



Continuous Aspiration of Subglottic Secretions in the Prevention of Ventilator-Associated Pneumonia in the Postoperative Period of Major Heart Surgery*

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Objective: Aspiration of endotracheal secretions is a major step in the prevention of ventilator-associated pneumonia (VAP). We compared conventional and continuous aspiration of subglottic secretions (CASS) procedures in ventilated patients after major heart surgery (MHS).

Materials and methods: Randomized comparison during a 2-year period.

Results: A total of 714 patients were randomized (24 patients were excluded from the study; 359 CASS patients; 331 control subjects). The results for CASS patients and control subjects (per protocol and intention-to-treat analysis) were as follows: VAP incidence, 3.6% vs 5.3% ($p = 0.2$) and 3.8% vs 5.1%, respectively; incidence density, 17.9 vs 27.6 episodes per 1,000 days of mechanical ventilation (MV) [$p = 0.18$] and 18.9 vs 28.7 episodes per 1,000 days of MV, respectively; hospital antibiotic use in daily defined doses (DDDs), 1,213 vs 1,932 ($p < 0.001$) and 1,392 vs 1,932, respectively ($p < 0.001$). In patients who had received mechanical ventilation for > 48 h, the comparisons of CASS patients and control subjects were as follows: VAP incidence, 26.7% vs 47.5% ($p = 0.04$), respectively; incidence density, 31.5 vs 51.6 episodes per 1,000 days of MV, respectively ($p = 0.03$); median length of ICU stay, 7 vs 16.5 days ($p = 0.01$), respectively; hospital antibiotic use, 1,206 vs 1,877 DDD ($p < 0.001$), respectively; *Clostridium difficile*-associated diarrhea, 6.7% vs 12.5% ($p = 0.3$), respectively; and overall mortality rate, 44.4% vs 52.5% ($p = 0.3$), respectively. Reintubation increased the risk of VAP (relative risk [RR], 6.07; 95% confidence interval [CI], 2.20 to 16.60; $p < 0.001$), while CASS was the only significant protective factor (RR, 0.40; 95% CI, 0.16 to 0.99; $p = 0.04$). No complications related to CASS were observed. The cost of the CASS tube was 9 vs 1.5 € for the conventional tube.

Conclusions: CASS is a safe procedure that reduces the use of antimicrobial agents in the overall population and the incidence of VAP in patients who are at risk. CASS use should be encouraged, at least in patients undergoing MHS. (CHEST 2008; 134:938–946)

Key words: intensive care; major heart surgery; prevention; subglottic aspiration; ventilator-associated pneumonia

Abbreviations: APACHE = acute physiology and chronic health evaluation; CASS = continuous aspiration of subglottic secretions; CDAD = *Clostridium difficile*-associated diarrhea; CI = confidence interval; DDD = daily defined dose; ETA = endotracheal aspiration; ETT = endotracheal tube; EuroSCORE = European System for Cardiac Operative Risk Evaluation; IQR = interquartile range; MHS = major heart surgery; MV = mechanical ventilation; RR = relative risk; VAP = ventilator-associated pneumonia

Ventilator-associated pneumonia (VAP) is the most frequent infection occurring in patients who are admitted to the ICU.^{1–3} The accumulation of respiratory secretions in the subglottic space is a well-proven cause of VAP. Therefore, prevention should include the aspiration of secretions from the subglottic space, and techniques to

avoid leakage between the tube and the tracheal wall.^{4–12} A conventional endotracheal tube (ETT) permits only intermittent aspiration of secretions through the central lumen, distal to the tracheal cuff, while new tubes with an independent dorsal lumen permit the continuous aspiration of secretions in the subglottic space.^{4,9,13–15}

Only five randomized prospective studies^{9,11,12,14,16} have assessed the effect of the continuous aspiration of subglottic secretions (CASS) in comparison with conventional aspiration. The results are inconclusive

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because the number of patients per study was limited, the population was not homogeneous, and the final conclusions regarding efficacy in the prevention of VAP were contradictory. Firm agreement in this area has not been reached, and the procedure is not yet common practice among ventilated patients despite appearing as a level I recommendation in the Centers for Disease Control and Prevention guidelines.^{2,17}

The incidence of VAP in patients undergoing major heart surgery (MHS) is particularly high, ranging from 3.2 to 8.3%.^{18–21} The only study to analyze this type of patient, by Kollef et al,¹⁴ found no significant reduction in the incidence of VAP with the implementation of CASS. Our study was a prospective, randomized, comparative study of CASS vs conventional intubation and aspiration in a large population of patients who were undergoing MHS.

MATERIALS AND METHODS

Hospital Setting and Patients

Our institution is a general reference hospital with 1,750 beds and 64,000 admissions per year. The study population included patients who underwent MHS from May 2004 to July 2006. Patients who gave their informed consent were randomly assigned to receive either conventional respiratory care or CASS. Informed consent was obtained by the anesthesiologist in charge in all cases. Our Ethics Committee approved the study. An infectious diseases physician who was aware of the treatment assignments followed up all patients to check for the presence of postoperative infections.

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Postoperative Management of ETTs and Respiratory Care

Randomization was performed by drawing a card from a sealed envelope. Thus, patients were intubated during the induction of anesthesia either with a conventional ETT (Hi-Contour; Mallinckrodt Medical; Athlone, Ireland) or with an ETT with CASS (HI-Lo Evac; Mallinckrodt; Hazelwood, MO). If reintubation was required at any time during the postoperative period, patients received the same type of tube to which they were initially randomized. Patients in whom tracheostomy was indicated at any time were also distributed according to initial randomization between conventional cannulas (Shiley Low Pressure Cuffed Tracheostomy Tube; Tyco Health Care, Mallinckrodt Medical) or cannulas allowing subglottic aspiration (Tracheostost Evac; Mallinckrodt Medical). The size of each ETT was selected by the attending anesthesiologist.

On admission to the ICU, both groups received common postoperative care. Tracheal aspiration through the lumen of the ETT was performed as requested by the nurse. Cuff pressure was maintained at between 20 and 30 mm Hg, and was controlled and registered during each shift.

On admission to the ICU, patients who were randomized to the CASS group were connected to a continuous system of subglottic aspiration with a negative pressure of between 100 and 150 mm Hg. Once per shift, and after checking the cuff pressure, 10 mL of distilled sterile water was instilled through the subglottic lumen in order to keep it patent. If obstruction was present, permeability was reestablished with an air bolus through the subglottic lumen. All patients received stress ulcer prophylaxis with pantoprazole.

Data Recorded

Clinical data were recorded according to a preestablished protocol, and no systematic surveillance respiratory tract cultures were performed. The presurgical information that was obtained included epidemiologic data, underlying diseases,²² and standard scores (*ie*, American Society of Anesthesiologists score,²³ European System for Cardiac Operative Risk Evaluation [EuroSCORE],²⁴ Charlson comorbidity index,²⁵ and acute physiology and chronic health evaluation [APACHE] II score²⁶ on admission to the ICU). Surgical information included the type of surgery, indication, duration, time spent on cardiopulmonary bypass, aortic cross-clamp time, transfusion needs, reinterventions, antimicrobial prophylaxis, and the need for inotropic support. Antimicrobial prophylaxis for surgery consisted of 2 g of cefazolin that was administered before surgery and every 8 h thereafter for a total of three doses (patients who were allergic to cefazolin received 1 g of vancomycin before surgery and every 12 h thereafter, up to two doses).

Postsurgical outcome events included ICU and hospital length of stay, the number of hours patients received mechanical ventilation (MV), and the need for tracheotomy. Infections other than VAP were recorded. In patients with sepsis, the Bone score for severity of sepsis²⁷ was also recorded. The patients who were enrolled into the study were prospectively followed up for the occurrence of VAP until they were successfully weaned from MV, discharged from the hospital, or died. Outcome variables also included antimicrobial administration, *Clostridium difficile*-associated diarrhea (CDAD), ICU length of stay, ICU mortality, hospital length of stay, and mortality on ICU discharge.

Demonstration of VAP

VAP was diagnosed in patients who received MV for ≥ 48 h when the presence of new and/or progressive pulmonary infiltrates was detected on a chest radiograph plus two or more of the

following criteria: fever (temperature $\geq 38.5^{\circ}\text{C}$) or hypothermia (temperature $< 36^{\circ}\text{C}$); leukocytosis ($\geq 12 \times 10^9$ cells/L); purulent tracheobronchial secretions; or a reduction in the $\text{PaO}_2/\text{fraction of inspired oxygen ratio} \geq 15\%$ according to Centers for Disease Control and Prevention definitions.²⁵ Patients with a clinical pulmonary infection score²⁹ > 6 were also considered to have pneumonia. The isolation of one or more pathogenic microorganisms in significant bacterial counts was required to confirm the diagnosis of VAP. We considered as nonpathogenic the isolation (at any concentration) of the following microorganisms, unless proven otherwise: viridans-group streptococci; coagulase-negative Staphylococcus; Neisseria spp; Corynebacterium spp; and Candida spp.

Sampling of the lower respiratory tract in cases of suspected VAP was performed either by endotracheal aspiration (ETA) and/or telescopic brush sampling of respiratory secretions. For ETA, we obtained undiluted tracheal secretions. When aspiration was unproductive, we irrigated with 5 mL of Ringer lactate solution. Secretions obtained by ETA were trapped in a Lukens specimen container (Sherwood Medical; Tullamore, Ireland). Samples were considered to be positive for VAP when bacterial counts $\geq 10^4$ cfu/mL for each microorganism were obtained by ETA, and $\geq 10^3$ cfu/mL obtained by telescopic brushing. All microorganisms were identified using standard methods, and antimicrobial susceptibility was determined according to Clinical and Laboratory Standards Institute recommendations.

Outcome Measures

The primary outcome measure of the study was to evaluate the incidence and incidence density of VAP in both study groups. Secondary outcome measures included days in the ICU, days of hospital stay, episodes of nonpneumonic nosocomial infections, and antimicrobial use determined as daily defined doses (DDDs). DDDs are the internationally accepted units of antimicrobial use, which accept a DDD of an antibiotic as being the average maintenance dose of that drug that is normally provided to an adult. Use of the DDD allows uniformity in the comparison of the consumption of antimicrobial agents between different patients and institutions.

Statistical Analysis

Relationships between baseline variables were evaluated for the randomized groups. Basal comparisons between groups were established by clinical relevance according to the Consolidated Standards of Reporting Trials (or CONSORT) recommendations. The qualitative variables appear with their frequency distribution. The quantitative variables are summarized as the mean and SD, and as the median and interquartile range (IQR) if their distribution was skewed. Continuous variables were compared using the *t* test for normally distributed variables and the Mann-Whitney test for nonnormally distributed variables. The χ^2 test or Fisher exact test was used to compare categorical variables. All statistical tests were two tailed. The level of significance was set at $p < 0.05$ for all the tests. The statistical analysis was performed using a statistical software package (SPSS, version 12.0; SPSS Inc; Chicago, IL; and Stata, version 9.0; StataCorp, LP; College Station, TX).

RESULTS

Study Population

Overall, 1,101 patients underwent MHS during the study period. Of them, 387 patients were ex-

cluded either because they did not give their consent (268 patients) or the consent could not be requested due to the emergent condition of the surgery (119 patients). Accordingly, 714 patients undergoing MHS were randomized immediately before undergoing anesthesia (24 patients were excluded from the study; CASS group, 359 patients; control group, 331 subjects). The exclusions were due to death during surgery or immediately after in 19 cases, and because the protocol was violated (*ie*, the wrong tube was used during reintubation) in 5 cases. Of the 24 patients who were excluded from the evaluation, 14 had been randomized to CASS group and 10 to the control group.

Comparison of the Characteristics of Both Populations

Preoperative and surgical characteristics of the patients in both groups are compared in Table 1. The mean (\pm SD) EuroSCOREs of both groups were comparable (control group, 5.7 ± 2.9 ; CASS group, 5.6 ± 2.9 ; $p = 0.45$).

Of the 690 patients, 85 patients (12.31%) remained under MV ≥ 48 h after undergoing surgery (CASS group, 45 patients [52.9%]; control subjects, 40 [47.1%]) [Table 2]. The mean EuroSCOREs in both groups of patients who were ventilated for ≥ 48 h were not significantly different (control group, 7.7 ± 3.6 ; CASS group, 7.5 ± 3.1 ; $p = 0.79$).

Table 3 compares the risk factors for the development of VAP in both groups. There were no significant differences in predisposing conditions between the groups.

Outcome Data of the Overall Population

The postoperative data for both groups in the overall population are shown in Table 4. The cumulative incidence of VAP during the study period was 4.5% (31 of 690 patients). The incidence density of VAP was 22.86 episodes per 1,000 days of MV. VAP occurred after a median of 8 days of MV (IQR, 6 to 12 days). The Kaplan-Meier plot showing the time for the development of VAP in both groups is shown in Figure 1. The 31 episodes of VAP had a positive quantitative ETA. In six of these cases, a telescopic brush sample was also obtained at the time of the diagnosis of the VAP; and the result was concordant with ETA samples in five of them (one negative telescopic brush sample finding). The microorganisms causing VAP in both groups are summarized in Table 5.

When all randomized patients with VAP were compared (*ie*, CASS patients and control subjects), the results were as follows: number of cases, 12 vs 19 cases, respectively; incidence, 3.6% vs 5.3% (relative risk [RR], 0.67; 95% confidence interval [CI], 0.32 to 1.40 [$p = 0.2$]), respectively; and incidence density, 17.9 vs 27.6 episodes per 1,000 days of MV

Table 1—Baseline Characteristics and Surgical Variables of Study Patients in the Overall Population (Per Protocol Analysis)*

Characteristics	CASS Group (n = 331)	Control Group (n = 359)	p Value
Preoperative			
Mean age, yr	65.7 ± 11.9	65.0 ± 12.0	0.48
Sex, No.			0.27
Male	191	198	
Female	140	161	
Underlying conditions			
Myocardial infarction	55 (16.6)	58 (16.2)	0.47
CNS	50 (15.1)	57 (15.9)	0.43
CNS disorder	31 (9.4)	33 (9.2)	0.52
COPD	29 (8.8)	47 (13.1)	0.045
Peripheral vascular disease	32 (9.7)	43 (12.0)	0.19
Ulcer disease	26 (7.9)	35 (9.7)	0.23
Diabetes mellitus	76 (23)	77 (21.4)	0.35
Renal disease	23 (6.9)	20 (5.6)	0.27
Malignant neoplasm	25 (7.6)	27 (7.5)	0.55
Liver disease	7 (2.1)	5 (1.4)	0.33
Severe pulmonary hypertension	23 (6.9)	25 (7.0)	0.55
Severe ventricular dysfunction	18 (5.4)	18 (5.0)	0.47
Previous cardiac surgery	39 (11.8)	34 (9.5)	0.19
NYHA functional class IV	11 (3.3)	12 (3.3)	0.58
EuroSCORE	5.6 ± 2.9	5.7 ± 2.9	0.45
Surgical			
Emergent indication	11 (3.3)	6 (1.7)	0.12
Type of surgery			
Valve replacement	182 (55.0)	227 (63.2)	0.02
CABG	81 (24.5)	74 (20.6)	0.13
Mixed (valve and CABG)	34 (10.3)	28 (7.8)	0.15
Heart transplantation	1 (0.3)	2 (0.6)	0.53
Aortic surgery	16 (4.8)	14 (3.9)	0.34
Other	17 (5.1)	14 (3.9)	0.27
CPBT, min	113.0 ± 49.2	112.5 ± 47.0	0.90
Aortic cross-clamp time, min	76.0 ± 38.9	75.1 ± 33.5	0.77
Surgery time, min	232.2 ± 87.9	230.0 ± 69.3	0.72

*Values are given as the mean ± SD or No. (%), unless otherwise indicated. NYHA = New York Heart Association; CABG = coronary artery bypass grafting; CPBT = cardiopulmonary bypass time.

[p = 0.18], respectively). VAP occurred after a median duration of 8.5 and 8 days of MV, respectively.

The results of the intention-to-treat analysis, including the overall 714 cases, were as follows: VAP patients, 13 (3.8%) vs 19 (5.1%), respectively; incidence density, 18.9 vs 28.7 episodes per 1,000 days of MV, respectively. Hospital antibiotic use was 1,392 vs 1,932 DDDs (p < 0.001), respectively.

We were not able to demonstrate significant differences between the groups regarding the duration of MV, the length of ICU or hospital stay, the number of episodes of CDAD, or mortality (Table 4). Overall, 19 patients died in the operating room (control group, 9 subjects; CASS group, 10 patients) and 5 patients died in the immediate postoperative period (control group, 1 subject; CASS group, 4 patients) because of cardiogenic shock. The protocol was violated (*ie*, the wrong tube was used during reintubation) in five cases in CASS group. The mortality rate in both groups including all patients

(intention-to-treat analysis) was 34 of 345 patients (9.9%) in the CASS group vs 35 of 369 subjects (9.5%; p = 0.86) in the control group. There was, however, a significant difference in the DDDs of antibiotics consumed, with a much lower number in patients with CASS (CASS group, 1,213.5 DDDs; conventional therapy group, 1,932.5 DDDs; p < 0.001).

Only nine patients required tracheostomy (CASS group, three patients; control group, six subjects). Tracheostomy was indicated between the second and third week of the ICU stay. Pneumonia developed in only three people after a tracheostomy (CASS group, one patient; control group, two subjects).

Outcome Data of the Risk Population

The risk population (*ie*, those receiving MV for > 48 h) showed a significant difference in VAP incidence in favor of CASS patients (26.7% vs 47.5%, respectively; RR, 0.40; 95% CI, 0.16 to 0.99; p = 0.04) as well as in

Table 2—Baseline Characteristics and Surgical Variables of Patients Receiving MV for > 48 h*

Characteristics	CASS Group (n = 45)	Control Group (n = 40)	p Value
Preoperative			
Mean age, yr	71 ± 11.2	67.5 ± 12.8	0.18
Sex, No.			0.28
Male	23	17	
Female	22	23	
Underlying conditions			
Myocardial infarction	13 (28.9)	7 (17.5)	0.16
Congestive heart failure	13 (28.9)	12 (30.0)	0.55
CNS disorder	8 (17.8)	4 (10.0)	0.23
COPD	6 (13.3)	7 (17.5)	0.40
Peripheral vascular disease	3 (6.7)	3 (7.5)	0.60
Ulcer disease	2 (4.4)	5 (12.5)	0.17
Diabetes mellitus	12 (26.7)	9 (22.5)	0.42
Renal disease	7 (15.6)	3 (7.5)	0.21
Malignant neoplasm	4 (8.9)	4 (10.0)	0.57
Liver disease	1 (2.2)	2 (5.0)	0.45
Severe pulmonary hypertension	6 (13.3)	6 (15.0)	0.53
Severe ventricular dysfunction	4 (8.9)	5 (12.5)	0.42
Previous cardiac surgery	6 (13.3)	4 (10.0)	0.44
NYHA functional class IV	1 (2.2)	3 (7.5)	0.26
EuroSCORE	7.5 ± 3.1	7.7 ± 3.6	0.79
APACHE II score	10.2 ± 2.4	10.4 ± 3.3	0.78
Surgical			
Emergent indication	6 (13.3)	3 (7.5)	0.30
Type of surgery			
Valve replacement	20 (44.4)	27 (67.5)	0.03
CABG	10 (22.2)	3 (7.5)	0.05
Mixed (valve and CABG)	11 (24.4)	8 (20.0)	0.41
Heart transplantation	1 (2.2)	0 (0.0)	0.53
Aortic surgery	3 (6.7)	2 (5.0)	0.55
CPBT, min	131.1 ± 61.2	141.6 ± 65.9	0.45
Aortic cross-clamp time, min	85.9 ± 53.2	86.5 ± 39.6	0.95
Surgery time, min	289.3 ± 149.5	284.2 ± 108.7	0.85

*Values are given as the mean ± SD or No. (%), unless otherwise indicated. See Table 1 for abbreviations not used in the text.

incidence density of VAP (31.5 vs 51.6 episodes per 1,000 days of MV, respectively; $p = 0.03$). The length of ICU stay and MV were also shorter in patients with CASS, and there was a very significant reduction in antibiotic DDDs in the CASS group (1,206.5 vs 1,877.5

DDDs, respectively; $p = <0.001$). The mortality rates in the CASS group and the conventional therapy group were 44.4% and 52.5% ($p = 0.3$), respectively (Table 6).

The statistical analysis of risk factors associated with VAP in the risk population showed that reintu-

Table 3—Risk Factors for VAP During the Study Period of Patients Receiving MV for > 48 h*

Factors	CASS Group (n = 45)	Control Group (n = 40)	p Value
Semirecumbent body position, No.			
Never	0	1	
Sometimes (when possible)	45	44	
Control of cuff pressure	42 (93.4)	37 (92.5)	0.60
Prevention of gastric overdistension	18 (40.0)	18 (46.2)	0.35
Received aerosol therapy	8 (17.8)	9 (23.1)	0.37
Reintubation†	12 (26.7)	14 (35)	0.27
Fiberoptic bronchoscopy	1 (2.2)	2 (5.1)	0.44
Prior antibiotic therapy	2 (4.4)	4 (10.3)	0.27
Blood units transfused, No.	4.4 ± 3.8	4.2 ± 3.5	0.76
Need to move with ETT	20 (44.4)	22 (56.4)	0.19

*Values are given as No. (%) or mean ± SD, unless otherwise indicated.

†The median time between reintubation and VAP was 6 days (IQR, 4 to 9 days) in the control group and 7.5 days (IQR, 1.5 to 9.5 days) in the CASS group.

Table 4—Clinical Outcome in All Randomized Patients (Per Protocol Analysis)*

Variables	CASS Group (n = 331)	Control Subjects (n = 359)	p Value
VAP	12 (3.6)	19 (5.3)	0.2
Episodes of VAP/1,000 d of MV, No.	17.9	27.6	0.18
Duration of mechanical ventilation, d	1.0 (1.0–1.0)	1.0 (1.0–1.0)	0.4
Length of ICU stay, d	3 (2–5)	3 (2–5)	0.3
Length of hospital stay, d	8 (7–12)	9 (8–13)	0.9
Mortality	23 (6.9)	26 (7.2)	0.5
DDD	1,213.5 (1,145.7–1,283.2)	1,932.5 (1,846.8–2,020.1)	< 0.001
Episodes of CDAD	3 (0.9)	5 (1.4)	0.4

*Values are given as No. (%) or median (IQR), unless otherwise indicated.

bation significantly increased the risk of VAP (RR, 6.07; 95% CI, 2.20 to 16.60; $p < 0.001$), while CASS was the only significant protective factor (RR, 0.40; 95% CI, 0.16 to 0.99; $p = 0.04$). A trend toward a reduction in the number of episodes of CDAD was observed in the CASS group.

No complications related to CASS were observed. Thanks to the maintenance of our tube protocol, none of the CASS patients experienced obstruction of the aspiration lumen. The cost of the CASS tube in our institution was 9 € compared to 1.5 € for the conventional tube. The extra cost of acquiring CASS tubes was estimated to be approximately 2,800 €. The savings in the acquisition of antibiotics in the CASS group was calculated to be approximately 21,600 €.

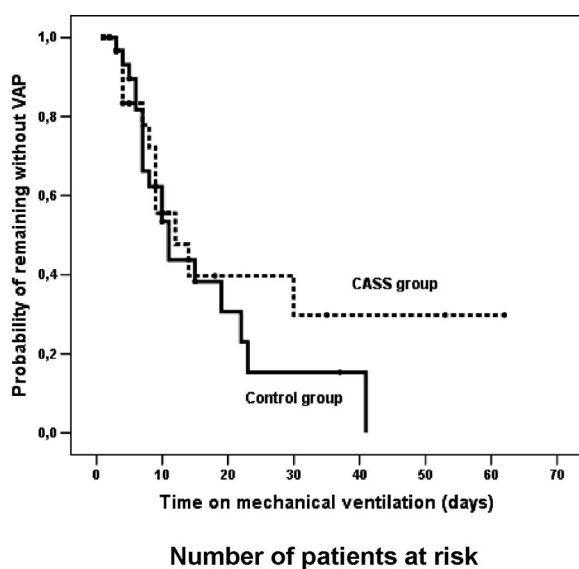


FIGURE 1. Kaplan-Meier plot showing the proportion of patients remaining without VAP, using an ETT with CASS vs a conventional ETT.

DISCUSSION

We found that using CASS in patients undergoing MHS is a safe procedure that significantly reduces the antibiotic burden. In the population that was at high risk (*ie*, those persons receiving MV for > 48h), CASS reduced the incidence and incidence density of VAP. It also reduced ICU stay, duration of MV, and antibiotic consumption.

VAP is a very severe disease that is associated with a high degree of mortality, and few of the variables influencing mortality can be modified.^{30–36} The incidence and severity of VAP are particularly high in patients undergoing MHS.^{2–4,21,36–38} Data for that population are scarce and are usually provided as the incidence but not as the incidence density. According to the National Nosocomial Infections Surveillance report of 2004,³⁹ the median incidence density of VAP was 6.3 episodes per 1,000 days of MV (IQR, 2.9 to 12.6 episodes per 1,000 days of MV) in cardiothoracic ICUs vs 3.7 episodes per 1,000 days of

Table 5—Microorganisms Causing VAP in Patients With and Without CASS*

Microorganisms	CASS Group	Control Subjects
Gram-positive microorganisms	2	4
MSSA	0	1
MRSA	2	2
<i>Streptococcus pneumoniae</i>	0	1
Total GNB	12	22
<i>Pseudomonas aeruginosa</i>	6	6
<i>Stenotrophomonas maltophilia</i>	0	1
<i>Escherichia coli</i>	0	3
<i>Klebsiella</i> spp	1	0
<i>Enterobacter</i> spp	3	2
<i>Serratia</i> spp	0	2
<i>H influenzae</i>	1	6
<i>Proteus mirabilis</i>	1	2
Polymicrobial	2/12	8/19

*GNB = Gram-negative bacilli; MSSA = methicillin-sensitive *Staphylococcus aureus*; MRSA = methicillin-resistant *S aureus*.

Table 6—Clinical Outcome in Patients Receiving MV for > 48 h*

Variables	CASS Group (n = 45)	Control Subjects (n = 40)	p Value
VAP	12 (26.7)	19 (47.5)	0.04
Episodes of VAP/1,000 d of MV, No.	31.5	51.6	0.03
Duration of mechanical ventilation, d	3 (2–9)	7 (3–11)	0.02
Length of ICU stay, d	7 (3–27)	16.5 (6.5–39.5)	0.01
Length of hospital stay, d	16 (7.5–47)	28 (11–62)	0.12
Mortality	20 (44.4)	21 (52.5)	0.3
DDDs	1,206.5 (1,138.9–1,276.0)	1,877.5 (1,793.0–1,963.9)	< 0.001
Episodes of CDAD	3 (6.7)	5 (12.5)	0.3

*Values are given as No. (%) or median (IQR), unless otherwise indicated.

MV (IQR, 2.1 to 6.2 episodes per 1,000 days of MV) in medical ICUs. The National Nosocomial Infections Surveillance data, however, refer to the situation in mixed cardiothoracic ICUs and not to the specific rates in patients following MHS. In the United States, Kollef et al¹⁴ reported an incidence density of 39.7 episodes per 1,000 days of MV in MHS patients. VAP was the most common infection after MHS in a prospective Cooperative European Study⁴⁰ carried out in 25 MHS ICUs in eight European countries. The global incidence was 3%, and the incidence density was 18.7 episodes per 1,000 intubation days.⁴⁰

Pathogenesis takes place mainly by the aspiration of secretions, with bacteria colonizing the upper respiratory tract passing into the lower respiratory tract via the leaks between the tracheal wall and the cuff of the ETT.^{5,8,41} Conventional ETTs do not permit the aspiration of secretions collected in the subglottic space proximal to the cuff.^{2,3,42–46} The development of ETTs with a lumen that permits the aspiration of subglottic secretions and the maintenance of monitored pressure of the tracheal cuff to ensure adequate sealing of the lower airway is an unquestionable advance.^{4,9,13–15} Nevertheless, although recommended by most recent guidelines,^{47,48} CASS it is not used by many ICUs.^{49,50} These inconsistencies may be due to the conflicting data from the five prospective studies⁵¹ that, to date, have investigated the value of CASS.

In a metaanalysis,⁵¹ only 5 of 110 articles selected were randomized trials and met the inclusion criteria. These five trials included a total of 896 patients.^{9,11,12,14,16}

Mahul et al⁹ published a study of 145 medical-surgical ICU patients who were expected to require > 72 h of MV. The drainage of subglottic secretions was associated with a lower incidence of VAP or a delay in the onset of VAP.

Vallés et al¹² performed a randomized, controlled, blinded study in 153 patients who had been admitted to a mixed medical-surgical ICU. They showed a reduction in VAP incidence density from 39.6 epi-

sodes per 1,000 days of MV in the control subjects to 19.9 episodes per 1,000 days of MV in CASS patients (RR, 1.98; 95% CI, 1.03 to 3.82; $p < .03$). The reduction was significant only in patients infected with Gram-positive organisms and *Haemophilus influenzae*. Episodes of VAP occurred later in patients receiving CASS, and the authors were not able to demonstrate significant differences in final outcome.

Smulders et al¹¹ studied 150 patients in a general ICU and found 3 patients (4%) with VAP in the CASS group vs 12 patients (16%) in the control group (RR, 0.22; 95% CI, 0.06 to 0.81; $p = 0.014$), with no significant differences in other outcome measures. The study by Bo et al¹⁶ involved only 68 surgical ICU patients expected to require > 72 h of MV and found reductions only in patients with early VAP caused by Gram-positive cocci or *H influenzae*.

Only the study by Kollef et al¹⁴ was performed in a MHS ICU and involved 343 patients. The incidence of VAP was 5.0% (8 cases) in patients receiving CASS and 8.2% (15 subjects) in the control group (RR, 0.61%; 95% CI, 0.27 to 1.40; $p = 0.238$). Episodes of VAP occurred statistically later among patients receiving CASS, but no significant differences for hospital mortality, duration of MV, or hospital stay were found between the two groups.

Not included yet in the metaanalysis was the recent article by Lorente et al,⁵² which also demonstrated the value of using an ETT with a polyurethane cuff and intermittent secretion drainage in the prevention of early-onset and late-onset VAP. This study included 280 medical-surgical ICU patients who were expected to require MV for > 24 h.

Our data represent the largest prospective and randomized study reported to date in a uniform type of patient who was randomized to one group or the other at the time of anesthesia induction. The largest proportion of that population required an ICU stay < 48 h and had very low rates of infection. In the overall population, we showed that fewer antimicrobial agents were used in patients who were randomized to receive CASS, which means, at the very least, a considerable reduction in hospital cost, clearly

outweighing the excess costs of the CASS tube. Our study showed a reduction in the episodes of *H influenzae* VAP in the CASS group. This is in agreement with the findings of Vallés et al,¹² who suggested that this procedure would be more efficacious in reducing the number of cases of pneumonia caused by less pathogenic microorganisms that require a high inoculum.

In patients undergoing MHS, the population at high risk of pneumonia and other infections is composed of those patients remaining in the ICU for > 48 h under MV. They represent 12.5% of our MHS population and, in that subpopulation, the incidence of postoperative pneumonia was 52%.⁵³ When the results of our study were evaluated in that specific subgroup of patients, CASS was able to reduce the incidence of VAP, the incidence density of VAP, and the length of ICU stay. We were not able to demonstrate a reduction in the length of hospital stay or mortality with CASS, and this may be due to the limited sample size.

One limitation of our article is the imbalance in the randomization of the patients regarding the indication for surgery (*ie*, there were more patients who had undergone valve replacement in the control group and more patients who had undergone coronary artery bypass grafting in the CASS group). However, the EUROSCORE, a well-recognized prognostic factor that includes the type of surgery and other important factors, was equivalent in both groups of patients.

We found that CASS was a safe procedure, that the price of the ETT was by far compensated by the reduction in the use of antimicrobial agents, and, in our opinion, that use of CASS should be part of the pack of measures used to decrease the incidence and consequences of VAP, at least in populations of patients who are undergoing MHS.

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