Extubation failure influences clinical and functional outcomes in patients with traumatic brain injury*

A falência da extubação influencia desfechos clínicos e funcionais em pacientes com traumatismo cranioencefálico

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Abstract

Objective: To evaluate the association between extubation failure and outcomes (clinical and functional) in patients with traumatic brain injury (TBI). **Methods:** A prospective cohort study involving 311 consecutive patients with TBI. The patients were divided into two groups according to extubation outcome: extubation success; and extubation failure (defined as reintubation within 48 h after extubation). A multivariate model was developed in order to determine whether extubation failure was an independent predictor of in-hospital mortality. **Results:** The mean age was 35.7 ± 13.8 years. Males accounted for 92.3%. The incidence of extubation failure was 13.8%. In-hospital mortality was 4.5% and 20.9% in successfully extubated patients and in those with extubation failure, respectively (p = 0.001). Tracheostomy was more common in the extubation failure group (55.8% vs. 1.9%; p < 0.001). The median length of hospital stay was significantly greater in the extubation failure group than in the extubation success group (44 days vs. 27 days; p = 0.002). Functional status at discharge was worse among the patients in the extubation failure group. The multivariate analysis showed that extubation failure was an independent predictor of in-hospital mortality (OR = 4.96; 95% CI, 1.86-13.22). **Conclusions:** In patients with TBI, extubation failure appears to lengthen hospital stays; to increase the frequency of tracheostomy and of pulmonary complications; to worsen functional outcomes; and to increase mortality.

Keywords: Brain injuries; Ventilator weaning; Intensive care units; Glasgow outcome scale.

Resumo

Objetivo: Avaliar a associação entre falência da extubação e desfechos clínicos e funcionais em pacientes com traumatismo cranioencefálico (TCE). **Métodos:** Coorte prospectiva com 311 pacientes consecutivos com TCE. Os pacientes foram divididos em dois grupos de acordo com o resultado da extubação: sucesso ou falência (necessidade de reintubação dentro de 48 h após extubação). Um modelo multivariado foi desenvolvido para verificar se a falência de extubação era um preditor independente de mortalidade hospitalar. **Resultados:** A média de idade foi de 35,7 ± 13,8 anos, e 92,3% dos pacientes eram do sexo masculino. A incidência de falência da extubação foi de 13,8%. A mortalidade hospitalar foi, respectivamente, de 20,9% e 4,5% nos pacientes com falência e com sucesso da extubação (p = 0,001). A realização de traqueostomia foi mais frequente no grupo falência da extubação (55,8% vs. 1,9%; p < 0,001). A mediana de tempo de permanência hospitalar foi significativamente maior nos pacientes com falência do que naqueles com sucesso da extubação (44 dias vs. 27 dias; p = 0,002). Os pacientes com falência da extubação apresentaram piores desfechos funcionais na alta hospitalar. A análise multivariada mostrou que a falência da extubação foi um preditor independente para a mortalidade hospitalar (OR = 4,96; IC95%, 1,86-13,22). **Conclusões:** A falência da extubação esteve associada a maior permanência hospitalar, maior frequência de traqueostomia e de complicações pulmonares, piores desfechos funcionais e maior mortalidade em pacientes com TCE.

Descritores: Traumatismos encefálicos; Desmame do respirador; Unidades de terapia intensiva; Escala de resultado de Glasgow.

Introduction

Patients with traumatic brain injury (TBI) commonly need mechanical ventilation (MV) in order to maintain ventilation, optimize oxygenation, and protect the airway; however, the use of MV is associated with adverse effects.[1,2]

The first phase of withdrawal of MV is designated discontinuation of ventilatory support, and studies have been conducted with the objective of determining the best timing for initiation of withdrawal. When ventilatory support can be withdrawn, the decision to extubate has to be made.[3-5]

Although most patients are successfully removed from MV, a proportion of patients experience extubation failure; that is, there is a need for reintubation within 24-72 h after extubation. The extubation failure rate ranges from 5% to 20% depending on the population studied. Extubation failure has been associated with prolonged ICU and hospital stays, as well as with higher rates of tracheostomy and mortality.[6-10]

This scenario seems to be more complicated in patients with neurological involvement, higher extubation failure rates having been observed in this population.[11] Despite reports of worse outcomes in patients with extubation failure, the impact of extubation failure on the evolution of patients with TBI remains unknown and is possibly underestimated. In addition, the association between functional outcomes and extubation failure has yet to be explored. Therefore, we conducted a prospective study in a trauma referral center with the objective of determining whether extubation failure had any influence on the length of hospital stay, the length of ICU stay, in-hospital mortality, and ICU mortality, as well as on functional outcomes at hospital discharge and at ICU discharge, in patients with TBI.

Methods

This was a prospective cohort study conducted between November of 2008 and December of 2010 and involving patients with TBI admitted to the ICU of the Bahia State General Hospital, located in the city of Salvador, Brazil. The present study was approved by the Research Ethics Committee of the Bahia Foundation for Science Development, and patients were included in the study after their legal guardians had given written informed consent.

We included adult patients ($\geq$ 18 years of age) who had been diagnosed with TBI, who had been on MV via an endotracheal tube for at least 48 h, and who passed the spontaneous breathing trial (SBT). We excluded patients with spinal trauma, those who subsequently died, those who underwent tracheostomy before the first extubation, and those who had unscheduled extubation.

The patients who met the inclusion criteria were observed daily until death or discharge from the ICU. For each patient included in the study, only the first extubation attempt was analyzed. Extubation outcome was classified as extubation success or extubation failure. Extubation failure was defined as reintubation within 48 h after extubation.[12]

All of the decisions regarding weaning, extubation, reintubation, tracheostomy, and use of noninvasive ventilation (NIV) were made by the teams of attending physicians, without the involvement of the researchers. In accordance with standard practices, the patients were considered eligible for an SBT when they showed reversal or control of the event that led to their being placed on MV, adequate gas exchange, and hemodynamic stability. The patients were extubated if they tolerated 30-120 min of spontaneous breathing on pressure support ventilation of 7 cmH$_2$O or unassisted through a T-tube.

For all of the patients who were reintubated, we collected the following data: date of reintubation; time of reintubation; and reason for reintubation. The time to reintubation was measured in hours, and the reasons for reintubation were dichotomized into airway problems (upper airway obstruction, aspiration/excess pulmonary secretions, and bronchospasm) and nonairway problems (excessive respiratory distress, reduced level of consciousness, and others).

The level of consciousness was assessed by the Glasgow Coma Scale (GCS) score. Because all of the patients had undergone orotracheal intubation and were on MV, those who gave a verbal response received a score of 1.

We analyzed the following clinical outcomes: death in the ICU; in-hospital death; need for tracheostomy; length of ICU stay and length of hospital stay; pulmonary complications in the ICU; and functional outcomes at ICU discharge and at hospital discharge.

Pulmonary complications during the ICU stay were defined as follows: pneumonia, defined as new or progressive pulmonary infiltrate on chest X-rays, accompanied by at least two of the following signs: purulent tracheal secretions, body temperature > 38.3°C, and 25% increase in baseline leukocyte count; atelectasis on chest X-rays, accompanied by acute respiratory symptoms; tracheobronchitis, defined as increased tracheobronchial secretion volume, changes in tracheobronchial secretion color, or purulent tracheobronchial secretion, accompanied by normal chest X-ray findings; and bronchospasm, defined as wheezing with acute respiratory symptoms requiring bronchodilator use.

The Glasgow Outcome Scale (GOS) has been widely used for evaluating outcomes in patients with TBI because the GOS addresses physical, social, and cognitive sequelae. We used the extended GOS in order to determine the functional outcome after TBI. The extended GOS consists of eight categories, the scores ranging from 1 to 8 points: total recovery (8 points); good recovery (7 points); upper moderate disability (6 points); lower moderate disability (5 points); upper severe disability (4 points); lower severe disability (3 points); persistent vegetative state (2 points); and death (1 point).[13] The patients were graded on the extended GOS at ICU discharge and at hospital discharge.

The extended GOS variable was dichotomized into independent (total recovery, good recovery, upper moderate disability, and lower moderate disability) and dependent (upper severe disability, lower severe disability, persistent vegetative state, and death).[14]

The patients who failed extubation were compared with those who were successfully extubated in terms of the length of ICU stay, the length of hospital stay, tracheostomy, ICU mortality, in-hospital mortality, pulmonary complications, and functional outcome.

Categorical variables were expressed as absolute and relative frequencies. Continuous variables were expressed as mean and standard deviation or as median and interquartile range (IR), when appropriate. In order to compare categorical variables, we used the chi-square test or Fisher's exact test, when appropriate. In order to establish the statistical significance of the difference between the means of the groups,

we used the Student's t-test or the Mann-Whitney test, when appropriate.

A multiple logistic regression model was used in order to assess the ability of each independent variable to predict the expected outcome (in-hospital mortality). After the univariate analysis, the independent variables were included in the logistic model if they had a value of $p < 0.10$ and remained in the model if they remained significant ($p < 0.05$). For inclusion and exclusion of variables, a manual procedure was used.

The level of significance was set at $p < 0.05$. Statistical analysis of the results was performed with the Statistical Package for the Social Sciences, version 12.0 (SPSS Inc., Chicago, IL, USA).

Results

During the study period, we included 311 consecutive patients with TBI extubated for the first time. The mean age of the patients was 35.7 ± 13.8 years. Of the 311 patients, 287 (92.3%) were male, and the mean GCS score was 9.7 ± 4.4 at admission. The most common type of accident was motorcycle accident, in 33.8%, followed by various causes, in 23.5%, automobile/automobile-pedestrian accident, in 18.0%, assault, in 16.4%, gunshot wound, in 5.8%, and stab wound, in 2.6%. Of the 311 patients, 232 (74.6%) underwent surgical treatment and 79 (25.4%) underwent conservative treatment. The median duration of MV was 7 h (IR, 5-10 h).

Extubation failure occurred in 43 patients (13.8%). The reasons for reintubation were respiratory failure, in 18 patients (41.9%); upper airway obstruction, in 11 (25.6%); reduced level of consciousness, in 7 (16.3%); excess pulmonary secretions/inability to protect the airways, in 4 (9.3%); bronchospasm, in 1 (2.3%); and other reasons, in 2 (4.7%). The median time to reintubation was 6.0 h (IR, 2.0-25.5 h). Most of the patients (27 cases, 62.8%) had extubation failure within up to 12 h after extubation; 4 (9.3%) had extubation failure within 12-23 h after extubation; 4 (9.3%) had extubation failure within 24-35 h after extubation; and 8 (18.6%) had extubation failure within 36-48 h after extubation. Of the 311 extubated patients, 18 (5.8%) received NIV after extubation. The need for NIV after extubation was more common in the patients who failed extubation than in those who were successfully extubated (11.6% vs. 4.9%, p = 0.086).

The patients who failed extubation had longer ICU and hospital stays. In addition, ICU mortality was significantly higher in the patients who failed extubation than in those who were successfully extubated. The need for tracheostomy was significantly more common in the extubation failure group than in the extubation success group (Table 1).

The results of the univariate analysis of in-hospital mortality are shown in Table 2. After adjustment for other variables, extubation failure was independently associated with in-hospital mortality (Table 3).

Regarding the evolution of the 43 patients with extubation failure, 23 underwent extubation again; of those, 6 (27.3%) failed extubation again. A tracheostomy was performed in 24 (55.8%) of the 43 patients who had failed extubation, being performed after the first extubation failure in 19 and after the second extubation failure in 5. One patient remained intubated after the first extubation failure until death. Only 1 patient was extubated for the third time and evolved successfully.

There was a statistically insignificant difference in mortality between the patients who were reintubated because of nonairway problems and those who were reintubated because of airway problems (25.9% vs. 12.5%; p = 0.45). Among the reintubated patients, in-hospital mortality tended to be lower in those who were reintubated within up to 12 h after extubation (14.8% vs. 31.3%; p = 0.26).

Pulmonary complications occurring during the ICU stay were evaluated in 256 of the 311 patients in the cohort, being more common in the extubation failure group than in the extubation success group (65.7% vs. 30.8%; p < 0.001).

On the basis of the extended GOS scores, the functional outcomes at ICU discharge and at hospital discharge were worse in the patients who failed extubation than in those who were successfully extubated. The patients with extubation failure had a lower mean extended

Table 1 – Comparison of morbidity and mortality between patients who were successfully extubated and those who failed extubation.[a]

Variable	Extubation success	Extubation failure	p
	(n = 268)	(n = 43)	
Length of ICU stay, days	9 (7-13)	15 (12-19)	< 0.001
Length of ICU stay after the first extubation, days	3.0 (2.0-5.0)	8.5 (5.8-14.0)	< 0.001
Length of hospital stay, days	27.0 (19.2-36.8)	40.0 (24.5-59.5)	0.002
Tracheostomy[b]	5 (1.9)	24 (55.8)	< 0.001
ICU mortality[b]	3 (1.1)	6 (14.0)	< 0.001
In-hospital mortality[b]	12 (4.5)	9 (20.9)	0.001

[a]Values expressed as median (interquartile range), except where otherwise indicated. [b]Values expressed as n (%).

Table 2 – Univariate analysis of the factors associated with mortality in patients with traumatic brain injury.[a]

Variable	Survivors	Death	p
	(n = 290)	(n = 21)	
Age, years	35.2 ± 13.5	43.2 ± 16.3	0.012
Male gender[b]	267 (92.1)	20 (95.2)	1.00
GCS score at hospital admission	9.7 ± 3.5	9.8 ± 3.3	0.91
GCS score on the day of extubation	10.7 ± 0.7	10.2 ± 0.8	0.01
Length of ICU stay, days[c]	10.0 (7.0-13.0)	14.0 (9.5-19.5)	0.006
Days on MV before the 1st extubation[c]	7.0 (5-10)	9.0 (5-10.5)	0.17
Type of treatment[b]			
Surgical	216 (74.5)	16 (76.2)	0.86
Conservative	74 (25.3)	5 (27.8)	
Use of NIV after extubation[b]	15 (5.2)	3 (14.3)	0.112
Extubation failure[b]	34 (11.7)	9 (42.9)	0.001

GCS: Glasgow Coma Scale; MV: mechanical ventilation; and NIV: noninvasive ventilation. [a]Values expressed as mean ± SD, except where otherwise indicated. [b]Values expressed as n (%). [c]Values expressed as median (interquartile range).

GOS score at ICU discharge (3.8 ± 2.2 vs. 5.5 ± 1.8; p < 0.001) and at hospital discharge (5.0 ± 2.4 vs. 6.0 ± 2.0; p = 0.036). The proportions of dependent patients at ICU discharge and at hospital discharge were significantly higher in the extubation failure group than in the extubation success group (67.1% vs. 33.3%, p < 0.001, and 43.8% vs. 24.0%, p = 0.018, respectively). Figure 1 shows a comparison between the extubation success group and the extubation failure group

in terms of the extended GOS categories at ICU discharge and at hospital discharge.

Discussion

The present study examined the association of extubation failure with clinical and functional outcomes in patients with TBI. The patients who failed extubation had longer ICU and hospital stays, higher rates of pulmonary complications, greater need for tracheostomy, worse functional outcome, and higher mortality.

In the present study, the incidence of extubation failure in patients with TBI was found to be 13.8%, which is consistent with the findings of a study evaluating a similar population.[15] The reported incidence of extubation failure varies widely, ranging from 2% to 25%.[16] Because of

Table 3 – Multivariate analysis of the risk factors for in-hospital mortality in patients with traumatic brain injury.

Variable	OR	95% CI	p
Age, years	1.04	1.01-1.07	0.019
Extubation failure	4.96	1.86-13.22	0.001
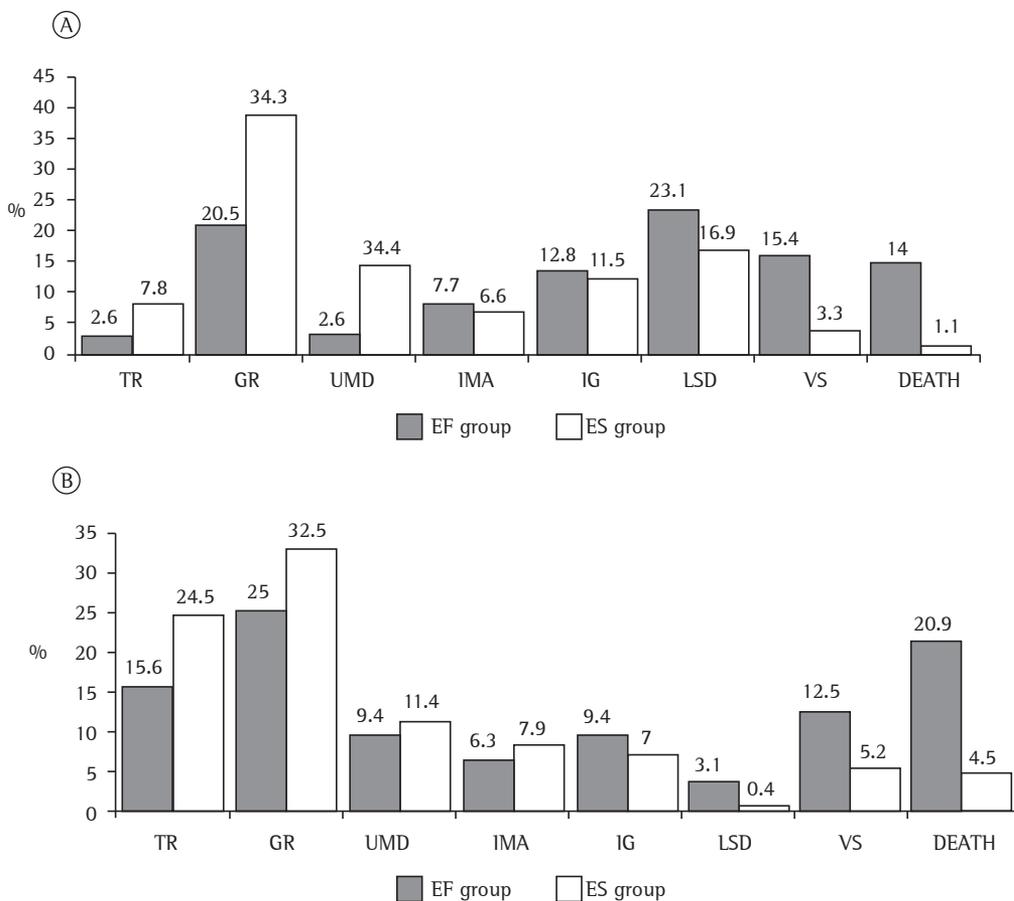
Figure 1 – Comparison of the Glasgow Outcome Scale scores at ICU discharge (in A) and at hospital discharge (B) between the patients in the extubation failure (EF) group and those in the extubation success (ES) group. TR: total recovery; GR: good recovery; UMD: upper moderate disability; LMD: lower moderate disability; USD: upper severe disability; LSD: lower severe disability; and VS: vegetative state.

the different definitions of extubation failure across studies, it can be difficult to compare the reported incidences of extubation failure. In addition, this variation can be partially explained by the heterogeneity of the populations studied. Karanjia et al. studied a heterogeneous cohort of neurological patients and found the incidence of extubation failure to be 6%, which is lower than the incidence found in the present study. This difference is due to the fact that those authors used the total number of intubated patients rather than the total number of extubated patients in order to calculate the incidence of extubation failure.[17]

Extubation failure rates have been reported to be higher in patients with neurological involvement.[11,18] However, the reported incidence is consistent with that found in other populations.[9,19] A recent study suggested that the "optimal" extubation failure rate is 5-10%.[20] In contrast, some authors have reported that extubation failure rates of 10-15% are acceptable.[5] It is not easy to determine the ideal extubation failure rate; however, it can be inferred that rates close to 0% indicate that many patients remained on MV for an unnecessarily long time and that extremely high rates are suggestive of premature withdrawal of MV.

The main reason for reintubation in the present study was respiratory failure, a finding that is consistent with those reported in previous studies.[21,22] We found no association between the reason for reintubation and in-hospital mortality, a finding that corroborates those of Menon et al.[23] In contrast with our results, the results of a study conducted by Epstein et al.[24] showed a higher mortality in patients who were reintubated because of nonairway problems. It is plausible that, in patients who are reintubated because of upper airway obstruction, acute respiratory failure can be immediately corrected, whereas organ dysfunction cannot.

Our univariate analysis showed that the need for NIV after extubation was more common in the patients with extubation failure. It has been suggested that, when used without an appropriate selection, NIV after extubation delays the initiation of appropriate therapy and results in worse outcomes.[25]

In the present study, the patients with extubation failure had unfavorable outcomes. This finding has been reported in previous studies,

ICU mortality rates having been reported to be higher in patients who failed extubation than in those who were successfully extubated.[24,26] In addition, we found that the patients who failed extubation had longer ICU and hospital stays, a finding that corroborates previous findings.[7]

In our study sample, the number of patients requiring tracheostomy was substantially higher in the extubation failure group than in the extubation success group. This finding is similar to that reported by one group of authors (66.6% vs. 8.6%).[10] It is possible that extubation failure, when associated with other factors, such as excess pulmonary secretions and reduced level of consciousness, led to the decision of performing a tracheostomy, given that 79% of all tracheostomies were performed after the first extubation failure.

In the present study, in-hospital mortality was found to be approximately five times as high in the patients who failed extubation as it was in those who were successfully extubated, a finding that corroborates those reported in the literature.[21,27] In addition, extubation failure was independently associated with in-hospital mortality in our sample of patients with TBI. In our multivariate analysis, age remained a risk factor for in-hospital mortality even after having been adjusted for extubation failure, a finding that is consistent with previous findings.[28]

Because of its invasive nature, reintubation is associated with increased life-threatening complications. Prolonged MV due to extubation failure can also lead to adverse outcomes. In addition, it is possible that extubation failure is only a marker of greater clinical severity. There is also the possibility that clinical deterioration occurs during the time elapsed between extubation and reintubation.[24] One study[24] showed that patients who were reintubated within up to 12 h after extubation had lower mortality than did those who were reintubated later (24% vs. 51%; p < 0.05). In the present study, mortality tended to be lower in the patients who were reintubated within up to 12 h after extubation.

Studies have concluded that the need for reintubation increases the risk of pulmonary complications.[24,29] A case-control study showed a higher incidence of pneumonia in patients requiring reintubation (47% vs. 10%).[29] A prospective study of neurological patients showed higher rates of respiratory complications in patients

who failed extubation than in those who were successfully extubated (85% vs. 15%).[8] In our study, the rate of pulmonary complications was more than twice as high in the patients who failed extubation as it was in those who were successfully extubated.

Another important finding of our study was the association between extubation failure and functional outcome. The association between extubation failure and mortality or that between extubation failure and length of hospital stay has been studied.[7-9,23,26] However, data on the association between extubation failure and physical sequelae are scarce. Cognitive disability, prolonged MV, and longer hospital stays are factors that might be related to a worse functional outcome in patients with TBI and extubation failure. In addition, critical illness polyneuropathy is one of the events that influence the decline in the functional capacity of ICU patients. One study demonstrated that critical illness polyneuropathy was an independent predictor of failure to wean from MV.[30]

The data on functionality reinforce the need for measures to prevent extubation failure, given that functional disability is related to health status and has an impact on activities of daily living. One issue to be addressed in future studies is the long-term monitoring of functional capacity in such patients.

Our study has limitations. Like any observational study, the present study is only a generator of hypotheses; however, it is reasonable to assume that the results obtained are representative of current clinical practice in the intensive care of patients with TBI. Another potential limitation is the fact that the study was conducted in a single center; nevertheless, the incidence of extubation failure was found to be within the range reported in the literature. Finally, we did not assess prognostic scores for severity. This issue was partially resolved by the inclusion of the GCS scores at admission. In addition, the impact of extubation failure on clinical outcomes was found to be consistent with that reported in previous studies. However, we recognize that future studies involving the use of prognostic scores will allow a more accurate determination of the predictive power of extubation failure for mortality in patients with TBI. Despite its limitations, the present study showed that extubation failure is a predictor of poor prognosis in patients with TBI.

In patients with TBI, extubation failure appears to lengthen hospital stays; to increase the frequency of tracheostomy and of pulmonary complications; to worsen functional outcomes; and to increase mortality.

Acknowledgments

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