in both groups, and VAP was polymicrobial in four patients of each group (data not shown).

Secondary End Points. The median duration of ventilation was 6 days, both in the semirecumbent group (range, 0–281) and in the supine group (range, 0–64). The median number of days in the study was also comparable for the two groups: 6 days (range, 0–34) and 5 days (range 0–64) in the semirecumbent and supine group, respectively. Differences in median number of days of ventilation and in study were caused by patients who were treated in prone position or in beds in which backrest position could not be elevated after the first 48 hrs of ventilation. Use of antibiotics at admission, mean number of antibiotic courses, and number of days on antibiotics were equal in the two study groups (Table 2).

Pressure sores developed in 33 patients (30%) in the supine group and in 31 (28%) in the semirecumbent group (NS). In both study groups, most patients had stage 1 or 2 pressure sores: 23 (70%) of 33 patients in the supine group and 22 (71%) of 31 patients in the semirecumbent group. In the majority of cases (93% and 91% of those with pressure sores in the supine group and semirecumbent group, respectively), pressure sores were present at the heel and/or sacral region. Mortality rates in the ICU were comparable in the two groups: 33 patients (29%)

Table 3. Backrest elevations and number of deviations in the semirecumbent and supine group during the first 7 days of ventilation

	Backrest Elevation in Degrees, Mean ± SD		No. of Deviations, Mean ± SD (Median; Range)	
Day	Semirecumbent	Supine	Semirecumbent	Supine
1	29.2 ± 10.3	9.8 ± 3.9	5.6 ± 3.6 (5; 0–16)	1.9 ± 2.6 (1; 0–14)
2	26.8 ± 11.4	10.8 ± 4.6	5.9 ± 4.3 (5; 0–23)	2.1 ± 2.9 (1; 0–18)
3	25.5 ± 9.8	12.0 ± 6.3	6.7 ± 4.3 (5; 0–20)	2.5 ± 2.6 (1; 0–13)
4	23.9 ± 9.1	12.5 ± 6.4	6.4 ± 4.1 (5; 1–17)	3.1 ± 2.7 (2; 0–11)
5	23.1 ± 8.3	13.6 ± 6.5	6.5 ± 4.7 (5; 1–16)	3.3 ± 3.5 (2; 0–18)
6	24.7 ± 6.8	14.4 ± 8.1	6.2 ± 4.2 (6; 1–22)	3.5 ± 4.3 (2; 0–25)
7	26.5 ± 8.2	14.8 ± 7.1	7.1 ± 3.7 (6; 2–19)	3.3 ± 2.8 (3; 0–12)

Table 4. Effect of different variables on mean backrest elevation during the first week for patients randomized to the semirecumbent position

Variable	No. of Patients	Backrest Elevation, Mean ± SD	*p* Value
Admittance type			
Medical	67	26.3 ± 9.0	
Surgical	17	25.9 ± 6.4	NS
APACHE at admittance			
≤20	16	28.2 ± 6.8	
21–30	43	25.2 ± 9.3	
≥30	24	26.5 ± 8.2	NS
Infection at admittance			
Yes	46	27.7 ± 9.4	
No	36	24.2 ± 7.2	.07 (−3.5; −7.3–0.25)
Age quartile			
1	21	27.4 ± 7.6	
2	20	26.4 ± 8.2	
3	21	24.8 ± 9.3	
4	22	26.2 ± 9.1	NS
Gender			
Male	51	27.0 ± 8.8	
Female	33	24.9 ± 9.1	NS
Hospital			
UHM/VUHA	58	23.6 ± 7.6	
UMCU	26	32.0 ± 7.6	<.0001 (8.4; 4.9–12.0)
Days of sedation			
≤4	50	27.0 ± 8.8	
≥5	34	25.1 ± 8.1	NS
SIRS during ICU stay			
Yes	74	26.7 ± 8.5	
No	10	22.5 ± 8.2	NS
Sepsis during ICU stay			
Yes	35	25.4 ± 6.7	
No	49	26.8 ± 9.6	NS

NS, not significant; APACHE, Acute Physiologic and Chronic Health Evaluation; UHM/VUHA, University Hospital Maastricht/Vrije Universiteit Medical Center Amsterdam; UMCU, University Medical Center Utrecht; SIRS, systemic inflammatory response syndrome; ICU, intensive care unit.

in the semirecumbent group and 33 patients (30%) in the supine group died (NS). In-hospital mortality rates were 39% (44 patients) and 38% (41 patients) in the semirecumbent and supine position (NS).

DISCUSSION

The main feature of the present study is that, despite the presence of dedicated research nurses to control and maintain patient positioning, the semirecumbent treatment position with an aimed backrest elevation of 45° is not feasible for mechanically ventilated patients. In our setting, a backrest elevation of nearly 30° was achieved. As compared with the 10° elevation that is the standard of care, semirecumbency did not prevent the development of VAP. These findings question the generally assumed efficacy of this intervention for prevention of VAP.

Our study is the second randomized trial evaluating the semirecumbent position as a VAP-preventive measure. In comparison with the only other randomized trial, our study is unique in three aspects: patient positioning was continuously monitored throughout the first week, the semirecumbent position was compared to the standard of care, and data were analyzed according to the intention-to-treat principle. In contrast to our findings, Drakulovic and co-workers (9) reported an 83% decrease of bacteriologically confirmed VAP in a group of patients treated in a semirecumbent position of 45°. Some important differences between the study of Drakulovic et al. and the present study deserve attention. In their study, backrest elevation was measured only once daily and, therefore, feasibility of the implemented position could not be examined.

One explanation for the difference in outcome between the studies may be the treatment position of control patients. In our study, control patients were not subjected to any intervention and had mean backrest elevations between 9.8° and 14.8° during the first 7 days of ventilation, representing the standard of care in our ICUs. Apparently, control patients were treated in complete horizontal position (0°) in the Drakulovic study, and 60% of them received enteral feeding in this position. Both enteral feeding and supine position were selected as the most important risk factors for VAP in that study. Therefore, the difference between the two studies seems to be explained, at least in part, by an increased incidence of VAP in patients treated in a more supine position than is generally practiced in ICUs. In the present study, start and duration of enteral feeding as well as amounts of gastric residues were comparable in the two groups. The type of drainage tube used in patients will be comparable, since randomization occurred within ICUs. Therefore, it is unlikely that differences in any of these variables have raised the incidence of VAP in patients treated in semirecumbent position, which could have explained the lack of benefit of this position.

Another difference between both studies is that Drakulovic and co-workers excluded patients being cared for in a deviating position for more than 45 mins. Our study was based on an intention-to-treat principle, and data of patients with a long-term change of body position were included in the analyses. In our opinion,

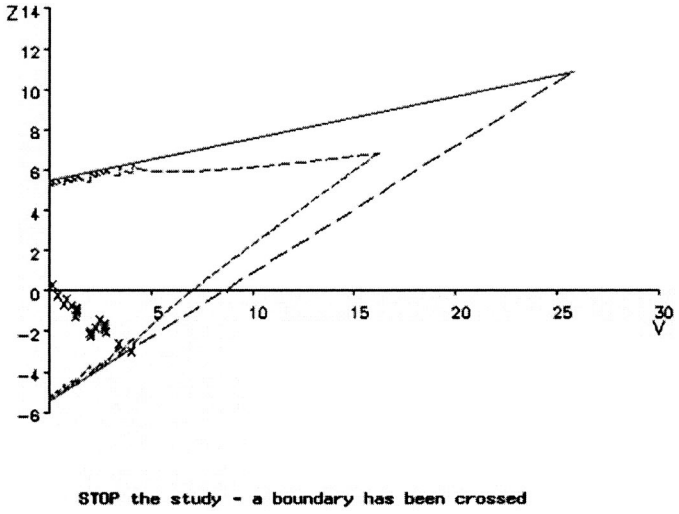

Figure 2. Results of group sequential analysis. On the horizontal axis (*V*), the cumulative amount of information in the trial, which is proportional to the sample size, is depicted. On the vertical axis (*Z*), the cumulative measure for the advantage of the semirecumbent position in reducing the incidence of ventilator-associated pneumonia (VAP) is depicted. The triangle boundaries represent the values where the null hypothesis can be rejected or accepted. Crossing of the upper boundary indicates that the semirecumbent position reduces the incidence of VAP. Crossing of the lower boundary indicates that the semirecumbent position does not reduce the incidence of VAP. The inner lines represent a continuity correction. The cumulative results of group sequential analyses are represented by X marks. The crossing of the X marks of the lower boundary indicates that the semirecumbent position did not reduce the incidence of VAP.

this reflects daily practice more properly and makes subsequent extrapolation of our findings more feasible. Excluding such patients, however, would not have influenced our findings, since mean backrest elevations were comparable for patients developing and not developing VAP in the semirecumbent group.

A potential and imaginable point of criticism is that we failed to treat patients in a semirecumbent position of 45°, despite daily control by research nurses in all participating centers. However, to the best of our knowledge, more detailed data on patient positioning have not been determined. Possibly, an average backrest of 30° is not enough for VAP prevention. Alternatively, 10° might be sufficient for prevention. Unfortunately, the reason why the aimed position of 45° was not achieved remains unclear. Nevertheless, the presence of a dedicated research nurse for the control and maintenance of patient positioning probably exceeds the possibilities in other wards and nonintervention settings. We could not identify patient-specific risk factors associated with this failure. However, a significant difference in patient position between the participating centers was observed, probably as a result of differences in daily patient care. These site-specific differences and the failure to reach the suggested 45° position, even in a study setting with dedicated research nurses, question the feasibility of this intervention. The differences probably result from healthcare-worker related factors such as motivation and commitment to adhering to scientific protocols, but these variables were not systematically analyzed.

Another possible limitation of the study was the mixed and nonprotocolized use of large and small nasogastric feeding tubes. Despite differences in local treatment policies, it is unlikely that this affected our results, since patient randomization was performed within each center. Moreover, gastric tube size was not a risk factor for gastroesophageal reflux and microaspiration (15).

Finally, the observed VAP rate was lower than the expected VAP rate, which was based on a study performed in one of the participating ICUs 3 yrs earlier (16). Incidences of VAP in the period before this trial had not been determined in the other two participating centers. Therefore, we cannot explain the difference between the expected and observed VAP rates. Yet, in another multicentered study on VAP prevention, performed in the 2 yrs after the current study in seven Dutch ICUs, incidences of VAP were, in a comparable population, again around 10% (personal communication, M.J.M. Bonten; publication in preparation). Without strictly defined interventions, incidences of VAP seem to have decreased in the past 10 yrs.

The achieved difference in treatment position (28° vs. 10°) did not prevent the development of ventilator-associated pneumonia.

Mean backrest elevation in our study was approximately 30° in the semirecumbent group. Nevertheless, although a difference in treatment position between both study groups was achieved, this did not prevent the development of VAP. Pooling of colonized oropharyngeal fluids above the inflated cuff of the endotracheal tube is common in mechanically ventilated patients (17). It is possible that the semirecumbent position stimulates leakage of oropharyngeal fluid by means of gravity. Furthermore, the more frequent changes in position necessary to restore the randomized position after medical or nursing-care procedures may have further facilitated aspiration. In this regard, one might speculate whether continuous subglottic aspiration of this fluid or high-volume, low-pressure cuffs could have prevented episodes of VAP. Preventive effects of these techniques have been reported, albeit with contrasting results (17–21).

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REFERENCES

1. Vincent JL, Bihari DJ, Suter PM, et al: The prevalence of nosocomial infection in intensive care units in Europe: Results of the European Prevalence of Infection in Intensive Care (EPIC) Study. EPIC International

Advisory Committee [see comments]. *JAMA* 1995; 274(8):639–644
2. Johanson WG Jr, Pierce AK, Sanford JP, et al: Nosocomial respiratory infections with gram-negative bacilli: The significance of colonization of the respiratory tract. *Ann Intern Med* 1972; 77(5):701–706
3. Johanson WG Jr, Woods DE, Chaudhuri T: Association of respiratory tract colonization with adherence of gram-negative bacilli to epithelial cells. *J Infect Dis* 1979; 139(6): 667–673
4. Bonten MJ, Gaillard CA, de Leeuw PW, et al: Role of colonization of the upper intestinal tract in the pathogenesis of ventilator-associated pneumonia [see comments]. *Clin Infect Dis* 1997; 24(3):309–319
5. Ibanez J, Penafiel A, Raurich JM, et al: Gastroesophageal reflux in intubated patients receiving enteral nutrition: effect of supine and semirecumbent positions. *JPEN J Parenter Enteral Nutr* 1992; 16(5):419–422
6. Torres A, Serra-Batlles J, Ros E, et al: Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: The effect of body position. *Ann Intern Med* 1992; 116(7):540–543
7. Centers for Disease Control and Prevention. Guidelines for prevention of nosocomial pneumonia. *MMWR Morb Mortal Wkly Rep* 1997; 46(RR-1):1–79
8. Cook DJ, Meade MO, Hand LE, et al: Toward understanding evidence uptake: Semirecumbency for pneumonia prevention. *Crit Care Med* 2002; 30(7):1472–1477
9. Drakulovic MB, Torres A, Bauer TT, et al: Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: A randomised trial [see comments]. *Lancet* 1999; 354(9193):1851–1858
10. Bergstrom N, Bennet MA, Carlson CE: Treatment of Pressure Ulcers. Rockville, MD, Agency for Health Care Policy and Research, 1994
11. de Brauwer E: Standardisation and applications of bronchoalveolar lavage cytology. Maastricht University, 2000
12. Pingleton SK, Fagon JY, Leeper KV Jr: Patient selection for clinical investigation of ventilator-associated pneumonia: Criteria for evaluating diagnostic techniques. *Chest* 1992; 102(5 Suppl 1):553S–556S
13. Whitehead J: The Design and Analysis of Sequential Clinical Trials. Second Edition. Baltimore, John Wiley & Sons, 1997
14. Pinheiro JC, Bates DM: Mixed Effect Models in S and S-Plus. Berlin, Springer-Verlag, 2000
15. Ferrer M, Bauer TT, Torres A, et al: Effect of nasogastric tube size on gastroesophageal reflux and microaspiration in intubated patients. *Ann Intern Med* 1999; 130(12): 991–994
16. Bergmans DCJJ, Bonten MJM, Gaillard CA, et al: Prevention of ventilator-associated pneumonia by oral decontamination: A prospective, randomized, double-blind, placebo-controlled study. *Am J Respir Crit Care Med* 2001; 164(3):382–388
17. Valles J, Artigas A, Rello J, et al: Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia [see comments]. *Ann Intern Med* 1995; 122(3):179–186
18. Rello J, Sonora R, Jubert P, et al: Pneumonia in intubated patients: role of respiratory airway care. *Am J Respir Crit Care Med* 1996; 154(1):111–115
19. Kollef MH, Skubas NJ, Sundt TM: A randomized clinical trial of continuous aspiration of subglottic secretions in cardiac surgery patients. *Chest* 1999; 116(5):1339–1346
20. Young PJ, Blunt MC: Improving the shape and compliance characteristics of a high-volume, low-pressure cuff improves tracheal seal. *Br J Anaesth* 1999; 83(6):887–889
21. Smulders K, Van der Hoeven H, Weers-Pothoff I, et al: A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation. *Chest* 2002; 121(3):858–862