



## **Pneumonia related to mechanical ventilation and its associated factors: an observational study**

Pneumonia associada à ventilação mecânica e seus fatores de riscos:  
um estudo observacional

Neumonía asociada al ventilador y sus factores de riesgo: un estudio observacional

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### **ABSTRACT**

**Objective:** To verify the profile of patients admitted to an adult ICU and the risk factors associated with the occurrence of VAP. **Methods:** This is a cross-sectional study, carried out between January 2018 and December 2020, whose participants were individuals admitted to the adult ICU of a hospital in ES. **Results:** A total of 425 people were included in the study. Multinomial binary logistic regression showed that patients with MV time between 10 and 14 days (OR = 6.94;  $p < 0.001$ ; 95% CI = 1.99 – 24.42) and more than 14 days (OR = 7.15;  $p < 0.001$ ; 95% CI = 2.78 – 20.94) were more prone to VAP. Associations were found between chronic obstructive pulmonary disease (OR = 2.75;  $p < 0.05$ ; 95% CI = 0.64 – 9.87), type 2 diabetes mellitus (OR = 2.70;  $p < 0.001$ ; CI 95% = 1.13 – 6.34), COVID-19 (OR = 2.07;  $p < 0.01$ ; 95% CI = 0.75 – 5.38) and occurrence of VAP. **Conclusion:** Patients with increased duration of MV, with comorbidities and hospitalized due to COVID-19 infection are at high risk of developing VAP.

**Keywords:** Artificial respiration, Respiratory infections, Risk factors, Prevention, Infection control.

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### **RESUMO**

**Objetivo:** Verificar o perfil de pacientes internados em UTI adulto e os fatores de risco associados à ocorrência de PAV. **Métodos:** Trata-se de um estudo transversal, que foi realizado entre janeiro de 2018 e dezembro de 2020, cujos participantes eram indivíduos internados na UTI adulto de um hospital do ES. **Resultados:** Um total de 425 pessoas foram incluídos no estudo. A regressão logística binária multinomial mostrou que pacientes com tempo de VM entre 10 e 14 dias (OR = 6,94;  $p < 0,001$ ; IC 95% = 1,99 – 24,42) e mais de 14 dias (OR = 7,15;  $p < 0,001$ ; IC 95% = 2,78 – 20,94) eram mais propensos a PAV. Associações foram encontradas entre doença pulmonar obstrutiva crônica (OR = 2,75;  $p < 0,05$ ; IC 95% = 0,64 – 9,87), diabetes

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mellitus tipo 2 (OR = 2,70;  $p < 0,001$ ; IC 95% = 1,13 – 6,34), COVID-19 (OR = 2,07;  $p < 0,01$ ; IC 95% = 0,75 – 5,38) e ocorrência de PAV. **Conclusão:** Pacientes com aumento do tempo de VM, com comorbidades e internados por infecção causada por COVID-19 têm alto risco de desenvolver PAV.

**Palavras-chave:** Respiração artificial, Infecções respiratórias, Fatores de risco, Prevenção, Controle de infecção.

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## RESUMEN

**Objetivo:** Verificar el perfil de los pacientes ingresados en una UTI de adultos y los factores de riesgo asociados a la ocurrencia de NAV. **Métodos:** Se trata de un estudio transversal, realizado entre enero de 2018 y diciembre de 2020, cuyos participantes fueron personas internadas en la UTI de adultos de un hospital de ES. **Resultados:** Un total de 425 personas fueron incluidas en el estudio. La regresión logística binaria multinomial mostró que los pacientes con tiempo de VM entre 10 y 14 días (OR = 6,94;  $p < 0,001$ ; IC 95 % = 1,99 – 24,42) y más de 14 días (OR = 7,15;  $p < 0,001$ ; 95 % IC = 2,78 – 20,94) eran más propensos a VAP. Se encontraron asociaciones entre enfermedad pulmonar obstructiva crónica (OR = 2,75;  $p < 0,05$ ; IC 95% = 0,64 – 9,87), diabetes mellitus tipo 2 (OR = 2,70;  $p < 0,001$ ; IC 95% = 1,13 – 6,34), COVID- 19 (OR = 2,07;  $p < 0,01$ ; IC 95% = 0,75 – 5,38) y aparición de VAP. **Conclusión:** Los pacientes con mayor duración de la VM, con comorbilidades y hospitalizados por infección por COVID-19 tienen alto riesgo de desarrollar NAVM.

**Palabras clave:** Respiración artificial, Infecciones respiratórias, Factores de riesgo, Prevención, Control de infección.

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## INTRODUCTION

Mechanical ventilation is an extensively utilized invasive technique within intensive care units (ICUs) that proves highly effective in preserving the lives of critically ill patients. The term ventilator-associated pneumonia (VAP) refers to inflammation of the lung parenchyma caused by infectious agents acquired specifically through invasive mechanical ventilation (MV) after 48 hours (PAPAZIAN L, et al., 2020; CRAVEN TH, et al., 2020). There is a 5% to 40% incidence of VAP in intensive care units (ICUs) and it is one of the most common Healthcare Associated Infections (HAIs). It should be noted that all mechanically ventilated patients are susceptible to VAP, and the first 5 days of ventilation concentrate the highest incidence of this type of infection (SHASH H, et al., 2022). A number of important points occur with ICU patients, such as a worse prognosis, increased treatment costs, and a longer length of stay in the intensive care units (KÓZKA M, et al., 2020; WU D, et al., 2019).

Although there have been great advances regarding the diagnosis and propaedeutics of VAP, high rates of morbidity and mortality related to this infection persist. In the literature, the incidence ranges from 20% to 75% of patients hospitalized using mechanical ventilation (SHASH H, et al., 2022). According to the Infectious Diseases Society of America, in the United States of America this rate reached values around 13% in 2016. It should be noted that one of the major challenges related to VAP is the growing resistance to antibiotic therapy, the absence of truly efficient preventive strategies, as well as the lack of a gold standard diagnosis for ventilator-associated pneumonia (WU D, et al., 2019).

According to the National Health Surveillance Agency and the Centers for Disease Control and Prevention, ventilator-associated pneumonia can be diagnosed clinically or microbiologically. The Infiltrate opacification, persistent, new or progressive, or the cavitation must be evident on serial chest radiographs of patients with an underlying heart or lung disease. Furthermore, they must have at least one of the following signs and symptoms: fever (temperature  $> 38^{\circ}\text{C}$ ) without any other cause, leukopenia (4000 cells/mm<sup>3</sup>), leukocytosis ( $> 12000$  cells/mm<sup>3</sup>), and confusion (ANVISA, 2017; CDC, 2023). Apart from, purulent secretions, changes in the characteristics of the secretions, an increase in the respiratory secretion, difficulties with gas exchange, an increase in oxygen requirements or increases in ventilator parameters, auscultation with snoring or rales, cough, dyspnea, and tachypnea are all common signs of VAP (ANVISA, 2017; CDC, 2023).

The incidence density of ventilator-associated pneumonia and rate of use of mechanical ventilation are two indicators of VAP surveillance. A database of all data is compiled and calculated periodically for internal service monitoring and for the purpose of presenting the results to the health care professionals, in that way, health care services are able to assess required preventive and care decisions to the suspected or confirmed cases of ventilator-associated pneumonia (ANVISA, 2017).

Additionally, the identification of modifiable and non-modifiable risk factors for infection permits a more rigorous observation of patients susceptible to ventilator-associated pneumonia (HASSOUN-KHEIR N, et al., 2020; KÓZKA M, et al., 2020). The incidence of VAP is directly related to an increase in length of stay and prolongs the period of mechanical ventilation for invasive support. In this context, there is an increase in the demand for medical and financial resources (WU D, et al., 2019).

The definition of risk factors enables early diagnosis in cases of emerging symptoms, reducing the incidence of VAP, as well as, patient morbidity and mortality rates; therefore, it is necessary to clarify the the main ones risk factors for this kind of pneumonia, as well as strategies to control and prevent this comorbidity (WU D, et al. 2019).

The Brazilian Society of Pulmonology and Tisiology classifies the risk factors for hospital-acquired pneumonia as modifiable or non-modifiable (SBPT, 2007). Non-modifiable risk factors include age, severity score, chronic obstructive pulmonary disease, neurological diseases, trauma and surgery, while the modifiable risk factors for hospital-acquired pneumonia are obvious targets for better clinical management and prophylaxis (ATS, 2005).

Patient characteristics (advanced age, male sex), increased MV time, disturbances in consciousness, comorbidities, burns, invasive operations, previous antibiotic therapy and genetic polymorphisms are internationally recognized risk factors (WU D, et al., 2019).

Considering cited above, the objective of the present study was to investigate the epidemiological profile of patients hospitalized in four adult intensive care units Brazilian Hospital and the factors associated with the occurrence of pneumonia resulting from mechanical ventilation.

## METHODS

This retrospective observational study was carried out between January 2018 and December 2020, with patients admitted in the adult intensive care unit of a hospital in the Espírito Santo, Brazil. Data were collected retrospectively from the records available in the "Magma Solution" software, a software for internal use at the hospital and of records of the institution's Hospital Infection Control Service. The diagnosis of ventilator-associated pneumonia was performed by hospital professionals and followed the criteria established by National Agency of Sanitary Vigilance (ANVISA).

The epidemiological criteria were the same for healthcare-related pneumonia in the patients with and without mechanical ventilation (ANVISA, 2017; ANVISA, 2021). There are different criteria for clinically and microbiologically defined pneumonia and for immunosuppressed patients. The three main assessment tools for the detection of ventilation-associated pneumonia using the current criteria are chest radiography, signs and symptoms, and laboratory tests (ANVISA, 2017; ANVISA, 2021).

With the emergence of the new coronavirus, Anvisa has proposed an alternative criterion for the epidemiological diagnosis of ventilator-associated pneumonia in patients with Coronavirus Disease (COVID-19) (HASSOUN-KHEIR N, et al., 2020).

The study population consisted of individuals over 18 years of age, of both sexes, and admitted to the intensive care units of the hospital. Patients who did not meet at least one of the following criteria were excluded from the study: (a) patients not exposed to mechanical ventilation, (b) patients exposed to mechanical ventilation for less than or equal to 48 hours and (c) patients who had missing data on any of the variables of interest to the study.

The outcome variable was the presence or absence of ventilator-associated pneumonia. Patients were followed-up from intensive care unit admission to the outcome, namely hospital discharge or death, and the follow-up period of each patient was recorded to avoid information bias.

The following variables were evaluated: presence of ventilator-associated pneumonia, sex, age group, use of alcohol and smoking, number of mechanical ventilation events and time of exposure to MV, type of hospitalization (clinical, elective surgical clinic, emergency, and coronary), readmission, renal replacement therapy, non-dialysis chronic renal failure, congestive heart failure, chronic coronary failure, chronic atrial fibrillation, systemic arterial hypertension, type 1 diabetes mellitus, type 2 diabetes mellitus, nutritional status (obese and non-obese), non-terminal chronic obstructive pulmonary disease, cancer, blood products, sepsis, ICU admission for COVID-19 and therapeutic restriction.

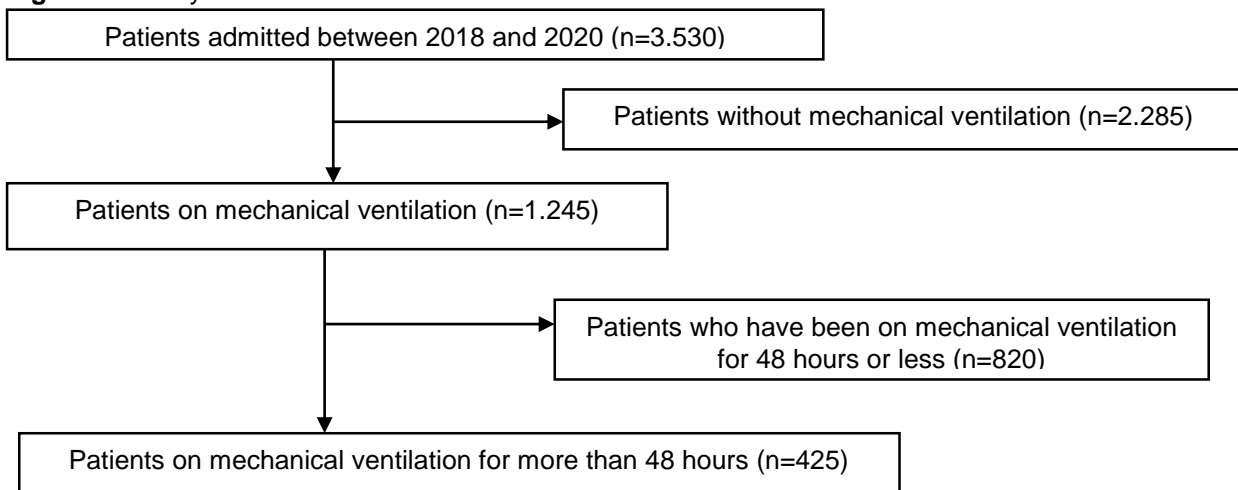
Patients were categorized according to age (adults: 18-60 years old; elderly  $\geq 60$  years old) and mechanical ventilation time (2-10 days; 10-14 days;  $>14$  days) when tracheostomy was indicated (ANDRIOLO BN, et al., 2015). Data are presented in n and percentages (%), the outcome variable was categorized (with and without VAP). The chi-square test was used to compare the proportions between the groups.

Multinomial logistic regression models were created (crude and adjusted) to verify the association with the significant variables in the bivariate analysis. A significance level of  $\alpha = 0.05$  was adopted for all hypothesis tests and the data were analyzed in the “R statistical computing and graphics” software. The article was approved by the Research Ethics Committee under the CAAE 47872921.0.0000.5062 and 4.782.897.

## RESULTS

Retrospective data of all patients over 18 years of age of both sexes who entered the intensive care units (n=3,530) of the study hospital during the years 2018, 2019, and 2020 were analyzed exclusion, a sample of 425 patients was obtained (**Figure 1**).

**Figure 1** - Study flowchart.



**Source:** Schrioder RP, et al., 2023.

The **table 1** shows the characteristics of the patients on mechanical ventilation according to the presence or absence of pneumonia. It was observed that most participants were men, over 60 years of age, non-alcoholic, non-smokers, with systemic arterial hypertension, non-obese, at their first and only event of mechanical ventilation, with MV time between 2 to 10 days, not readmitted to the hospital, and in the intensive care units for causes other than COVID-19. When comparing the presence or absence of pneumonia, it was observed that the highest proportion of the two variables was found in non-smokers, with the absence of DM2, COPD, and intensive care units for causes other than COVID-19.

**Table 1** - Characterization of patients on mechanical ventilation with and without pneumonia.

	Total		With VAP		Without VAP		P-value
	N	%	N	%	N	%	
<b>General features</b>							
<b>Sex</b>							
Feminine	188	44,20	10	32,30	178	45,20	<b>0,160</b>
Masculine	237	55,80	21	67,70	216	54,80	
<b>Age group</b>							
Up to 60 years	94	22,10	8	25,90	86	21,90	<b>0,600</b>
60 years or older	331	77,90	23	74,10	308	78,10	
<b>Alcohol use</b>							
Non-alcoholic	391	92,00	28	90,30	363	92,10	<b>0,720</b>
Alcoholic	34	8,00	3	9,70	31	7,90	
<b>Smoking</b>							
Non-smoker	349	82,10	22	71,00	327	83,00	<b>0,090</b>
Smoker	76	17,90	9	29,00	67	17,00	
<b>Mechanical ventilation</b>							
<b>Mechanical ventilation events</b>							
1 event	331	77,90	21	67,80	310	78,70	<b>0,200</b>
2 events	76	17,90	7	22,60	69	17,50	
3 or more events	18	4,20	3	9,70	15	3,80	
<b>Mechanical ventilation time</b>							
2 to 10 days	270	63,50	6	19,40	264	67,00	<b>&lt; 0,001</b>
10 to 14 days	50	11,80	6	19,40	44	11,20	
14 or more days	105	24,70	19	61,30	86	21,80	
<b>Hospital conduct</b>							
<b>Type of hospitalization</b>							
Clinical	315	74,10	23	74,20	292	74,10	<b>0,300</b>
Elective surgical	53	12,50	4	12,90	49	12,40	
Emergency surgery	48	11,30	2	6,50	46	11,70	
Coronary	9	2,10	2	6,50	7	1,80	
<b>Readmission</b>							
Not readmitted	372	87,50	30	96,80	342	86,80	<b>0,110</b>
Readmitted	53	12,50	1	3,20	52	13,20	
<b>Health conditions</b>							
<b>Renal replacement therapy</b>							
No	222	52,20	14	45,10	208	52,80	<b>0,410</b>
Yes	203	47,80	17	54,90	186	47,20	
<b>Non-dialytic chronic renal failure</b>							
No	391	92,00	29	93,50	362	91,90	<b>0,740</b>
Yes	34	8,00	2	6,50	32	8,10	
<b>Congestive heart failure</b>							
No	396	93,20	28	90,30	368	93,40	<b>0,510</b>
Yes	29	6,80	3	9,70	26	6,60	
<b>Chronic coronary insufficiency</b>							
No	412	96,90	29	93,50	383	97,20	<b>0,250</b>
Yes	13	3,10	2	6,50	11	2,80	
<b>Chronic atrial fibrillation</b>							
No	397	93,40	29	93,50	368	93,40	<b>0,970</b>
Yes	28	6,60	2	6,50	26	6,60	
<b>Systemic arterial hypertension</b>							
No	187	44,00	9	29,00	178	45,20	<b>0,080</b>
Yes	238	56,00	22	71,00	216	54,80	
<b>Type 1 Diabetes Mellitus</b>							
No	396	93,20	30	96,80	366	92,90	<b>0,410</b>
Yes	29	6,80	1	3,20	28	7,10	



	Total		With VAP		Without VAP		P-value
	N	%	N	%	N	%	
<b>Type 2 Diabetes Mellitus</b>							
No	345	81,20	18	58,10	327	83,00	< 0,001
Yes	80	18,80	13	41,90	67	17,00	
<b>Nutritional status</b>							
Not obese	386	90,80	26	83,90	360	91,40	0,160
Obese	39	9,20	5	16,10	34	8,60	
<b>Non-terminal Chronic obstructive pulmonary disease</b>							
No	407	95,80	27	87,10	380	96,40	0,050
Yes	18	4,20	4	12,90	14	3,60	
<b>Cancer</b>							
No	360	84,70	29	93,50	331	84,00	0,160
Yes	65	15,30	2	6,50	63	16,00	
<b>Hemoderivatives</b>							
No	213	50,10	12	38,70	201	51,00	0,190
Yes	212	49,90	19	61,30	193	49,00	
<b>Sepsis</b>							
Admitted with sepsis	179	42,10	10	32,30	169	42,90	0,250
<b>Covid-19</b>							
ICU for other causes	370	87,10	22	71,00	348	88,30	< 0,001
Exclusive ICU for Covid-19	55	12,90	9	29,00	46	11,70	

**Legends:** VAP (Ventilator-associated pneumonia), ICU (Intensive Care Units), Test: Chi-square; n = number of participants.

**Source:** Schrioder RP, et al., 2023.

Most patients with ventilator-associated pneumonia displayed mechanical ventilation time higher than 14 days and systemic arterial hypertension. For those without VAP, a statistically significant association was found for MV time between 2 to 10 days and SAH. The **Table 2** demonstrates variables associated with pneumonia caused by mechanical ventilation. It was observed that there is a dose-response relationship with MV time and the risk of pneumonia: the longer in this condition, the greater the probability of presenting pneumonia. Patients with DM2 were more likely to present VAP even after statistical adjustment.

**Table 2** - Measures of association with ventilator-associated pneumonia by unadjusted odds ratio.

	Gross OR	CI (95%)	OR Ajusted	CI (95%)
<b>General features</b>				
<b>Sex</b>				
Feminine				
Masculine	1,73	0,79 - 3,77		
<b>Age group</b>				
Up to 60 years	1	1		
60 years or older	0,81	0,35 - 1,86		
<b>Alcohol use</b>				
Non-alcoholic	1	1		
Alcoholic	1,25	0,36 - 4,36		
<b>Smoking</b>				
Non-smoker	1	1		
Smoker	2,00	0,88 - 4,53		
<b>Mechanical ventilation</b>				
<b>Mechanical ventilation events</b>				
1 event	1	1		
2 events	1,50	0,61 - 3,66		
3 or more events	2,95	0,79 - 11,01		
<b>Mechanical ventilation time</b>				
2 to 10 days	1	1	1	1
10 to 14 days	6,00	1,85 - 19,44	6,94	1,99 - 24,42
14 or more days	9,72	3,76 - 25,12	7,15	2,78 - 20,94

	Gross OR	CI (95%)	OR Adjusted	CI (95%)
<b>General features</b>				
<b>Type of hospitalization</b>				
Clinical	1	1		
Elective surgical	1,04	0,34 - 3,13		
Emergency surgery	0,55	0,13 - 2,42		
Coronary	3,63	0,71 - 18,47		
<b>Readmission</b>				
Not readmitted	1	1		
Readmitted	0,22	0,03 - 1,64		
<b>Health conditions</b>				
<b>Renal replacement therapy</b>				
No	1	1		
Yes	1,36	0,65 - 2,83		
<b>Non-dialytic chronic renal failure</b>				
Non-dialysis non-CRF patient	1	1		
Patient with non-dialysis CRF	0,78	0,18 - 3,42		
<b>Congestive heart failure</b>				
Patient without CHF	1	1		
Patient with CHF	1,52	0,43 - 5,32		
<b>Chronic coronary insufficiency</b>				
Patient without CCI	1	1		
Patient with CCI	2,4	0,51 - 11,35		
<b>Chronic atrial fibrillation</b>				
Patient without chronic atrial fibrillation	1	1		
Patient with chronic atrial fibrillation	0,98	0,22 - 4,32		
<b>Systemic arterial hypertension</b>				
Patient without SAH	1	1		
Patient with SAH	2,01	0,9 - 4,49		
<b>Type 1 Diabetes Mellitus (DM1)</b>				
Individual without DM1	1	1		
Individual with DM1	0,44	0,06 - 3,31		
<b>Type 2 Diabetes Mellitus (DM2)</b>				
Individual without DM2	1	1	1	1
Individual with DM2	3,52	1,65 - 7,54	2,7	1,13 - 6,34
<b>Nutritional status</b>				
Not obese	1	1		
Obese	2,04	0,73 - 5,64		
<b>Non-terminal chronic obstructive pulmonary disease</b>				
Patient without non-terminal COPD	1	1	1	1
Patient with non-terminal COPD	4,02	1,24 - 13,06	2,75	0,64 - 9,87
<b>Cancer</b>				
Patient without cancer	1	1		
Cancer patient	0,36	0,08 - 1,56		
<b>Hemoderivatives</b>				
No	1	1		
Yes	1,65	0,78 - 3,49		
<b>Sepsis</b>				
Admitted with sepsis	1	1		
No sepsis	0,63	0,29 - 1,38		
<b>Covid-19</b>				
Admitted to ICU for other causes	1	1	1	1
Admitted to exclusive ICU for Covid-19	3,09	1,34 - 7,13	2,07	0,75 - 5,38

**Legend:** ICU (Intensive Care Units). **Source:** Schrioder RP, et al., 2023.

## DISCUSSION

In the present study it was observed that mechanical ventilation time, the presence of comorbidities, and the hospitalization in the exclusive intensive care unit for COVID-19 were associated with the risk of VAP. A total of 435 people participated in the study, in which 31 patients developed ventilator-associated pneumonia, where 6 patients used MV during approximately 10 days and 19 patients used more than 14 days. Some patients with COVID-19 infection were hospitalized and were diagnosed with VAP. Regarding comorbidities,

chronic obstructive pulmonary disease and type 2 diabetes mellitus were the most prevalent in the sample group. The epidemiological profile of patients demonstrated no significantly higher overall incidence of healthcare associated infections in hospitalized older patients (aged  $\geq 60$  years) when compared with patients more younger than 60 years.

In contrast, Zhao X, et al. (2020) showed an increase of healthcare associated-infections in elderly inpatients  $\geq 60$  compared to non-elderly inpatients  $< 60$  years, it was attributed to the higher rates of comorbidities and special medical procedures in the elderly group. Some studies observed another independent risk factor for ventilator-associated pneumonia is the sex, male patients are more sensible to development the VAP (CUI JB, et al., 2020; DANANCHÉ C, et al., 2007). Similar results were found by researcher Nseir and collaborators (NSEIR S, et al., 2021), which concluded that obesity has no significant impact on the incidence of ventilator-associated pneumonia.

In the present study it was verified that the duration of mechanical ventilation had a significant influence on the occurrence of ventilator-associated pneumonia, as well as, in the study performed previously, which observed that on the fifteenth day of hospitalization, pneumonia was diagnosed in many intubated patients (KÓZKA M, et al., 2020).

One factor that may explain the increased risk over time is that the artificial airway established by mechanical ventilation alters the mucosal defense function of the normal airway. Swallowing ability and the ability to clear cilia for mucus are weakened, and bacteria enter the lower respiratory tract directly or pass through the space between the wall of the tracheal tube and the airway, leading to infection (WU D, et al., 2019).

The incidence of VAP is also directly related to the type of invasive device in the airways of patients. In the research by Kózka M, et al. (2020) pneumonia was more common in patients intubated (6%) than in those with a tracheostomy (less than 0.5%). To minimize the risk of oropharyngeal bacteria entering the lower respiratory tract through the endotracheal tube cuff, preventive measures include minimizing the administration of sedative and paralytic agents that suppress cough and other protective mechanisms of the body. Additionally, it is important to maintain the endotracheal cuff pressure above 20 cmH<sub>2</sub>O (ATS, 2005).

There was a higher risk of infection in the 80 subjects with type 2 diabetes mellitus than in those without this disease. Furthermore, half of patients with ventilator-associated pneumonia presented type 2 diabetes mellitus. However, the relationship between pneumonia and type 2 diabetes mellitus has not been extensively investigated in the literature, but type 2 diabetes mellitus has been recently reported as an independent predictor of VAP (LOPEZ-DE-ANDRES A, et al., 2021).

A possible explanation for the higher occurrence of VAP in diabetic patients is related to the clinical characteristics of this group associated with poor glycemic control, microaspirations, increased disease severity and duration of mechanical ventilation, according to Razazi K, et al. (2023). Furthermore, the incidence of pneumonia associated with mechanical ventilation was higher in diabetic men when compared to diabetic women, in all age groups, in addition to having a worse prognosis, according to Diling Wu, et al (2019).

Corroborating with the present study, in the systematic review and meta-analysis it was observed that chronic obstructive pulmonary disease is another important risk factor for the development of nosocomial infections of the lower respiratory tract (YIN M and LIU M, 2020).

Patients with chronic obstructive pulmonary disease (COPD) often experience exacerbations and infections as part of the natural progression of the disease. In such cases, the management typically involves assisted ventilation and hospitalization. The incidence of ventilator-associated pneumonia in intubated chronic obstructive pulmonary disease patients range from 18.6% to 60% and affect the outcomes of hospitalized patients (YIN M and LIU M, 2020). Specifically, in this investigation, 18 individuals had chronic obstructive pulmonary disease as a comorbidity and 4 patients developed VAP.

One of the possible explanations is that the immune system of chronic obstructive pulmonary disease in patients can be weakened by prolonged use of corticosteroids, reduced mucociliary clearance, prolonged



duration of invasive mechanical ventilation (muscle weakness), and high incidence of microaspiration (YIN M and LIU M, 2020). In addition, the association of chronic obstructive pulmonary disease and VAP significantly increases mortality and length of stay in the ICU (NÚÑEZ SA, et al., 2021).

Regarding the assessment of the presence of ventilator-associated pneumonia in patients with COVID-19, there was statistical relevance in the crude model; however, this significance was lost after adjustment. In a retrospective observational study conducted at a university hospital in the United Kingdom, a hazard ratio of 2.1 was reported, compared with non-COVID-19 patients, and a 79% incidence of VAP similarly, a cohort study carried out by Baccolini et al. Baccolini V, et al. (2005) reported that the incidence of VAP was significantly higher in the Severe Acute Respiratory Syndrome Coronavirus 2 positive patient group.

Grasselli and collaborators (2021), in a retrospective study including 774 critically ill patients admitted to the ICU for COVID-19, reported that the majority were men, mostly elderly, and with the presence of various comorbidities (hypertension, diabetes, chronic obstructive pulmonary disease), requiring invasive MV in almost 90% of cases. Of the Healthcare-associated Infections analyzed by the group, VAP was the most common infection (51%) and the most common one associated with septic shock (54%). Acute Respiratory Distress Syndrome is an established risk factor for ventilator-associated pneumonia. Patients with COVID-19 experience a complex dysregulation of their immune function, with features of hyperinflammatory activation and organ damage, as well as impaired antimicrobial functions (MAES M, et al., 2021).

Among the factors that explain the link between the incidence of ventilator-associated pneumonia and patients infected with COVID-19 are the long duration of invasive ventilatory support, the use of immunosuppressive therapy, such as corticosteroids, and the high rates of acute respiratory distress in these patients. Apart from, it is worth noting that SARS-CoV-2 itself causes the formation of lung lesions, together with the interaction between bacteria and viruses in the lung microbiota, which may corroborate the incidence of VAP. Authors such as Razazi K, et al (2023), suggest the hypothesis that specific mutations in SARS-CoV-2, in the spike protein, or in other viral proteins may justify such an association, since the composition of the microbiota of the upper respiratory tract changes significantly and proportional to the severity of the COVID-19 infection.

Among the limitations of our study, we highlight that the protocols related to hospital care for patients on mechanical ventilation can change between centers and have heterogeneous populations. In addition, the retrospective design of this study may introduce inherent biases to this type of research. Some variables and confounding factors may not have been considered because of the nature of the design of this study. In contrast, the research is important to understand the importance of controlling for VAP for the logistics of the service and hospital clinical practice, given that patients who are more susceptible due to their morbidities and profile need more attention during monitoring. Thus, patients with longer MV time and those with diabetes, chronic obstructive pulmonary disease or COVID-19 need more intensive follow-up.

## CONCLUSION

The identification of ventilator-associated pneumonia risk factors plays an important role in guiding clinical prevention. Based on our findings, patients with increased mechanical ventilation time, comorbidities such as chronic obstructive pulmonary disease and type 2 diabetes mellitus, and those hospitalized due to infection caused by COVID-19 are at high risk of developing VAP. Multicenter studies that address global risk factors for the development of ventilator-associated pneumonia are necessary, especially in the scenario of the COVID-19 pandemic. In order to effectively guide clinical prevention measures against VAP, it is crucial to enhance efforts aimed at preventing health issues, particularly those associated with COPD and diabetes. Regarding COPD, smoking is widely recognized as a significant risk factor, in fact, the most significant one. The study was conducted during a period when COVID-19 vaccines were not yet available. It is evident that the disease had a significant impact during that time. Moreover, for the prevention of VAP, it is essential to implement stringent assistance protocols in ICUs. These protocols should ensure precise indications for both intubation and early extubation, as well as proper management of critically ill patients.

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