ORIGINAL RESEARCH

Risk factors of ventilator-associated pneumonia in elderly patients receiving mechanical ventilation

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Purpose: The aim of this study was to verify the potential risk factors of ventilator-associated pneumonia (VAP) in elderly Chinese patients receiving mechanical ventilation (MV). The secondary aim of this study was to present logistical regression prediction models of VAP occurrence in elderly Chinese patients receiving MV.

Methods: Patients (aged 80 years or above) receiving MV for ≥ 48 h were enrolled from the Chinese People's Liberation Army (PLA) General Hospital from January 2011 to December 2015. A chi-squared test and Mann–Whitney U-test were used to compare the data between participants with VAP and without VAP. Univariate logistic regression models were performed to explore the relationship between risk factors and VAP.

Results: A total of 901 patients were included in the study, of which 156 were diagnosed as VAP (17.3%). The incidence density of VAP was 4.25/1,000 ventilator days. Logistic regression analysis showed that the independent risk factors for elderly patients with VAP were COPD (OR =1.526, $P<0.05$), intensive care unit (ICU) admission (OR=1.947, $P<0.01$), the MV methods ($P<0.023$), the number of antibiotics administered (OR=4.947, $P<0.01$), the number of central venous catheters (OR=1.809, $P<0.05$), the duration of indwelling urinary catheter (OR=1.805, $P<0.01$) and the use of corticosteroids prior to MV (OR=1.618, $P<0.05$). Logistic regression prediction model of VAP occurrence in the Chinese elderly patients with mechanical ventilation:

$$Logit\ (P) = (-6.468) + 0.423X1 + 0.666X2 + 0.871X3 + (-0.501)X5 + 0.122X6 + 0.593X7 + 0.590X8 + 1.599X9.$$

Conclusion: VAP occurrence is associated with a variety of controllable factors including the MV methods and the number of antibiotics administered. A model was established to predict VAP occurrence so that high-risk patients could be identified as early as possible.

Keywords: aged, 80 and over, pneumonia, ventilator-associated, risk factors, prediction model

Introduction

Ventilator-associated pneumonia (VAP) is defined as pneumonia that occurs 48–72 h (or later) following endotracheal intubation. VAP is characterized by the presence of new or progressive infiltrates, systemic infection (fever, altered white blood cell counts), changes in sputum characteristics, and the detection of a causative agent.[1] VAP is the most frequent cause of nosocomial infections amongst patients requiring mechanical ventilation (MV).[2,3] It has been reported that the incidence of VAP is 9–27% with a mortality of 25–50%.[4–6] VAP can lead to the deterioration of a patient's condition, endanger the patient's life, and increase the health-care burden.[6–8] As the average age of the Chinese population is increasing, the number of elderly patients requiring MV is rising. Elderly patients have a compromised

immune system and are more prone to opportunistic infections, increasing the likelihood of VAP. The factors affecting the occurrence of VAP are complex and diverse, making its management difficult. Specific risk factors include tracheal catheterization, MV, the duration of intensive care unit (ICU) stay, nursing measures, increased colonization of upper gastrointestinal pathogens and the aspiration of contaminated secretions.[9,10] The risk factors for VAP in elderly patients have not been assessed in detail. Clinical practices possess no effective theoretical based evidence for the prevention of VAP in elderly patients. This study retrospectively analyzed the incidence of VAP and related risk factors in elderly patients receiving MV to provide suggestions for the prevention of VAP and elderly patient care.

Methods
Participants
Elderly patients who underwent MV from the Chinese People's Liberation Army (PLA) General Hospital from January 2011 to December 2015 were included. A total of 901 patients were enrolled, including 755 males and 146 females, with an average age of (86.73 ± 4.818) years. Inclusion criteria for the study were: 1) ventilator use ≥ 48 h; 2) no VAP infection prior to MV; 3) ≥ 80 years old. Exclusion criteria were: 1) pneumonia diagnosed before MV; (2) death, ceased treatment, discharged or transferred within 48 h; (3) patients with incomplete clinical data.

Data collection
Retrospective survey methods were used to collect data on elderly patients who underwent MV from the Chinese People's Liberation Army (PLA) General Hospital from January 2011 to December 2015. The investigation was conducted with the assistance of staff from the Hospital Infection Management Section. The investigating members consisted of three nursing staff and one hospital infection management staff, all of whom received uniform training. For patients with MV, routine VAP prevention protocols were available in our hospital. All procedures involving human participants were performed in accordance with the basic principles of the Declaration of Helsinki. Ethical approval was obtained from the Beijing Municipal Commission of Science and Technology Program. Informed consent was waived due to the retrospective design. The electronic database at the Chinese People's Liberation Army General Hospital includes discharge records for all patients treated in the hospital. All patient data were anonymized and maintained with confidentiality.

Study variables
Study variables included basic patient characteristics (gender, disorder of consciousness, smoking, alcohol consumption, nutritional status, surgery, ICU admission, underlying diseases, hospitalization length of stay, ICU stay, origin of patients, duration and number of catheters), MV related data (MV methods, duration of MV and number of reintubations), and medication-related data (antibiotics use after surgery, duration of antibiotics use after surgery, number of antibiotics administered, duration of antibiotics administered, combined application of antibiotics, number of combined antibiotics administered, duration of the combined antibiotics, use of acid suppressant agent, use of sedation, and use of corticosteroids).

Diagnosis of VAP
Chest radiograph or CT showing new or progressive infiltration, consolidation, or ground glass, and at least two of the following criteria: 1) fever $(>38.3°C)$ or hypothermic $(<36°C)$; 2) leukocytosis $(>11×10^9/L)$ or leukopenia $(<4×10^9/L)$; and 3) purulent tracheal secretions confirmed by microscopic examination, and a quantitative bacterial cultures of 10^6 CFU/mL from an endotracheal specimens or 10^4 CFU/mL from bronchoalveolar lavage fluid. Pulmonary edema, acute respiratory distress syndrome (ARDS), tuberculosis, pulmonary embolism, and other diseases were discounted.[11] VAP rate was defined as the number of VAPs/1,000 ventilator days.[12] It can be of two types: 1) early-onset VAP, which is defined as VAP that occurs within the first 4 days of ventilation; and 2) late-onset VAP, which is defined as VAP that occurs more than 4 days after initiation of mechanical ventilation.[13]

Statistical analysis
Statistical analysis was performed using SPSS 22.0 software. The Kolmogorov–Smirnov test was used to determine the normality of distributions. Continuous variables were presented as median, max, and min, while categorical variables were presented as percentages. Mann–Whitney U-test or chi-squared test was used to compare the data between participants with VAP and participants without VAP. Univariate logistic regression models were used to analyze the risk factors of VAP. The hypothesis test significance level was 0.05. OR>1 was a risk factor and

OR<1 was a protective factor. When $P \leq 0.05$ (bilateral), differences were considered statistically significant.

Quality control

According to the criteria for the inclusion and exclusion of cases, completed unified data collection forms were used to screen and collect cases that met the study criteria. Double data entries and logic verification were used to ensure data accuracy. Upon completion, all data were checked, missing data were completed, and duplicated or erroneous data were removed.

Results

VAP incidence

From January 2011 to December 2015, a total of 901 elderly patients receiving MV who met the criteria for inclusion were assessed. Of these patients, 156 had VAP (17.3%). The incidence of VAP in elderly patients receiving MV significantly decreased from 23.4% to 8.4% over the five-year study period (χ^2=23.634, P<0.001). VAP incidence was calculated as follows: (number of cases with VAP/total number of patients who received MV×100)= VAP rate per 100 patients. See Table 1. The VAP incidence density was calculated as follows: (number of cases with VAP/number of ventilator days)×1,000= VAP rate per 1,000 ventilator days.[14] The incidence density of VAP was 4.25/1,000 ventilator days (156/36,720×1,000=4.25 per 1,000 ventilator days). Out of the 156 cases, 47 (30.13%) were categorized under early-onset group and 109 (69.87%) under the late-onset group.

Patient characteristics

Analysis of the basic characteristics of the elderly patients who received MV showed significant differences in the effects of surgery (χ^2=5.018, P<0.05) and ICU admission (χ^2=8.445, P<0.05). COPD influenced the occurrence of VAP (χ^2=6.264, P<0.05). VAP occurred in 22.6% of COPD patients, which was higher than patients with other diseases. Compared with the non-VAP group, the hospitalization

length of stay in the VAP group was prolonged, and the difference was statistically significant (Z=−4.677, P<0.01). ICU length of stay also significantly differed between the VAP group and the non-VAP group (Z=−4.938, P<0.01). According to patient origin, we sub-divided the patients into internal medicine, surgery, emergency department, ICU and others. Statistical analysis showed a large number of internal medicine patients had VAP (12.9%) and the incidence of VAP was influenced by patient origin (χ^2=13.519, P<0.05). The analysis of central venous catheter and indwelling urinary catheter in elderly patients receiving MV showed that the duration of central venous catheter >90 days had a significant influence on VAP (P<0.01). Patients with indwelling urinary catheter >90 days had a higher incidence of VAP compared to patient's ≤90 days. The number of central venous catheters also significantly influenced VAP (χ^2=18.350, P<0.001) (Table 2).

Effects of MV on VAP occurrence

From 2011 to 2015, the number of elderly patients with tracheal intubation was the highest (596) and the rate of VAP was 13.4%. However, the incidence of VAP in patients with tracheotomy was 28.4%, followed by 23.7% in patients who underwent tracheotomy after tracheal intubation. Chi-squared tests of the patient's MV methods revealed its influence on VAP (χ^2=19.616, P<0.001). When the duration of ventilation between groups was compared, significant differences were observed (Z=−5.983, P<0.01). The number of MVs received also significantly influenced VAP (χ^2=7.633, P<0.01). The incidence of VAP in patients suffering the number of reintubations >2 (28.4%) was higher than the number of reintubations ≤2 (16.2%) (Table 3).

Medication use

The analysis of medication use in elderly patients receiving MV in hospital showed that the use of antibiotics after surgery (χ^2=4.652, P<0.05), the duration of

Table 1 Incidence of VAP in elderly patients receiving MV

Year	Number (N)	VAP, n (%)	NVAP, n (%)	χ^2	p
2011	154	36（23.4）	118 (76.6)		
2012	255	40（15.7）	215 (84.3)		
2013	288	44（15.3）	244 (84.7)		
2014	312	32 (10.3)	280 (89.7)		
2015	285	24（8.4）	261 (91.6)		
Total	901	156（17.3）	745 (82.7)	23.634	0.000

Abbreviations: MV, mechanical ventilation; NVAP, non-ventilator-associated pneumonia; VAP, ventilator-associated pneumonia.

Table 2 Characteristics between elderly patients receiving MV with VAP and without VAP

Patient characteristics	VAP（N=156）	NVAP（N=745）	χ^2/Z	p
Gender			1.591	0.207
Male	136（18.0）	619（82.0）		
Female	20（13.7）	126（86.3）		
Disorder of consciousness			3.806	0.051
Yes	58（21.0）	218（79.0）		
No	98（15.7）	527（84.3）		
Smoking			0.090	0.764
Yes	64（17.8）	296（82.2）		
No	92（17.0）	449（83.0）		
Alcohol consumption			1.028	0.311
Yes	45（15.5）	246（84.5）		
No	111（18.2）	499（81.8）		
Nutritional status			1.301	0.522
Poor	26（17.0）	127（83.0）		
Moderate	86（18.6）	376（81.4）		
Good	44（15.4）	242（84.6）		
Surgery			5.018	0.025
Yes	73（20.9）	277（79.1）		
No	83（15.1）	468（84.9）		
ICU admission			9.594	0.002
Yes	101（21.0）	381（79.0）		
No	55（13.1）	364（86.9）		
Underlying diseases				
Hypertension	83（19.1）	352（80.9）	1.833	0.176
Diabetes	27（14.4）	161（85.6）	1.446	0.229
COPD	45（22.6）	154（77.4）	5.009	0.025
Respiratory failure	32（13.3）	209（86.7）	3.744	0.053
Heart dysfunction	44（14.9）	252（85.1）	1.847	0.174
Brain infarction	47（19.9）	189（80.1）	1.511	0.219
Malignancy	41（16.7）	204（83.3）	0.014	0.907
Renal insufficiency	29（15.7）	156（84.3）	0.305	0.581
Origin of patients				
Internal medicine	59（12.9）	397（87.1）	13.519	0.009
Surgery	10（18.9）	43（81.1）		
Emergency department	1（11.1）	8（88.9）		
ICU	85（22.5）	293（77.5）		
Others	1（20.0）	4（80.0）		
Hospitalization length of stay	120（9, 2,535）	70（4, 1,607）	−4.677	<0.01
ICU length of stay	25（0, 1,263）	4（0, 1,548）	−4.938	<0.01
Duration of catheters(days)				

(*Continued*)

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Table 2 (Continued).

Patient characteristics	VAP（N=156）	NVAP（N=745）	χ^2/Z	p
Central venous catheter 　0–90 　>90	 90（15.3） 66（21.1）	 498（84.7） 247（78.9）	 4.767	 0.029
Indwelling urinary catheter 　0–90 　>90	 92（13.6） 64（28.2）	 582（86.4） 163（71.8）	 25.090	 <0.001
Number of catheters				
Central venous catheter 　0–2 　>2	 118（15.2） 38（30.9）	 660（84.8） 85（69.1）	 18.350	 <0.001
Indwelling urinary catheter 　0–2 　>2	 112（14.7） 44（19.3）	 651（85.3） 184（80.7）	 0.839	 0.360

Note: Data are shown as number (percentage) or median (min and max).
Abbreviations: ICU, intensive care unit; MV, mechanical ventilation; NVAP, non-ventilator-associated pneumonia; VAP, ventilator-associated pneumonia.

Table 3 Comparison of MV characteristics between VAP group and non-VAP group

Ventilation characteristics	VAP（N=156）	NVAP（N=745）	χ^2/Z	p
MV methods 　Tracheal intubation 　Tracheostomy 　Tracheotomy after tracheal intubation	 80（13.4） 21（28.8） 55（23.7）	 516（86.6） 52（71.2） 177（76.3）	 19.615	 <0.001
Duration of MV	71.5（4, 1,588）	34（2, 1,584）	−5.983	<0.01
Number of reintubations 　0–2 　>2	 133（16.2） 23（28.4）	 687（83.8） 58（71.6）	 7.633	 0.006

Note: Data are shown as number (percentage) or median (min and max).
Abbreviations: MV, mechanical ventilation; NVAP, non-ventilator-associated pneumonia; VAP, ventilator-associated pneumonia.

antibiotics use post-surgery (χ^2=6.868, $P<0.05$), the number of antibiotics (χ^2=18.645, $P<0.05$), the duration of antibiotic administered (χ^2=6.101, $P<0.05$), the combined application of antibiotics (χ^2=5.098, $P<0.05$), the number of combined antibiotics (χ^2=9.508, $P<0.05$), the duration of combined antibiotics (χ^2=16.732, $P<0.05$) and the use of corticosteroids prior to MV (χ^2=5.483, $P<0.05$) all significantly influenced VAP (Table 4).

Logistical analysis of factors related to VAP infection

Retrospective analysis of elderly patients with MV was performed from 2011 to 2015. Two-class logistic analysis was performed to identify whether VAP was a dependent variable and to perform single-factor analysis of the risk factors for VAP ($P<0.05$). Using the forward conditional method for stepwise regression, the significance level α of the selected variables was determined as 0.05. Dummy variables were set for multi-category variables such as MV methods and the origin of patients. The results showed that the COPD (X1) (OR=1.526, $P<0.05$), the ICU admission (X2) (OR=1.947, $P<0.01$), the MV methods ($P<0.023$) (tracheal intubation (X3), tracheostomy (X4), tracheotomy after tracheal intubation (X5)), the number of central venous catheter (X6) (OR=1.809, $P<0.05$), the duration of indwelling urinary catheter (X7) (OR=1.805, $P<0.01$), the number of antibiotics administered (X8) (OR=4.947, $P<0.01$) and the use of corticosteroids prior to MV (X9) (OR=1.618, $P<0.05$) were all single risk factors of VAP (Table 5).

Table 4 Effects of medication use on the occurrence of VAP

Medication use	VAP (N=156)	NVAP (N=745)	χ^2	p
Antibiotics use after surgery			4.652	0.031
Yes	72（20.7）	275（79.3）		
No	84（15.2）	470（84.8）		
Duration of antibiotics use after surgery (days)			6.868	0.009
≤14	93（15.1）	524（84.9）		
>14	63（22.2）	221（77.8）		
Number of antibiotics administered			18.645	<0.001
≤3	4（3.4）	115（96.7）		
>3	152（19.4）	630（80.6）		
Duration of antibiotics administered (days)			6.101	0.014
≤14	6（5.1）	112（94.9）		
>14	150（18.3）	670（81.7）		
Combined application of antibiotics			5.098	0.024
Yes	151（18.1）	682（81.9）		
No	5（7.4）	63（92.6）		
Number of combined antibiotics administered			9.508	0.002
≤3	22（10.3）	191（89.7）		
>3	134（19.5）	554（80.5）		
Duration of combined antibiotics administered (days)			16.732	<0.001
≤14	20（8.6）	213（91.4）		
>14	136（20.4）	532（79.6）		
Before mechanical ventilation				
Use of acid suppressant agent	107（19.2）	451（80.8）	3.548	0.060
Use of sedation	48（19.5）	198（80.5）	1.142	0.285
Use of corticosteroids	58（21.9）	207（78.1）	5.483	0.019
After mechanical ventilation				
Use of acid suppressant agent	135（17.1）	655（82.9）	0.228	0.633
Use of sedation	88（16.4）	449（83.6）	0.797	0.372
Use of corticosteroids	65（18.3）	290（81.7）	0.406	0.524

Note: Data are number (percentage).
Abbreviations: NVAP, non-ventilator-associated pneumonia; VAP, ventilator-associated pneumonia.

Establish logistic regression prediction model

Logistic regression prediction model

Logistic regression prediction model of VAP infection in elderly patients with mechanical ventilation:

$$\text{Logit(P)} = (-6.468) + 0.423X1 + 0.666X2 + 0.871X3 + (-0.501)X5 + 0.122X6 + 0.593X7 + 0.590X8 + 1.599X9$$

The model is used for the preliminary prediction of VAP, predicting whether VAP will occur in patients undergoing mechanical ventilation. The closer the P-value is to 1, the more likely VAP will occur in patients undergoing mechanical ventilation. The closer the P-value is to 0, the less likely the patient will have VAP.

Prediction effect evaluation of logistic regression models

The likelihood ratio test, Hosmer–Lemeshow goodness-of-fit test and receiver-operating characteristic (ROC)

Table 5 Logistic regression analysis of VAP risk factors in elderly patients with MV

Risk factors	B	SE	Wald	p	OR	95%CI
COPD	0.423	0.211	4.015	0.045	1.526	1.009–2.308
ICU admission	0.666	0.199	11.239	0.001	1.947	1.319–2.875
Mechanical ventilation methods						
Tracheal intubation			7.584	0.023		
Tracheostomy	−0.501	0.222	5.123	0.024	0.606	0.392–0.935
Tracheotomy after tracheal intubation	0.122	0.321	0.145	0.703	1.130	0.602–2.122
Number of central venous catheter	0.593	0.234	6.424	0.011	1.809	1.144–2.860
Duration of indwelling urinary catheters	0.590	0.206	8.226	0.004	1.805	1.206–2.701
Number of antibiotics administered	1.599	0.525	9.263	0.002	4.947	1.767–13.852
Before mechanical ventilation						
Use of corticosteroids	0.481	0.195	6.075	0.014	1.618	1.104–2.372
Constant	−6.468	1.100	34.557	<0.001	0.002	

Abbreviations: MV, mechanical ventilation; ICU, intensive care unit; VAP, ventilator-associated pneumonia.

curve were used to evaluate the prediction effect of the model.

Overall validity of the model. The likelihood ratio test showed that χ^2=315.332, df=1, P<0.001, indicating that the prediction model has statistical significance. The Wald test demonstrated that χ^2=34.557, df=1, P<0.001, that is, the coefficients of the regression equation were statistically significant.

Goodness-of-fit of logistic regression equations. Hosmer–Lemeshow goodness-of-fit test showed that the goodness of fit model was favorable (χ^2=4.613, df=7, P=0.707).

Discriminant ability of logistic regression equations. The ROC curve was drawn with "1-specificity" as the abscissa and "sensitivity" as the ordinate. When 0.5≤ the area under the curve (AUC) <0.7, it was considered that the discriminant value of the model was acceptable. When 0.7≤AUC<0.9, it was considered that the discriminant value of the model was favorable. When 0.9≤AUC, the value of the model was considered outstanding.

The results of this study show that the AUC of the prediction probability of the new variable was 0.722, indicating that the discriminant effect of the model was very good. The AUC of the comprehensive index was higher than that of other indices (P<0.05), indicating that the comprehensive index more accurately identified VAP, and performed better than that of the single index for the identification of VAP (Figure 1 and Table 6).

Discussion

VAP is a common complication during MV and a leading cause of death in MV patients.[15,16] The clinical symptoms of VAP are complex and early diagnosis is difficult. Once VAP occurs, patients suffer difficulties withdrawing from MV, have prolonged hospitalization, increased hospitalization expenses and an increased danger to life.[6–8] Of the 901 elderly MV patients observed in this study, 156 met the diagnostic criteria for VAP (incidence=17.3%). The incidence density of VAP in our hospital was 4.25‰, which was mainly classed as late onset. This was less than previously reported values that ranged from 18% to 32%.[17–19] The incidence of VAP varied because of the target population and methods of diagnosis. In this study, the target population was elderlyChinesepatients. Analyzing the risk factors for the occurrence of VAP provides a theoretical basis for effective preventive measures. Logistic regression revealed that the risk factors of VAP in elderly patients were COPD, ICU admission, the MV methods, the number of central venous catheters, the duration of an indwelling urinary catheter, the number of antibiotics administered and the use of corticosteroids prior to MV.

MV methods are VAP risk factors

The methods of MV influenced the occurrence of VAP. The incidence of VAP was 13.4% for tracheal intubation, 28.4% for tracheostomy, and 23.7% for tracheostomy after tracheal intubation. The incidence of VAP in patients with tracheotomy was lower than that of patients who underwent tracheostomy after tracheal intubation. This is contrary to previous clinical data. Patients with MV should therefore undergo tracheotomy as quickly as possible to reduce the risk of secondary catheterization and the incidence of VAP. Wang[20] and
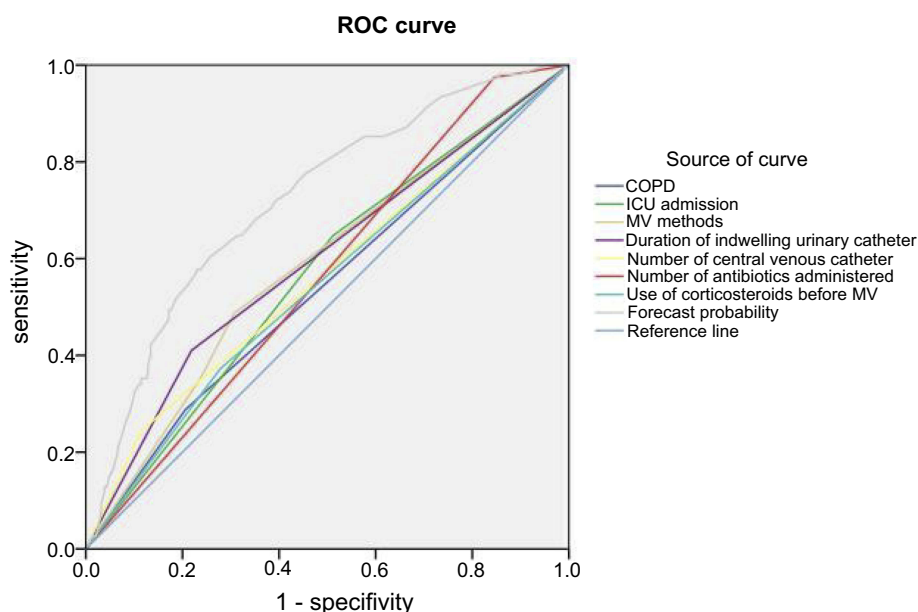
ROC curve

Figure 1 Logistic regression prediction model ROC curve.
Abbreviation: ROC, receiver-operating characteristic.

Table 6 Area under curve

Test result variable	Area chart	The standard error[a]	Asymptotically significant level[b]	95% CI	
				Lower limit	Upper limit
COPD	0.541	0.026	0.108	0.490	0.592
ICU admission	0.568	0.025	0.007	0.519	0.617
Duration of mechanical ventilation	0.586	0.025	0.001	0.536	0.636
Number of central venous catheter	0.565	0.027	0.001	0.513	0.617
Duration of indwelling urinary catheter	0.596	0.026	0.000	0.545	0.647
Number of antibiotics use	0.564	0.023	0.011	0.519	0.610
Use of corticosteroids before MV	0.547	0.026	0.065	0.496	0.598
Forecast probability	0.722	0.022	0.000	0.679	0.765

Notes: [a]Assume nonparametric. [b]Original hypothesis: real area =0.5
Abbreviations: ICU, intensive care unit; MV, mechanical ventilation.

Griffiths et al[21] found that early tracheotomy failed to reduce the incidence of VAP and did not shorten the duration of MV or the duration of ICU stay. This is because tracheotomy damages the normal physiological and anatomical function of the trachea. The respiratory tract directly contacts the external environment and the protective effects of upper respiratory tract filtration and humidification are weakened. This leads to a loss of cough and reflex function of the trachea, leading to pathogenic microorganisms colonizing in the tracheal tube. Colonized pathogens form biofilms, increasing the likelihood of lower respiratory tract infections.[22,23] In this study, the incidence of VAP in patients suffering >2 (28.4%) reintubations was higher than those with ≤2 (16.2%) reintubations. These differences, however, were not statistically significant. This differed from previous studies that identified reintubation as an important predictor of VAP development.[24–26] This may have been due to the number of re-intubations we compared, as opposed to the number of re-intubations that occurred.

ICU admission and COPD are VAP risk factors

Patients admitted to ICU are between 5 and 10 times more likely to acquire a nosocomial infection than patients in other hospital areas.[27] VAP is the most common hospital-associated infection among adult patients in ICUs, with frequencies of 15–45%. The reported rate of VAP in North American and European ICU settings is 1–53 cases per 1,000 ventilator days, affecting up to 30% of patients receiving MV.[28–30] A 2005 study across 14 ICUs revealed a rate of 28%.[31] The incidence of VAP varied according to the type of ICU (medical, surgical, coronary). This was higher amongst patients with burns, or in those within neurosurgical or trauma units (17–20%).[32] These findings did not agree with Torres et al, who found that the type of ICU population did not influence VAP occurrence.[33] In this study, ICU admission was the major risk factor for the occurrence of VAP. We also found that patients who developed VAP had longer ICU stays than those who did not, which was consistent with other reports.[34] ICU patients have more chronic co-existing diseases and more severe acute physiological dysfunction and suffer more invasive procedures, so they are in a state of relative immunosuppression.[3] In addition, due to the widespread use of antibiotics and improper isolation measures, cross-infection is also increasing, and the possibility of infection is increasing. Therefore, reducing the incidence of ventilator-associated pneumonia and exploring the related factors causing ventilator-associated pneumonia in ICU have been the main research focus in this field.

COPD is a well-recognized risk factor for community-acquired pneumonia.[35,36] A history of COPD has also been identified as a risk factor for VAP development.[37] The duration of MV and ICU stay were both longer in COPD patients with VAP.[38] The development of VAP in COPD patients resulted in an increase of 17% in mortality rates compared to COPD patients that did not develop VAP.[39] In this study, COPD was the major risk factor of VAP occurrence (χ^2=6.264, P<0.05). VAP occurred in 22.6% of COPD patients, which was higher than in patients with other diseases. This may be due to the patient's advanced age, high colonization of the lower airways, the inhibition of mucociliary function due to cigarette smoking, the inability to generate an effective cough response due to airway obstruction, and the suppressive effects of corticosteroids on lung host defenses.[40] When patients with COPD develop VAP, they present an increased risk of infection of specific pathogenic bacterial species.[41] COPD leads to physiological changes which predispose patients to infections, particularly from Gram-negative bacilli.[42]

Impact of medication on the occurrence of VAP

The number of antibiotics administered by patients was a risk factor for VAP. Logistic regression showed that the incidence of VAP in patients using the number of antibiotics >3 was 4.947 times higher than those receiving ≤3, the differences of which were statistically significant. A large number of antibiotics can alter the parasitism of normal microorganisms, leading to infection by opportunistic pathogens or the emergence of drug-resistant bacterial strains, increasing the incidence of VAP.[43–45] Prior antibiotic therapy has been recognized as a risk factor for VAP in adults.[46,47] However, it is unclear whether the number of antibiotics prolongs hospitalization or intubation, both of which are risk factors for VAP. This relationship requires further exploration and clarification. A controversial issue is the selection of antibacterials. The judicious use of appropriate antibiotics may reduce patient colonization and subsequent infections with multi-drug-resistant bacteria. Data from global studies suggest that multi-resistant bacteria are increasing, but these data may not be applicable to local hospitals. Therefore, based on our knowledge of bacterial flora in our hospital, the selection of adequate therapeutic regimens will decrease both morbidity and mortality.

Reports on the effects of corticosteroids on VAP have been variable. Both experimental[48] and clinical[49] data suggest that corticosteroid use decreases the occurrence and severity of nosocomial pneumonia in patients treated in the ICU. In the case of ARDS patients, corticosteroids reduce the incidence of suspected VAP.[50,51] A multicenter trial that included 150 intubated patients admitted to the ICU due to severe trauma showed that the use of intravenous hydrocortisone over a period of seven consecutive days resulted in a decreased risk of hospital-acquired pneumonia and an increased duration of MV-free days.[51] Mortality rates, the length of the ICU stay and the length of MV were all significantly lower in VAP patients receiving corticosteroids.[52] Alternative results have however been reported. For patients with traumatic brain injury, the use of corticosteroids failed to reduce the incidence of VAP.[53] In other studies, the use of low-dose steroids to prevent VAP was not favored.[54] However, we found that

the use of corticosteroids prior to intubation in patients with MV increases the occurrence of VAP. The use of corticosteroids prior to MV was the major risk factor of VAP. The reason might be that the use of corticosteroids leads to myelosuppression, liver and kidney dysfunction, decreased immune function, and infection. In addition, corticosteroids can increase the incidence of ulcers and damage the integrity of the gastrointestinal mucosal tissue structure, leading to the adsorption and transplantation of gastrointestinal pathogens, an important risk factor of VAP. Thus, corticosteroids should be administered reasonably to elderly patients when required.

Invasive procedures influence the occurrence of VAP

The number of central venous catheters and the duration of indwelling urinary catheters were identified as risk factors for VAP. Logistic regression showed that the incidence of VAP in the number of central venous catheter >2 of patients was 1.809 times higher than those receiving ≤2, the differences of which were statistically significant. The incidence of VAP in the duration of indwelling urinary catheters >90 days of patients was 1.805 times higher than those receiving ≤90 days. Indwelling catheters bypass the host's natural defense mechanisms with high frequency, providing a method through which microbes invade important organs in the body. In the process of maintaining these catheters, medical personnel require frequent patient contact, leaving the patients vulnerable to the colonization and infection of hospital pathogens. In addition, maintenance devices act as reservoirs for pathogens, leading to the horizontal spread of pathogens between patients.[55] More regular catheters of prolonged duration is more likely to damage a patient's resistance and provide opportunities for pathogenic bacteria to enter the body, increasing the risk of infection. Therefore, invasive procedures in patients should be minimized to reduce the incidence of infection.

Establishment of VAP prediction model in elderly patients with MV

There are many factors affecting the occurrence of VAP. A model was constructed to predict the probability of VAP occurrence in patients with mechanical ventilation in Chinese elderly, to find high-risk patients infected with VAP as early as possible, to strengthen prevention measures in time, and to effectively reduce the occurrence of VAP. In this study, logistic regression was used to establish the prediction model of VAP infection in elderly patients with mechanical ventilation for the preliminary identification of VAP. By the logistic regression prediction model it is found that the number of antibiotics administered and mechanical ventilation methods have important effects on the occurrence of VAP, especially tracheotomy on the impact of VAP. Therefore, this study provides evidence for the clinical research to focus on the mechanical ventilation methods and the number of antibiotics administered to prevent VAP.

This study had several potential limitations. First, this was a cross-sectional study. Only correlations rather than causal relationships were established due to the study design. Secondly, this was a single-center study and all participants were from the same tertiary hospital in China. As such, the results cannot be generalized to other demographic groups. Further multicenter, prospective cohort studies that enroll participants with different demographic characteristics are now required.

Conclusion

The incidence of VAP in elderly patients with MV was 17.3%. The incidence density of VAP was 4.25/1,000 ventilator days. The risk factors of VAP mainly include the MV methods and the number of antibiotics administered. Based on the risk factors of VAP in the elderly Chinese patients, a prediction model was established to facilitate the early detection of high-risk patients. Further multicentered, prospective cohort studies are needed.

Ethical approval

The ethical approval was obtained from Beijing Municipal Commission of Science and Technology Program.

Disclosure

The authors report no conflicts of interest in this work.

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