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Rate of orotracheal extubation failure in a sample of cancer patients

Falência da extubação orotraqueal em uma amostra de pacientes oncológicos

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ABSTRACT: *Objective*: To classify the rate of orotracheal extubation failure (EF) in a sample of cancer patients and to evaluate the association between FE, mortality index and clinical events. *Methods:* A retrospective descriptive study was carried out to collect data from the medical records from March 2012 to May 2017 involving 1,088 medical records that required invasive ventilatory support during ICU admission. *Results:* 39 patients required early reintubation during ICU stay, in which the EF incidence rate was 3.6%, mean age 59.6 years, with a predominance of males, with a high incidence of respiratory complications and pneumonia. The mean reintubation time after extubation was 16.5 ± 14.0 h, with respiratory fatigue (48.7%) being the main reason for reintubation, and the main outcome was death (56.4%). Three univariate and multivariate regression models were used for the reintubation time, days of ICU stay (R2: 61.7%) and death (R2: 78.8), which demonstrated independent variables capable of predicting change in the models studied. The model that best responded to our goal was death with explained variance of 78.8%. *Conclusion:* Our findings demonstrated a low incidence of extubation failure and the importance of identifying specific risk factors for the cancer population, predicting that such factors could influence the need for reintubation.

Keywords: Physiotherapy; Extubation; Intensive care; Oncology; Intensive care units; Weaning; Intubation.

RESUMO: *Objetivo:* Classificar a taxa de falha de extubação orotraqueal (FE) em uma amostra de pacientes oncológicos e avaliar a associação entre FE, índice de mortalidade e eventos clínicos. *Métodos:* Estudo descritivo, retrospectivo, para coleta de dados do prontuário no período de março de 2012 a maio de 2017 envolvendo 1.088 prontuários que necessitaram suporte ventilatório invasivo durante a internação na UTI. *Resultados:* 39 pacientes necessitaram de reintubação precoce durante a estadia em UTI, no qual a taxa de incidência de FE foi de 3,6%, média de idade de 59,6 anos com predomínio do sexo masculino, com uma alta incidência de complicações respiratórias e pneumonia. O tempo médio de reintubação após a extubação foi de 16,5 ± 14,0 h, tendo como principal motivo da reintubação fadiga respiratória (48,7%) e o principal desfecho foi óbito (56,4%). Foram elaborados três modelos de regressão univariada e multivariada para o tempo de reintubação, dias de internação na UTI (R^2: 61,7%) e o óbito (R^2: 78,8) que demonstrou variáveis independentes capazes de predizer a mudança nos modelos estudados. O modelo que melhor respondeu à nossa meta foi óbito com variância explicada de 78,8%. *Conclusão:* Nossos achados demonstraram uma baixa incidência da falência na extubação e a importância da identificação de fatores de risco específicos para a população oncológica, predizendo que tais fatores poderiam influenciar a necessidade de reintubação.

Palavras-chave: Fisioterapia; Extubação; Terapia intensiva; Oncologia; Unidades de terapia intensiva; Desmame; Intubação

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INTRODUCTION

Mechanical ventilation (MV) is a method of ventilatory support that involves either partial or total replacement of spontaneous ventilation. Positive pressure facilitates the delivery of oxygen to the lungs by equipment such as artificial mechanical ventilators. The aim of MV is to maintain adequate gas exchange, relieve the respiratory muscles, allow specific interventions, and reduce lung injury[1,2] .

The indications for MV include respiratory failure, inadequate blood oxygen and carbon dioxide levels, cardiorespiratory arrest, respiratory muscle weakness, or unstable breathing commands[1].

Intensive care units (ICUs) specific to patients with cancer may have particular requirements because the therapies used to treat neoplasia can cause clinical complications, side effects, compromised organic functions, and general weakness; in some cases, patients with cancer require MV, which is therefore a routine procedure in ICUs[3,4].(

If a patient no longer requires MV within 48 hours of extubation, their weaning from MV is considered successful. Intolerance to the spontaneous breathing test (SBT) after extubation is defined as weaning failure[2]. In most patients, MV weaning occurs successfully, but some have extubation failure (EF) and require reintubation after 24–72 hours[5]. Specifically, EF occurs in 30%–40% of patients[6] and is associated with prolonged stay in ICUs and hospitals, as well as higher rates of tracheostomy and mortality[7-10].

There are some requirements for initiating weaning, such as a favorable clinical status, resolution or stabilization of the underlying disease, hemodynamic stability, and the ability to breathe spontaneously. As such, before weaning is initiated, weaning predictive indexes are applied[2].

Several researchers have suggested that EF is associated with a high mortality rate, although this remains unclear. Moreover, although some studies have evaluated failure of orotracheal extubation and its correlation with mortality[5,6,11-13], little is known about EF in cancer patients[14]. For this reason, a data survey must be conducted to assess whether the need for reintubation is an important predictor of prognosis and mortality rate.

OBJECTIVES

To assess the failure rate of orotracheal extubation in a sample of patients with cancer from a teaching hospital in São Paulo, as well as to ascertain the main clinical outcomes in patients who required reintubation, the present study aimed to evaluate whether EF was associated with mortality rate or clinical events.

METHODOLOGY

Study Design

This was a descriptive, retrospective study, which was carried out by reviewing the clinical history and analyzing the medical records of patients who required early intubation at the ICU of AC Camargo, which is a teaching hospital specializing in cancer treatment located in the city of São Paulo. The hospital has 55 adult ICU beds. We collected demographic data (sex, age, weight, and height), cancer diagnosis, comorbidities, reason for admission to the ICU, date of intubation, reason for intubation, success on the SBT, date of extubation, date of reintubation, reason for reintubation, use of non-invasive ventilation (NIV) after extubation, sedative drugs, vasoactive drugs, chemotherapy during the orotracheal intubation (OI) period, complications after reintubation (pulmonary, cardiovascular, and neurological), and outcomes after early reintubation.

Sample

All patients who required reintubation during their ICU stay between March 2012 and December 2017 were included. All data were collected from patients' electronic medical records and entered into a digitalized electronic spreadsheet (Excel®, Microsoft Office). The study was approved by the Research Ethics Committee (Protocol 1.849.306), and informed consent was not required for data analysis.

Exclusion criteria

The following exclusion criteria were applied: age < 18 years, medical records that did not mention the need for reintubation, insufficient data, OI period of < 48 hours.

Statistical analysis

The variables of interest collected were inserted into a digitalized electronic spreadsheet (Excel) and standardized. They were then statistically analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0.

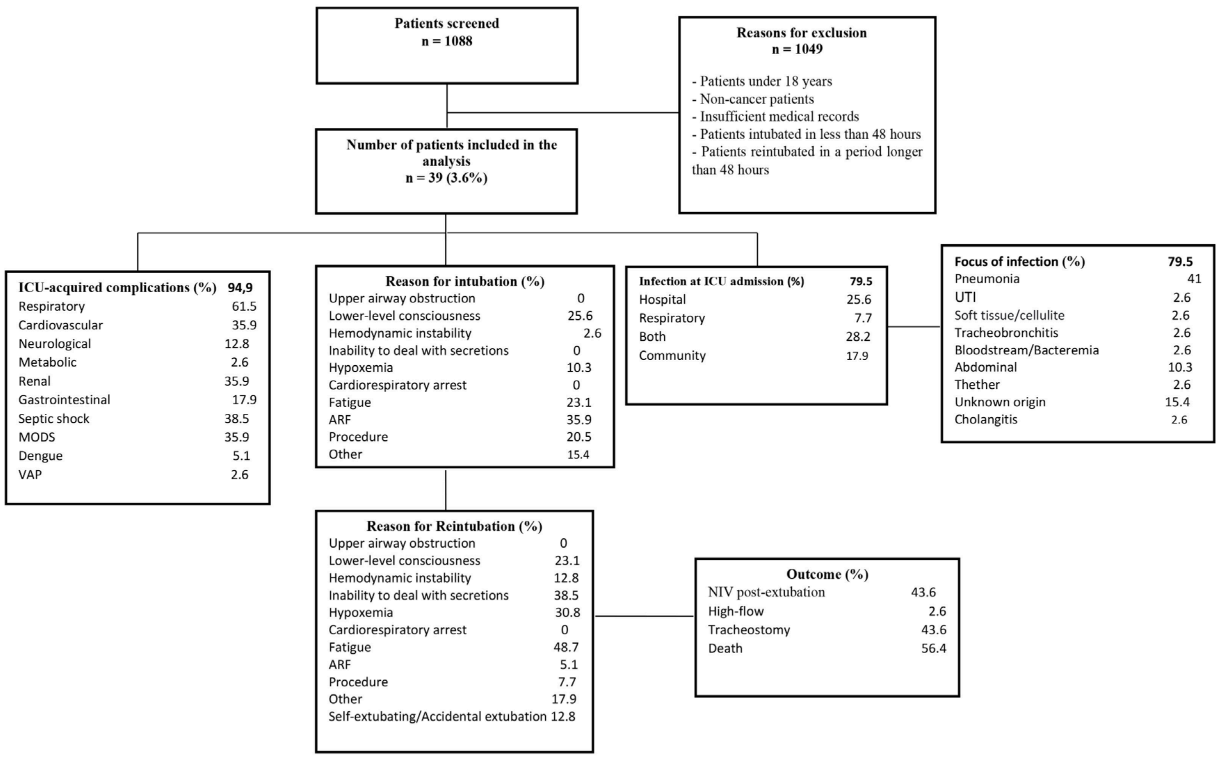
A descriptive analysis was performed to determine the characteristics of the study population, with categorical variables presented as absolute numbers and percentages. Continuous variables that showed normal distribution were expressed as mean and standard deviation, whereas those that did not show normal distribution were expressed as median and interquartile range.

Both univariate and multivariate regression models were incorporated to verify whether the independent variables were associated with the dependent variables. The independent variables were as follows: sex, age, body mass index, comorbidities, cancer diagnosis, reason for admission to the ICU, presence of infections upon admission to the ICU, location of such infections, reason for initial OI, reason for early reintubation, complications, surgical approaches during the ICU stay, use of chemotherapy, vasoactive and antiarrhythmic drugs, outcome after early reintubation, such as the use of NIV after extubation and the need for tracheostomy, while the dependent variables were as follows: time of reintubation, length of ICU stay in days, and death.

Categorical variables were coded as dummy variables. In the sequence, all variables that showed a p-value ≤ 0.20 in the univariate linear regression analysis were included in the multivariate regression model. The multivariate regression analysis used the backward elimination method, which was considered complete when all variables reached a p-value < 0.05. The assumptions of linearity and multicollinearity were not violated in either model.

RESULTS

We analyzed the medical records of 1088 patients who underwent OI and remained for more than 48 hours on invasive ventilatory support between March 2012 and Dec 2017. Of these, 1049 patients were excluded for specific reasons, as shown in the flowchart in Figure 1. The final sample thus consisted of 39 (3.6%) patients who underwent failed extubation during their stay in the ICU and required reintubation within 48 hours. Table 1 shows the anthropometric and clinical characteristics of the study population.



Subtitle: ARF: Acute respiratory failure; n: number of patients; ICU: Intensive care unit; MODS: Multiple Organ Dysfunction Syndrome; NIV: Non--invasive ventilation; UTI: Urinary tract infection; VAP: Ventilator-associated pneumonia. Values are expressed as a percentage

Figure 1: Study of flowchart

Table 1. General characteristics of patients

Variables	n = 39
Age	59.5 ± 13.3
Sex	
Female	14 ± 35.9
Male	25 ± 64.1
BMI	26.1 ± 5.1
ECOG	1.47 ± 1.19
Comorbidities, n (%)	35 (89.7)
Respiratory	6 (15.4)
Cardiovascular	23 (59)
Neurological	6 (15.4)
Metabolic	16 (41)
Renal	5 (12.8)
Gastrointestinal	2 (5.1)
Smoker / ex-smoker	21 (53.8)
Alcoholic / ex-alcoholic	4 (10.3)
Diagnosis of ICU admission, n (%)	
Postoperative monitoring	5 (12.8)
Lower-level consciousness	5 (12.8)
Hypovolemic or hemorrhagic shock	2 (5.1)
ARF	11 (28.2)
Sepsis, Septic shock	11 (2.8)
Arrhythmia	2 (5.1)
Agitation, state of mental confusion	2 (5.1)
Other	1 (2.6)
Clinical or Surgical Patient, n (%)	
Clinical	32 (82.1)
Surgical	7 (17.9)
Hematological or Solid Tumor, n (%)	
Hematological	6 (15.4)
Solid	33 (84.6)
Disease progression	22 (56.4)
In cancer treatment	30 (76.9)
Chemotherapy treatment	29 (74.4)
ICU Surgical Approaches	26 (66.7)
Use of Vasoactive Drugs	34 (87.2)
Use of Antiarrhythmic Drugs	12 (30.8)
State of mental confusion	33 (84.6)
Reintubation time (hours)	16.5 ± 14.0
Length of ICU stay (days)	22.4 ± 13.5

Subtitle: ARF: Acute respiratory failure; BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; ICU: Intensive care unit; n: number of patients.
Categorical variables are expressed as absolute numbers and percentages (%) and continuous variables are expressed as mean ± standard deviation; median (interquartile range) *.

Reintubation time

The patients were reintubated at an average of 16.5 ± 14.0 hours after extubation. Table 2 presents the results of the univariate and multivariate regression models for reintubation time. The final equation to predict the intubation time, derived from the multivariate model, was as follows:

Reintubation time = 11.08 + (0.32 × CT treatment) + (-0.38 × self-extubation or accidental extubation).

A value of 1 was assigned if patients were undergoing chemotherapy or if they showed self-extubation or accidental extubation. Patients with none of these criteria were given a value of 0. For example, comparing a patient who underwent OI with a patient who did not undergo chemotherapy, both of whom had self-extubation/extubation-accidental, the difference in reintubation time was only 0.31 hours (18 minutes).

Days in ICU

The patients stayed a mean of 22.4 ± 13.5 days in the ICU. Table 3 presents the results of the univariate and multivariate regression models analyzing the length of the ICU stay in days. The final equation derived from the multivariate model to predict the number of hospitalization days was as follows:

Days in ICU = 34.23 + (-0.42 × sex) + (0.27 × fatigue) + (-0.25 × self-extubation or accidental extubation) + (0.46 × tracheostomy)

A sex value of 1 was assigned to females while 2 was assigned to males; similarly, a value of 1 was assigned for the events, while 0 was assigned when no events took place. For example, a female patient who suffered reintubation due to fatigue and her outcome was submitted to tracheostomy compared to a male patient who suffered reintubation for the same reason and with the same outcome the difference was only 0.42 days of hospitalization in ICU.

Death

Of the patients included in the present study, an average of 54.6% died as the final outcome. Table 4 shows the results of univariate and multivariate regression models for death. The final equations derived from the multivariate model to predict death after reintubation are as follows:

Death

Surgical patient= 0.17 + (0.26 × ECOG) + (-0.60 × surgical patient) + (0.63 chemotherapy treatment) + (0.32 × postoperative monitoring) + (0.39 × use of vasoactive drugs).

Clinical Patient= 0.17 + (0.26 x ECOG) + (-0.60 × clinical patient) + (0.63 chemotherapy treatment) + (0.32 × hypovolemic or hemorrhagic shock) + (0.39 × use of vasoactive drugs).

By performing a comparison of a surgical patient or a clinical patient who underwent an assessment of the impact of the disease on their daily activities using the Eastern Cooperative Oncology Group (ECOG) scale, we obtained a score of 1 (one) on the scale and another who obtained a value of 4; considering the other variables of both patients a value of 1, the difference between them was 0.24, that is, on a scale between 0 and 1, these patients would evolve with a 0.24 probability of the outcome of death.

Table 2. Univariate and Multivariate regression analysis for the Reintubation time

	Univariate Regression				Multivariate Regression		
					R^2: 23,5%	F: 5,07	Constancy: 11,087
Independent variables	**Beta (IC to 95%)**	**p**	**R^2(%)**	**F**	**Beta (IC95%)**	**p**	
Age	-0,262 (- 0,653 a 0,081)	0,122*	0,069	2,511			
Sex	-0,003 (-10,256 a 10,555)	0,984	0	0			
BMI	-0,012 (- 1,049 a 0,977)	0,942	0	0,005			
ECOG	-0,053 (- 4,460 a 3,408)	0,786	0,003	0,075			
Comorbidities	-0,174 (- 25,692 a 8,424)	0,311	0,03	1,058			
Clinical or Surgical Patient	0,340 (0,450 a 24,611)	0,042*	0,116	4,443			
Hematological Tumor	-0,088 (-17,295 a 10,283)	0,609	0,008	0,267			
Solid Tumor	0,088 (-10,283 a 17,295)	0,609	0,008	0,267			
Disease progression	0,168 (- 4,833 a 14,074)	0,328	0,028	0,987			
In cancer treatment	-0,034 (-12,644 a 10,373)	0,842	0,001	0,04			
Chemotherapy treatment	0,299 (-1,079 a 20,024)	0,077*	0,089	3,328	0,316 (0,200 a 19,871)	0,046**	
Diagnosis of ICU admission							
Postoperative monitoring	0,314 (-0,730 a 28,194)	0,062*	0,099	3,723			
Lower-level consciousness	-0,051 (-15,841 a 11,810)	0,769	0,003	0,088			
Hypovolemic or hemorrhagic shock	-0,214 (-33,256 a 7,575)	0,210*	0,046	1,634			
ARF	0,065 (-8,432 a 12,309)	0,706	0,004	0,144			
Sepsis, Septic shock	0,013 (-10,275 a 11,100)	0,938	0	0,006			
Arrhythmia	-0,121 (-27,985 a 13,510)	0,483	0,015	0,503			
Agitation, state of mental confusion	-0,105 (-37,717 a 20,227)	0,544	0,011	0,376			
Others	-0,142 (-40,670 a 17,008)	0,410	0,02	0,695			
Infection at ICU admission	-0,066 (-14,372 a 9,767)	0,701	0,004	0,15			
ICU Surgical Approaches	-0,028 (-10,752 a 9,174/)	0,873	0,001	0,026			
Use of Vasoactive Drugs	-0,007 (-14,111 a 13,575)	0,969	0	0,002			
Use of Antiarrhythmic Drugs	-0,104 (-13,449 a 7,224)	0,545	0,011	0,374			
State of mental confusion	0,110 (-19,966 a 10,315)	0,522	0,012	0,42			
Reason for Reintubation							
Upper airway obstruction							
Lower-level consciousness	-0,043 (-12,395 a 9,697)	0,806	0,002	0,062			
Hemodynamic instability	0,060 (-11,440 a 16,196)	0,729	0,004	0,122			
Inability to deal with secretions	-0,023 (-10,455 a 9,181)	0,896	0,001	0,017			
Hypoxemia	0,054 (-8,561 a 11,721)	0,753	0,003	0,1			
Cardiorespiratory arrest							
Fatigue	0,303 (-0,813 a 17,467)	0,073*	0,092	3,428			
ARF	0,008 (-20,417 a 21,382)	0,963	0	0,002			
Procedure	0,152 (-11,573 a 29,745)	0,378	0,023	0,799			
Others	-0,037 (-13,362 a 10,814)	0,832	0,001	0,046			
Self-extubation/Accidental extubation	-0,368 (-27,488 a -1,744)	0,027*	0,135	5,325	-0,383 (-27,513 a -2,883)	0,017**	
Outcome							
NIV postextubation	0,270 (-1,970 a 17,053)	0,116*	0,073	2,602			
Tracheostomy	-0,135 (-13,290 a 5,801)	0,431	0,018	0,636			

Subtitle: ARF: Acute respiratory failure; BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; ICU: Intensive care unit; NIV: Non-invasive ventilation
Univariate regression: values of $p \leq 0.20$; **Multivariate regression:** ** statistically significant values

Table 3: Univariate and Multivariate regression analysis for ICU admission days

Univariate Regression					Multivariate Regression		
					R²: 61,7%	F: 13,670	Constancy: 34,228
Independent variables	**Beta (IC to 95%)**	**p**	**R² (%)**	**F**	**Beta (IC95%**	**p**	
Age	-0,150 (-0,487 a 0,182)	0,362	0,022	0,851			
Sex	-0,486 (-21,708 a -5,457)	0,002*	0,237	11,472	-0,425 (-18,051 a -5,665)	0,000**	
BMI	0,106 (-0,600 a 1,161)	0,522	0,011	0,417			
ECOG	-0,241 (-6,877 a 1,373)	0,183*	0,058	1,856			
Comorbidities	-0,109 (-19,425 a 9,810)	0,509	0,012	0,444			
Clinical or Surgical Patient	0,224 (-3,503 a 19,155)	0,170*	0,05	1,959			
Hematological Tumor	0,087 (-9,091 a 15,545)	0,599	0,008	0,282			
Solid Tumor	-0,087 (-15,545 a 9,091)	0,599	0,008	0,282			
Disease progression	-0,172 (-13,512 a 4,213)	0,295	0,03	1,13			
In cancer treatment	0,045 (-9,145 a 12,011)	0,785	0,002	0,075			
Chemotherapy treatment	0,107 (-6,883 a 13,434)	0,518	0,011	0,427			
Diagnosis of ICU admission							
Postoperative monitoring	0,091 (-9,660 a 16,919)	0,583	0,008	0,306			
Lower-level consciousness	-0,041 (-14,980 a 11,686)	0,804	0,002	0,063			
Hypovolemic or hemorrhagic shock	-0,242 (-34,314 a 4,936)	0,138*	0,059	2,3			
ARF	-0,020 (-10,519 a 9,305)	0,902	0	0,015			
Sepsis, Septic shock	0,031 (-8,997 a 10,822)	0,853	0,001	0,035			
Arrhythmia	-0,034 (-22,255 a 18,174)	0,839	0,001	0,042			
Agitation, state of mental confusion	0,175 (-9,307 a 30,523)	0,287	0,031	1,165			
Others	0,007 (-27,645 a 28,803)	0,967	0	0,002			
Infection at ICU admission	-0,315 (-20,944 a 0,025)	0,051*	0,099	4,086			
ICU Surgical Approaches	0,405 (-2,846 a 20,154)	0,011*	0,164	7,25			
Use of Vasoactive Drugs	0,196 (-5,245 a 20,927)	0,232	0,038	1,474			
Use of Antiarrhythmic Drugs	0,032 (-8,726 a 10,596)	0,846	0,001	0,038			
State of mental confusion	0,014 (-11,849 a 12,879)	0,933	0	0,007			
Reason for Reintubation							
Upper airway obstruction							
Lower-level consciousness	-0,163 (-15,636 a 5,258)	0,321	0,027	1,013			
Hemodynamic instability	-0,173 (-20,067 a 6,220)	0,293	0,03	1,139			
Inability to deal with secretions	-0,022 (-9,768 a 8,568)	0,895	0	0,018			
Hypoxemia	0,443 (4,185 a 21,518)	0,005*	0,196	9,028			
Cardiorespiratory arrest							
Fatigue	0,286 (-0,884 a 16,221)	0,077*	0,082	3,301	0,272 (1,457 a 13,141)	0,016**	
ARF	-0,129 (-27,895 a 12,219)	0,434	0,017	0,627			
Procedure	-0,088 (-21,121 a 12,232)	0,592	0,008	0,292			
Others	-0,225 (-19,172 a 3,484)	0,169*	0,051	1,968			
Self-extubation/Accidental extubation	-0,270 (-23,672 a 2,025)	0,096*	0,073	2,914	-0,253 (-18,812 a -1,469)	0,023**	
Outcome							
NIV postextubation	-0,018 (-9,660 a 8,685)	0,915	0	0,012			
Tracheostomy	0,574 (8,126 a 22,864)	0,000*	0,329	18,151	0,460 (6,428 a 18,396)	0,000**	

Subtitle: ARF: Acute respiratory failure; BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; ICU: Intensive care unit; NIV: Non-invasive ventilation
Univariate regression: values of p≤ 0.20; Multivariate regression: ** statistically significant values.

Table 4: Univariate and Multivariate Regression Analysis for death

Univariate Regression					Multivariate Regression		
					R^2: 78,8%	F: 15,531	Constancy: 0,166
Independent variables	**Beta (IC to 95%)**	**p**	**R^2 (%)**	**F**	**Beta (IC95%)**	**p**	
Age	-0,104 (-0,016 a 0,009)	0,531	0,011	0,401			
Sex	-0,011 (-0,356 a 0,333)	0,947	0	0,005			
BMI	0,012 (-0,032 a 0,034)	0,944	0	0,005			
ECOG	0,514 (0,082 a 0,353)	0,003*	0,264	10,766	0,265 (0,023 a 0,201)	0,016**	
Comorbidities	0,044 (0,472 a 0,615)	0,792	0,002	0,071			
Clinical or Surgical Patient	-0,532 (-1,052 a - 0,323)	0,000*	0,283	14,61	-0,599 (-1,175 a 0,348)	0,001**	
Hematological Tumor	0,375 (0,091 a 0,940)	0,019*	0,14	6,048			
Solid Tumor	-0,375 (-0,940 a -0,091)	0,019*	0,14	6,048			
Disease progression	0,270 (-0,051 a 0,591)	0,096*	0,073	2,911			
In cancer treatment	-0,113 (-0,523 a 0,256)	0,492	0,013	0,481			
Chemotherapy treatment	0,431 (0,148 a 0,831)	0,006*	0,186	8,45	0,629 (0,465 a 0,976)	0,000**	
Diagnosis of ICU admission							
Postoperative monitoring	-0,436 (-1,092 a -0,202)	0,005*	0,19	8,697	0,318 (-0,013 a 0,968)	0,056**	
Lower-level consciousness	0,028 (-0,453 a 0,535)	0,867	0,001	0,029			
Hypovolemic or hemorrhagic shock	0,204 (-0,274 a 1,193)	0,212*	0,042	1,613	0,317 (0,328 a 1,478)	0,003**	
ARF	0,091 (-0,265 a 0,466)	0,58	0,008	0,311			
Sepsis, Septic shock	-0,024 (-0,393 a 0,341)	0,887	0,001	0,021			
Arrhythmia	-0,030 (-0,816 a 0,681)	0,856	0,001	0,033			
Agitation, state of mental confusion	0,204 (-0,274 a 1,193)	0,212*	0,042	1,613			
Others	0,143 (-0,587 a 1,482)	0,386	0,02	0,768			
Infection at ICU admission	0,322 (0,008 a 0,782)	0,046*	0,104	4,274			
ICU Surgical Approaches	-0,183 (-0,537 a 0,152)	0,265	0,033	1,279			
Use of Vasoactive Drugs	0,282 (-0,056 a 0,892)	0,082*	0,079	3,186	0,387 (0,281 a 0,880)	0,001**	
Use of Antiarrhythmic Drugs	0,138 (-0,206 a 0,503)	0,403	0,019	0,717			
State of mental confusion	-0,088 (-0,577 a 0,335)	0,593	0,008	0,29			
Reason for Reintubation							
Upper airway obstruction							
Lower-level consciousness	0,236 (-0,103 a 0,659)	0,148*	0,056	2,183			
Hemodynamic instability	0,028 (-0,453 a 0,535)	0,867	0,001	0,029			
Inability to deal with secretions	0,057 (-0,281 a 0,397)	0,729	0,003	0,122			
Hypoxemia	-0,198 (-0,564 a 0,138)	0,226	0,039	1,513			
Cardiorespiratory arrest							
Fatigue	0,029 (-0,301 a 0,359)	0,86	0,001	0,032			
ARF	-0,030 (-0,816 a 0,681)	0,856	0,001	0,033			
Procedure	0,060 (-0,508 a 0,730)	0,718	0,004	0,132			
Others	0,007 (-0,421 a 0,439)	0,967	0	0,002			
Self-extubation/Accidental extubation	0,182 (-0,215 a 0,756)	0,266	0,033	1,274			
Outcome							
NIV postextubation	0,017 (0,102 a 0,920)	0,92	0	0,01			
Tracheostomy	-0,166 (-0,494 a 0,163)	0,313	0,027	1,046			

Subtitle: ARF: Acute respiratory failure; BMI: body mass index; ECOG: Eastern Cooperative Oncology Group; ICU: Intensive care unit; NIV: Non-invasive ventilation. Univariate regression: values of p≤ 0.20; Multivariate regression: ** statistically significant values.

DISCUSSION

The use of MV and EF are associated with a prolonged ICU stay and are important predictive factors of prognosis and mortality. Therefore, it is important that interdisciplinary teams treating patients with cancer who undergo MV identify these factors. The present study involved patients with cancer who underwent reintubation within a 48-hour period. Most patients a comorbidity, the most prevalent of which was cardiovascular disease (59%). The prevalence of admission to the ICU was greater in clinical patients (82.1%) who were hospitalized for respiratory failure, followed by postoperative monitoring and lower-level consciousness (28%). After conducting the study and comparing it with the bibliography, we identified variables of interest to be verified and hypothesized that patients with cancer have specific and unique risk factors for EF.

Chemotherapy data were collected in the present study, with most of the population studied undergoing chemotherapy (74.4%). The most prevalent chemotherapy drugs were carboplatin (23.1%), paclitaxel (20.5%), 5-fluorouracil (15.4%), cisplatin (15.4%), etoposide (15.4%), and docetaxel (Taxotere; 10.3%). We found no studies that assessed whether EF was associated with chemotherapy. In addition, patients were treated using different chemotherapy protocols, and the cancer population was heterogeneous, although solid tumors were predominant (84.6%).

Retrospective studies[15–17] have evaluated different populations presenting with EF, dividing them into two groups: patients successfully extubated and those who presented EF. In a study by Li et al.[17], the studied population was reintubated because of airway obstruction after previous cervical surgery. Nantsupawat et al.[16] studied patients with chronic obstructive disease (COPD) who were reintubated due to respiratory failure. Finally, the study by Brown et al.[15] evaluated patients who suffered trauma and were admitted to the ICU requiring MV.

In previous, prospective studies[6,13], the impact of EF on the general population has been assessed. Thille et al.[13] compared patients undergoing planned and unplanned extubation. In a study by Epstein et al.[6], patients were allocated into two groups: surviving and non-surviving patients. These authors identified mortality associated with reintubation time and categorized patients according to the causes of EF, as follows: airway etiology (obstruction, aspiration, excess pulmonary secretions) and extrapulmonary etiology (congestive heart failure, encephalopathy, etc.).

Among the studies described, the populations that presented EF had an average age between 55 and 65 years, with a predominance of males, corroborating our findings. In addition, patients who smoked were predominant at 71.42%[17]. In our study, 53.8% of the patients were smokers or ex-smokers, and 84.6% had altered mental status occurred while in the ICU. This was much higher than in the study by Brown et al.[15], in which 47% of patients in ICU showed altered mental status.

In their study, Brown et al.[15] found pulmonary infections to be the most prevalent complication (35%), corroborating our findings, in which the most prevalent complication was of respiratory origin (61.5%). In addition, in the study by Thille et al.[13], 27% of patients with EF developed pneumonia; in the present study, we found an infection rate of 79.5% upon admission to the ICU, with the most prevalent being pneumonia (41%).

In the literature[6,13], the requirement for reintubation is considered EF, even after more than 72 hours. In contrast, the present study, considered EF as the requirement for reintubation after more than 48 hours. In previous studies, EF rates have varied between 1.81% and 19%[3,13,17]; these values differ according to the population studied and the time of OI. In the study by Santos et al.[3], the authors investigated a heterogeneous cancer population and found high EF values (17.5%); these results that differ from the present study, in which occurred in only 3.6% of patients, even though the population was similar. In addition, the study by Thille et al.[13] found that patients undergoing unplanned extubation had a higher incidence of EF (65%).

Although several hypotheses have been suggested, it is not yet clear whether EF is associated with high mortality rates. Studies[6,18] have reported that the act of reintubation itself results in complications, and that clinical deterioration occurs during the time without ventilatory support between extubation and reintubation. Studies have found high rates of hospital mortality[4,18–22] in patients with cancer who required ventilatory support, ranging from 50% to 83%.

Raymond et al.[14] analyzed the predictors of morbidity and mortality after resection of esophageal cancer and observed that mortality rates (12.2%) were related to various events, including reintubation. In the present study, we found a significantly high mortality rate of 54.8%. In the study by Thille et al.[13] in the general population and by Nantsupawat et al.[16] among patients diagnosed with COPD, about 50% of patients died after reintubation, which corroborates our findings.

Previous authors[6,15] have reported that the average length of stay in the ICU after reintubation was between 15 and 21 hours. In the present study, we found an average reintubation time of 16.5 hours. Nantsupawat et al.[16] reported that the ICU stay was three times longer in patients with EF than in those who underwent successful extubation (mean of 14 days). In our study, we found a higher average, with 22.44 days of hospitalization. Previous studies[22,23] have also verified the effectiveness of early-use, non-invasive MV immediately after extubation. In the present study, prophylactic NIV reduced reintubation rates and mortality in patients at high risk for EF. Moreover, the use of NIV was instituted in approximately 43.6% of the population to avoid early reintubation.

The reasons for reintubation found in a study by Epstein et al.[6] showed a higher incidence of EF prompted by extrapulmonary etiologies than the present study, which found a higher incidence of EF prompted by fatigue, inability to deal with secretions, and hypoxemia. The reasons for reintubation in the study by Brown et al.[15] included respiratory failure (76%) and accumulation of secretions (18%), which is consistent with our findings.

Some studies in the literature[6,15,16] performed univariate and multivariate regression models, which were used in the present study. Epstein et al.[6] found that the reason for EF and the time to reintubation were independently associated with hospital mortality. They concluded that the etiology of EF and the time to reintubation were independent predictors of outcome in the study population. Similarly, in the study by Brown et al.[15], the risk of reintubation did not depend on factors that affected EF in the study population, which included fracture of the spine and airway as an indication for initial intubation, as well as delirium and lower Glasgow Coma Scale (GCS) score during extubation; however, there was no difference in mortality between the groups studied. Nantsupawat et al.[16] demonstrated that reintubation was significantly associated with sedative and analgesic drugs administered before extubation, with reintubation being more frequent in patients with acute exacerbations of COPD.

It was not possible to compare all significant variables found in previous studies that performed regression analysis and test the confidence of the models because some studies reported too few details of their analysis, while others used different dependent variables, independent variables, and objectives from the present study.

Regarding the regression analysis carried out in the present study, all variables included in the univariate models ($p < 0.20$) could predict some changes in the models studied: time of reintubation, days in the ICU, and death; however, after the analysis of multivariate variables, we found unique variables that predicted changes.

Thus, after multivariate analysis, the only variables that could predict change in reintubation time were treatment with chemotherapy ($\beta = 0.32$) and self-/accidental extubation (β: - 0.38), presenting an explained variance of only 23.5%. In the hospitalization days model, we found that sex (β: 0.42), reintubation due to fatigue (β: 0.27), reason due to self-/accidental extubation (β: -0.25), and tracheostomy outcome (β: 0.46) had an explained variance of 61.7%.

Finally, in the death model, ECOG score (β: 0.26), type of patient (clinical or surgical) (β: -0.60), treatment with chemotherapy (β: 0.63), ICU admission based on postoperative monitoring (β: 0.32), ICU admission based on hypovolemic or hemorrhagic shock (β: 0.32), and surgical approaches in ICU (β: 0.39) had an explained variance of 78.8%.

Another important finding after multivariate regression analysis, with statistically significant death as the dependent variable, was that the scale for assessing the impact of the disease on daily activities (ECOG; $p < 0.01$), had a β-value of 0.26. In addition, this analysis showed that, each year a patient lives, 0.2 points would be added to their ECOG scale, and higher ECOG scores indicated greater possibility of death. Other significant variables were treatment with chemotherapy ($p < 0.00$), type of clinical or surgical patient ($p < 0.00$), surgical approach during ICU stay ($p < 0.00$), diagnosis prompting ICU admission ($p < 0.05$), and hypovolemic shock ($p < 0.00$). However, it is impossible to measure the clinical significance of each of these variables.

Comparing the three models, the models that best answered our objective were those that considered whether length of ICU stay and death were associated with EF, with an explained variance of 61.7% and 78.8%, respectively. Thus, the most reliable model is composed of the dependent variable death, which is closest to the R2 value of 100%.

The present study had some limitations. Firstly, none of the measures or data collections were related to the spontaneous breathe test (SBT)[24], maximum respiratory pressure test, or MV time preceding extubation, which are important data in intensive care clinical practice because they inform the protocols for discontinuing MV. Furthermore, the patients' medical records contained insufficient data to classify the Sequential Organ Failure Assessment (SOFA) or Acute Physiology and Chronic Health Evaluation (APACHE) score. These systems use physiological data, information related to the patient's disease, and conditions to predict the likelihood of death. Such models can facilitate risk stratification in the context of intensive care.

CONCLUSION

The incidence of EF in the studied cancer population was low (3.6%), and EF was associated with more clinical events involving respiratory complications and pneumonia. Fatigue was the main reason for reintubation, and death was the main outcome. Therefore, to avoid EF, clinicians must identify specific risk factors that can influence the need for reintubation in the oncology population.

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