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Incidence and risk factors for ventilator-associated pneumonia after major heart surgery

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Abstract *Purpose:* Major heart surgery (MHS) patients are a particularly high-risk population for nosocomial infections. Our objective was to identify risk factors for ventilator-associated pneumonia (VAP) in patients undergoing MHS. *Methods:* Prospective study including 1,844 patients operated from 2003 to 2006. *Results:* Overall 106 patients (140 episodes) developed one or more episodes of VAP (5.7%, 22.2 episodes per 1,000 days of mechanical ventilation). VAP incidence was 45.9% in those patients requiring more than 48 h of MV. Enterobacteriaceae (32.8), *Pseudomonas aeruginosa* (28.6%) and *Staphylococcus aureus* (27.1%, of which 65.8% were methicillin resistant) were the principal microorganisms causing VAP. The independent risk factors for VAP were: age >70, perioperative transfusions, days of mechanical ventilation, reintubation, previous cardiac surgery, emergent surgery and intraoperative inotropic support. Median length of stay in the ICU for patients who developed VAP or not was, respectively, 25.5 versus 3 days ($P < 0.001$), and mortality was, respectively, 45.7 versus 2.8% in both populations ($P < 0.001$). We developed a predictive preoperative score with a sensitivity of 93% and a specificity of 40%. *Conclusions:* VAP is common in patients undergoing MHS that require more than 48 h of MV. In that "high-risk" population, innovative preventive measures should be developed and applied.

Keywords Ventilator-associated pneumonia · Heart surgery · Nosocomial infection · Nosocomial pneumonia · Risk factors for ICU nosocomial infection

Introduction

Ventilator-associated pneumonia (VAP) is the most frequent intensive care unit (ICU) acquired infection among patients receiving mechanical ventilation (MV) and is associated with prolonged hospitalization [1–3], increased health care costs [4], and a 15–45% attributable mortality [5, 6].

Patients undergoing major heart surgery (MHS) are a particularly high-risk population for nosocomial infections during the postoperative period with a high incidence and related mortality [7–11]. However, information regarding the risk factors and outcome of VAP in this setting is scarcely available [12] and needs to be permanently updated.

We carried out a prospective study of VAP in patients undergoing MHS in our institution during a 4-year period in order to assess the differential characteristics of patients who develop VAP and to identify risk factors

amenable to intervention. Some of the results of this study were presented as an abstract at the 46th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in San Francisco, CA.

Materials and methods

Study design

All patients who were admitted to the heart surgery ICU after MHS at our institution [procedures that require extracorporeal circulation (ECC) or surgical revascularizations without ECC] between January 2003 and December 2006 and who survived for at least 48 h were included in the study. All patients were prospectively followed by an infectious diseases (ID) physician who recorded clinical data on a pre-established form and collaborated in the management of infections.

We analyzed the incidence of VAP, its etiology, risk factors, and impact on clinical outcome. Patients were followed up until death or ICU discharge. Informed consent was not required as confidentiality was guaranteed, and no interventions were performed.

Setting

Our hospital is a 1,750-bed tertiary referral general teaching institution, attending a population of approximately 750,000 inhabitants, with a very active program of MHS that includes heart transplantation.

The heart surgery ICU is a separate unit of 16 beds exclusively for patients who undergo MHS. During the study period, there were no major outbreaks of nosocomial respiratory pathogens in this unit. Our practices for respiratory care include: patient placement in an upright position and perioperative rinsing with chlorexidine gluconate. Prompt extubation was intended, and 'breath spontaneously trial' (SBT) was performed daily. Patients intubated for >2 weaks underwent tracheostomy [13]. Sedative protocol was: remifentanil plus propofol and switching to morphine if the patient required sedation over 7 days. Nurses adjusted the dosage and rate of infusion to achieve a Ramsay score of 3 or 4 on the sedation scale. Daily interruption of the sedative infusion was performed as described by Kress et al. [14].

Clinical protocol

Clinical data were recorded according to a pre-established protocol, and no systematic surveillance of respiratory tract cultures were performed because they were not useful to predict pneumonia in a previous study in our ICU [12].

Pre-surgical, surgical, and post-surgical characteristics were recorded according to a pre-established protocol. The surgical risk was evaluated by the European system for cardiac operative risk evaluation (EuroSCORE) [15]. Antimicrobial prophylaxis for surgery consisted of 2 g of cefazolin given before surgery and every 8 h thereafter, for a total of three doses (allergic patients received vancomycin).

Definitions

Ventilator-associated pneumonia was diagnosed upon the presence of new and/or progressive pulmonary infiltrates on chest radiograph in a patient ventilated more than 48 h plus two or more of the following criteria: fever $\geq$38.5°C or hypothermia <36°C, leukocytosis $\geq 12 \times 10^9$/l, purulent tracheobronchial secretions or a reduction of PaO_2/FiO_2 $\geq$15% in the last 48 h according to the Center for Disease Control (CDC) definitions [16]. We also included as pneumonia those with a clinical pulmonary infection score (CPIS) [17] $\geq$6. Early-onset VAP was defined as occurring within the first 4 days of hospitalization and late-onset VAP as occurring in day 5 or later on [18]. The isolation of one or more microorganisms in significant bacterial count was required to confirm the diagnosis. The clinical, radiological, and microbiologic data for the diagnosis of VAP were systematically reviewed by an independent investigator.

We considered the isolation (at any concentration) of the following microorganisms as non-pathogenic: Viridans group streptococci, coagulase-negative *Staphylococcus*, *Neisseria* spp., *Corynebacterium* spp., and *Candida* spp., unless proven otherwise.

Microbiological protocol

Sampling of the lower respiratory tract in cases suspected of VAP was performed by endotracheal aspiration (ETA) of respiratory secretions. For ETA, we obtained undiluted tracheal secretions. When aspiration was unproductive we irrigated with 2 ml of ringer lactate. Positive samples were considered as those with bacterial counts $\geq 10^5$ cfu/ml of each significant microorganism. Occasionally, bronchoalveolar lavage samples or protected specimen brushes were obtained. In these cases, the cut-offs for positive samples were $\geq 10^4$ and $\geq 10^3$ cfu/ml, respectively.

All microorganisms were identified using standard methods, and antimicrobial susceptibility was determined according to clinical laboratory standard recommendations (CLSI) [19].

Statistical analysis

Data were entered and categorized using Microsoft ACCESS®. For univariate analysis, continuous variables were assessed using the Mann–Whitney U test, and qualitative variables were studied with Fisher's exact test or χ^2 test. All statistical tests were two-tailed.

A multivariable logistic regression model was used to assess the independent value of predictor variables using SPSS software (SPSS Inc., Chicago, IL). For this analysis, quantitative variables were categorized establishing optimum cutoff thresholds selected from their ROC curves. A forward stepwise approach was followed, including as candidate variables all those that showed univariate significance better than $P < 0.1$. Results are presented as adjusted risk ratios with 95% confidence intervals. The models were validated by means of a jackknifing technique [20]. Variables that yielded the same results in all the runs were qualified as "stable," while those variables that did not appear in at least 50% of the runs were discarded. No significant first-order interactions were found in the models.

From the final models we made an attempt to define predictive scores aiming to identify a subgroup of patients with higher risk of developing VAP. To this end we defined the scores as the addition of the significant variables weighted by their respective regression coefficients (β). Two scores were studied: the day 0 score, including only variables available before surgery, and the day 3 score, selecting only patients who remained intubated >48 h and incorporating surgical and perisurgical data.

The aim of choosing these days was: (1) to create an early score to help the anesthetist in the decision of using or not a subglottic continuous aspiration tube before surgery (day 0 score) and (2) identify patients with a higher risk of VAP within the subset who remain intubated more than 48 h (day 3 score). In this latter score, only patients who remained ventilated on day 3 were included. Our objective was to study if a risk-stratified preventive approach was feasible or if universal prevention is the most advisable option. Finally, to assess the clinical relevance of the scores (beyond its statistical significance) we conducted a ROC analysis to determine the sensitivity/specificity achieved.

Results

During the study period a total of 1,934 consecutive patients underwent MHS. Overall, 90 patients were excluded due to intraoperative or early postoperative (48 h) death, leaving a study population of 1,844 patients. Preoperative and surgical characteristics of the patients are shown in Table 1.

Table 1 Preoperative and surgical characteristics of patients who underwent major heart surgery

Characteristics	Global
Preoperative	
No. of patients	1,844
Mean age in years (SD)	64.7 ± 12.5
Sex, male/female	1,058 (57.4)/786 (42.6)
Underlying conditions (%)	
Myocardial infarction (<90 days)	229 (12.4)
Congestive heart failure (Framingham criteria)	189 (10.2)
Central nervous system disorder	140 (7.6)
Chronic obstructive pulmonary disease(GOLD criteria)	205 (11.1)
Peripheral vascular disease	134 (7.3)
Gastrointestinal ulcer disease	98 (5.3)
Diabetes mellitus	437 (23.7)
Renal disease (creatinine ≥2 mg/dl)	133 (7.2)
Malignant neoplasm	48 (2.6)
Severe pulmonary hypertension (mPAP ≥60 mmHg)	196 (10.6)
Severe ventricular dysfunction (EF ≤ 30%)	153 (8.3)
Previous cardiac surgery (%)	185 (10.0)
New York Heart Association functional class (%)	
I	403 (21.8)
II	883 (47.9)
III	435 (23.6)
IV	123 (6.7)
EuroSCORE (%)	
Low risk (0–2)	160 (8.7)
Moderate risk (3–6)	815 (44.2)
High risk (>6)	869 (47.1)
Surgical	
Indication (%)	
Elective	1,699 (92.1)
Emergent	145 (7.9)
Type of surgery (%)	
Valvular replacement	971 (52.7)
Coronary artery bypass grafting (CABG)	393 (21.3)
Mixed (valvular and CABG)	176 (9.5)
Aortic surgery	129 (7.0)
Heart transplantation	61 (3.3)
Other	114 (6.2)
Mean cardiopulmonary bypass time (min) mean ± SD	112.6 ± 43.6
Mean aortic cross-clamp time (min) mean ± SD	74.4 ± 32.2

EF Ejection fraction, *GOLD* global initiative for chronic obstructive lung disease, *mPAP* mean pulmonary artery pressure

Incidence and etiology of VAP

The cumulative incidence of VAP during the study period was 5.7% (106/1,844 patients). Of the 140 total episodes, 27 patients had more than 1 VAP episode. The incidence density of VAP in our population was 22.2 episodes per 1,000 days of mechanical ventilation. Mechanical ventilation >48 h was required by 231 patients (12.5%), and in this sub-group of patients VAP incidence was 45.9%.

Table 2 Organisms isolated in patients with pneumonia

Organisms	Total episodes $n = 140$ (%)
P. aeruginosa	40 (28.6)
S. aureus	38 (27.1)
MRSA	25 (17.8)
MSSA	13 (9.3)
H. influenzae	24 (17.1)
Enterobacter spp.	16 (11.4)
E. coli	13 (9.3)
Klebsiella spp.	7 (5.0)
Proteus spp.	7 (5.0)
S. maltophilia	5 (3.6)
Acinetobacter spp.	4 (2.8)
Serratia spp.	3 (2.0)
Moraxella spp.	2 (1.4)
Polymicrobial	19 (13.5)

MRSA Methicillin-resistant *S. aureus*, *MSSA* methicillin-susceptible *S. aureus*

Tracheostomy was performed in 57 patients (3%), usually after 2 weeks of ventilation. These patients had 43 episodes of VAP (75.4%), which in 63% of cases occurred before tracheostomy. Overall, VAP was diagnosed after a median of 9 days of MV (IQR 5.7–24.0). Considering the day of hospital admission before surgery, only 4.7% (5/106) of our VAP cases could be considered as early onset (within $\leq$4 days of hospital stay).

There were significant differences in the incidence of VAP according to the type of surgery: valve replacement 4.6% (45/971), coronary artery bypass graft (CABG) 5.3% (21/393), mixed surgeries 10.2% (18/176), aortic surgery 8.5% (11/129), heart transplantation 3.3% (2/61), and other 7.9% (9/114) ($P = 0.03$). Overall, 30 (1.6%) of the 1,844 patients presented sternal wound infections, 6 of which (20%) developed VAP.

Table 2 summarizes the microorganisms causing VAP in our study (140 episodes). Overall, 32.8% of VAP were caused by Enterobacteriaceae, 28.6% were caused by *Pseudomonas aeruginosa*, and 27.1% by *Staphylococcus aureus* (of them 65.8% were MRSA). VAP was polymicrobial in 13.5% of cases. All but 15 episodes had $\geq 10^6$ cfu in the culture. These 15 patients usually had 10^5 cfu.

Risk factors and predictive scores for VAP

Preoperative, operative and postoperative risk factors for development of VAP are shown in Table 3. As for the logistic regression model, the variables that yielded stable results in all the runs of the jack-knifing technique were: age >70 (RR = 4.0), number of blood units transfused perioperatively (RR = 1.1 per unit), days of mechanical ventilation (RR = 1.1 per day), and reintubation (RR = 14.3). The variables that appeared as significant in

Table 3 Univariate analysis of preoperative, operative and postoperative risk factors of VAP in patients underwent MHS

	Infection $n = 106$ (%)	No infection $n = 1{,}738$ (%)	RR (95% CI)	*P* value
Preoperative risk factors				
Age >70 years	73 (68.9)	730 (42.0)	3.1 (2.0–4.6)	<0.001
Intra-aortic balloon	6 (5.7)	40 (2.3)	2.6 (1.1–6.1)	0.04
Severe pulmonary hypertension	20 (18.9)	176 (10.1)	2.1 (1.2–3.4)	0.006
More than one previous heart surgery	25 (23.6)	160 (9.2)	3.0 (1.9–4.9)	<0.001
Peptic disease	15 (14.2)	83 (4.8)	3.3 (1.8–5.9)	<0.001
COPD	19 (17.9)	186 (10.7)	1.8 (1.1–3.1)	0.02
Diabetes	34 (32.1)	403 (23.2)	1.6 (1.0–2.4)	0.04
Peripheral vasculopathy	15 (14.2)	119 (6.8)	2.2 (1.3–4.0)	0.01
Neoplasia	9 (8.5)	39 (2.2)	4.0 (1.9–8.6)	0.001
Creatinine levels >1.5 mg/dl	19 (17.9)	114 (6.6)	3.1 (1.8–5.3)	<0.001
NYHA IV	20 (18.9)	103 (5.9)	3.7 (2.2–6.2)	<0.001
EuroScore, mean ± SD	9.2 ± 3.3	6.4 ± 3.2		<0.001
Operative risk factors				
Emergency	19 (17.9)	126 (7.2)	2.8 (1.6–4.7)	0.001
Intra-aortic balloon	19 (17.9)	70 (4.0)	5.2 (3.0–9.0)	<0.001
Perioperative myocardial infarction	9 (8.5)	38 (2.2)	4.2 (1.9–8.8)	0.001
Inotropic support	75 (70.8)	662 (38.1)	3.9 (2.6–6.0)	<0.001
CPBT, mean ± SD	137.8 ± 53.6	111.0 ± 42.4		<0.001
Mean aortic cross-clamp time ± SD	83.3 ± 44.7	73.2 ± 31.8		0.02
Postoperative risk factors				
Transfused units*, median (range)	9 (3–18)	2 (0–5)	4.9 (3.0–8.2)	<0.001
Reintervention	24 (22.6)	97 (5.6)		<0.001
Reintubation	65 (61.3)	67 (3.9)	39.5 (25–63)	<0.001
Days of MV median (IQR)	9 (5.7–24.0)	1.0 (1.0–1.0)		<0.001

COPD Chronic obstructive pulmonary disease, *CPBT* cardiopulmonary bypass time, *MV* mechanical ventilation, *NYHA* New York Heart Association functional class

*Intraoperative and in the first 24 h

Table 4 Multivariate analysis of risk factors for VAP in patients who underwent MHS

	RR (95% CI)	*P*
Age >70 years	4.0 (2.1–7.7)	<0.001
Number of transfused blood units	1.1 (1.04–1.1)	<0.001
Days on mechanical ventilation	1.1 (1.1–1.2)	<0.001
Reintubation	14.3 (7.9–25.8)	<0.001
Emergent surgery	42.5 (1.1–5.5)	0.02
Intraoperative inotropic support	2.1 (1.1–3.9)	0.01
Previous cardiac surgery	2.2 (1.1–4.5)	0.03

Table 5 Independent predictive variables used to calculate the "day 0 VAP predictor score" and the "day 3 VAP predictor score"

Variable	Exp (β)	95% CI	*P*	Coefficient (β)	Standard error
Day 0 score					
NYHA IV	2.2	1.2–4.1	0.009	0.8	0.3
Age >70 years	3.5	2.2–5.5	<0.001	1.2	0.2
Previous cardiac surgery	3.0	1.8–5.0	<0.001	1.1	0.2
Emergent surgery	2.6	1.4–4.8	0.003	0.9	0.3
Peripheral vasculopathy	2.0	1.1–3.7	0.03	0.7	0.3
Previous neoplasia	3.4	1.5–7.5	0.003	1.2	0.4
Creatinine >1.5 mg/dl	2.3	1.3–4.0	0.004	0.8	0.3
Constant	0.01		<0.001	−4.1	0.2
Day 3 score					
Age > 70 years	3.3	1.9–5.9	<0.001	1.2	0.3
Constant	0.4		<0.001	−0.8	0.2

at least 50% of the jack-knifing runs were emergent surgery (RR = 2.5), intraoperative inotropic support (RR = 2.1), and previous cardiac surgery (RR = 2.2) (Table 4).

We developed two scores to help the clinicians to identify the subset of patients with a higher risk of developing VAP at two time points: before surgery, including all patients, and on day 3, including only patients who remained ventilated. Independent predictor variables at the operation day before intubation were: age >70 years (RR = 3.5), previous cardiac surgery (RR = 3), emergent surgery (RR = 2.6), NYHA IV (RR = 2.2), peripheral vasculopathy (RR = 2.0), previous neoplasia (RR = 3.4), and creatinine level >1.5 mg/dl (RR = 2.2) (Table 5). As their β coefficients were quite similar, we assigned 1 point to each variable. Results of the ROC analysis performed with the score values are presented in Fig. 1**.** As shown in the figure, a threshold value of ≥1 point shows a sensitivity of 93% and specificity of 40%; if the cutoff of ≥2 points is selected, the achieved sensitivity and specificity would be 51 and 84%, respectively.

For creating the second score (day 3 score), we selected the population who remained intubated at that time and included in the model all the preoperative and perioperative variables. The only independent predictor for VAP identified in this population was: age >70 years (RR = 16.8). The sensitivity and specificity values obtained with this factor were 69.5 and 56%, respectively.

Outcome

The median length of stay in the ICU was significantly longer in patients with VAP (25.5 days RIQ: 10–51.2) than in patients without VAP (3 days RIQ: 2–5) ($P < 0.001$).

Overall in-hospital mortality in our study population was 6.9% (127/1,844), with a mortality rate in patients with VAP of 45.7 versus 2.8% in patients without VAP ($P < 0.001$). Overall mortality of the 231 patients who required MV during more than 48 h was 43.7% (101) and was significantly higher in the subgroup who developed VAP (58/106; 54.7% vs. 43/125; 34.4%. $P = 0.002$).

Discussion

Our paper demonstrates a high incidence density of VAP in patients undergoing MHS and that most predictive risk factors are not amenable to intervention. The combination of the VAP predictive score and/or the need of ventilation for more than 48 h identify a population in such high-risk of VAP that, in our opinion, justifies the prospective study of preemptive measures.

Of the 1,844 patient evaluated, 231 (12.5%) remained ventilated more than 48 h. In this high-risk population, we detected 140 episodes of VAP in 106 patients, with an overall incidence of 45.9%. VAP was diagnosed in 75.4% of patients requiring tracheostomy. Patients mostly developed VAP before tracheostomy, which was usually performed 2 weeks after surgery. Some authors recommend early tracheostomy, but its impact is not clear in MHS patients. The overall incidence of VAP was of 5.7% (22.2 episodes per 1,000 days of mechanical ventilation). This incidence density of VAP, as well as the high number of patients on prolonged MV, reflects the complexity of the patients operated on in our center (47% in Euroscore's high-risk category). In other series the incidence of VAP ranged from 7 to 40% [21–24], depending on age group, underlying condition, and other risk factors. Incidence is generally higher in surgical ICUs than in medical or mixed ones [6, 7]. We do not think that the use of the CPIS influenced our incidence, since it was only used as an adjunctive tool to establish the diagnosis and for early discontinuation of empiric treatment.

MHS patients usually have advanced age, severe underlying conditions, and a high rate of in-hospital instrumentation [7, 25]. Nosocomial infections are

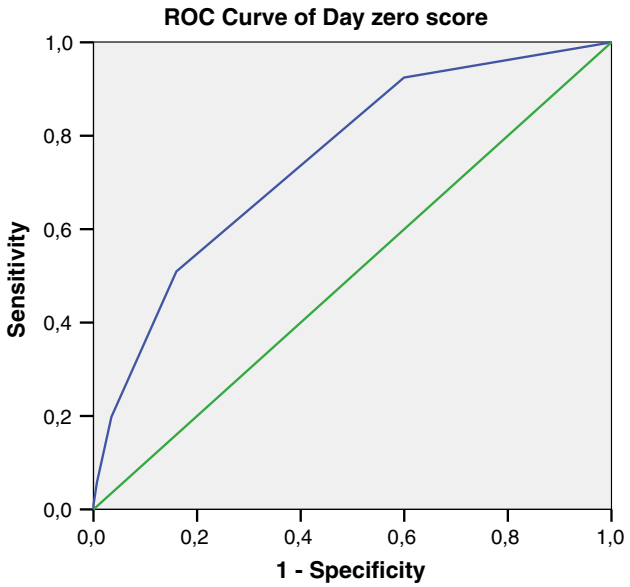

Fig. 1 Receiver operating characteristic (ROC) curve of day 0 score and coordinates of the curve showing the specificity, sensitivity, likelihood ratio for positive test (LR+), and likelihood ratio for negative test (LR−)

Coordinates of the ROC curve

Test Result Variable(s)	Positive if Greater Than or Equal To	Sensitivity (%)	Specificity (%)	LR+	LR-
Day zero score					
	0.5	93	40	1.55	0.17
	1.5	51	84	3.18	0.58
	2.5	20	97	6.66	0.82
	3.5	6	99	6.0	0.94
	4.5	1	99	1	1
	6	0	100		

common among this population, and VAP is the most frequent infectious disease [8, 11]. We believe the expertise of our cardiac catheterization team has made valvular replacement the most common type of surgery.

Etiology

We have included in this series microbiologically confirmed VAPs, as suggested by the recent ATS recommendations. In the absence of a new antibiotic in the past 72 h, a sterile culture of respiratory secretions almost rules out the diagnosis of bacterial pneumonia. In most reports, *P. aeruginosa*, Enterobacteriaceae, and *S. aureus* are the three leading etiologies of VAP. Our study confirmed this data; 32.8% of VAP were caused by Enterobacteriaceae, 28.6% by *P. aeruginosa*, and 27.1% by *S. aureus*, of which 65.8% were MRSA.

MRSA is increasing in importance as a cause of VAP worldwide [26]. Risk factors for VAP caused by MRSA include COPD, longer duration of MV, prior antibiotic therapy, prior steroid treatment, and prior bronchoscopy [27, 28]. The risk of MRSA VAP is higher in endemic areas [28]. This is the case of our hospital, where MRSA represent almost 50% of all *S. aureus* infections.

Risk factors

Our study of risk factors indicates that the variables independently related to VAP development (older age, previous cardiac surgery, previous neoplasia, cardiopulmonary bypass time, duration of VM, reintubation, blood transfusion) are hardly amenable to intervention when best-practice surgical, respiratory, and analgesic/sedation protocols are applied to prevent further complications.

The intubation process itself contributes to the risk of pneumonia [29]. Strategies aimed to reduce the days of ventilation, the rates of reintubation, or to promote non-invasive-ventilation (NIV) may decrease the risk for development of VAP [30–33]. A study has shown that the use of a pre-established protocol for respiratory care and sedation reduces the duration of MV and ICU stay [13].

Several studies in non-ICU patients have suggested that RBC transfusion increases the risk for nosocomial infection, including VAP. In a secondary analysis of data from a large study ($n = 4{,}892$) of transfusion practices in critically ill patients, RBC transfusions were found to be an independent risk factor for VAP [34]. RBC transfusions may represent a partially modifiable risk factor, especially since a recent study by Levy et al. [35] has shown that patients receiving MV received transfusions at

higher pre-transfusion hemoglobin levels than patients not receiving MV (8.7 ± 1.7 vs. 8.2 ± 1.7 g/dl, respectively; $P < 0.001$), although the reason is not clear.

We developed a "day 0 score" to identify a population at high risk of pneumonia with the variables available before surgery. This idea derives from our recent demonstration in a prospective study of the protective value of continuous aspiration of subglottic secretions (CASS) in MHS patients [36]. The three-lumen tube required to perform CASS has a higher cost than the conventional endotracheal (two lumen) tube and would be desirable to select the subpopulation more likely to benefit of the triple lumen tube. Our score would accurately identify 93% of the patients who will develop pneumonia, with a specificity of 40%. Further studies are required to decide the cost efficacy of using CASS tubes for all or only part of the population.

The aim of the "day 3 score" was to identify patients at higher risk of developing pneumonia among those who remained ventilated >48 h. These patients could be candidates for antimicrobial preventive measures. However, in our model the only independent predictor factor for VAP in this subgroup was age >70 years. In the past, strategies employing prophylactic antibiotics have included selective digestive decontamination (SDD) [37, 38]. The mortality benefit of SDD appears to occur in surgical/trauma patients and to be associated primarily with the administration of parenteral antibiotics. Unfortunately, the application of SDD has been associated with the emergence of antibiotic-resistant bacterial strains, limiting its overall utility.

Impact on morbidity and mortality

The overall mortality rate of our series was 11.3%, almost exactly the EuroSCORE's expected mortality (11.8%). VAP mortality ranges from 20 to 70% in specific settings such as late-onset VAP or infections caused by high-risk pathogens [1, 18, 39, 40]. VAP also prolongs the duration of ventilation and ICU stay. In our study the median ICU length of stay for patients with and without VAP was, respectively, 25.5 and 3 days ($P < 0.001$), and the mortality rate was, respectively, 45.7 and 2.8% in both populations ($P < 0.001$).

Our study has some limitations. As our institution is a referral hospital, patient selection bias is present. In addition, although the normalization of blood glucose levels is a standard in our unit, we did not include it in the model. We tried to develop a VAP predictive score that could help clinicians to recognize especially high-risk patients; however, the relatively small sample size of our cohort (106 patients) may have contributed to its somewhat low sensitivity and specificity values.

In conclusion, we have found that, in patients undergoing MHS, the incidence density of VAP is high, and most predictive risk factors are not amenable to intervention. The combination of a risk score and/or the need of ventilation for more than 48 h identifies a population at such a high risk of VAP that, in our opinion, it justifies the prospective study of preemptive measures.

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Conflict of interest statement The authors do not have any association that might pose a conflict of interest.

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