# Sevrage ventilatoire chez les patients trachéotomisés aux soins intensifs

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# Sevrage ventilatoire chez les patients trachéotomisés aux soins intensifs

THESE

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par

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***Sevrage ventilatoire chez les patients trachéotomisés aux soins intensifs***

sans se prononcer sur les opinions exprimées dans cette thèse.

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# RÉSUMÉ DE LA THÈSE

Lors de leur séjour aux soins intensifs, certains patients ont besoin une assistance ventilatoire invasive (ou ventilation invasive), délivrée au moyen d'un tube endotrachéal ou d'une canule de trachéostomie. Sa durée doit rester la plus courte possible puisqu'une ventilation prolongée est associée à un séjour prolongé aux soins intensifs et à une mortalité élevée. Chez le patient ventilé au moyen d'un tube endotrachéal, une stratégie proactive de sevrage de la ventilation mécanique permet de réduire la durée de ventilation mécanique. Cette stratégie consiste en la recherche systématique de prérequis au sevrage, la réalisation de tests de ventilation spontanée (ou tests de déventilation) et une extubation sans délai une fois les critères de déventilation satisfaits. Néanmoins, malgré une stratégie de sevrage bien conduite, 10.1% des patients sont considérés comme difficiles à sevrer et 8.7% présentent un sevrage prolongé. Dans ces situations, bien qu'il s'agisse d'un geste chirurgical invasif, une trachéostomie est souvent réalisée afin de diminuer le travail respiratoire, diminuer les besoins de sédation, améliorer la communication, faciliter la mobilisation et augmenter le confort du patient. L'optimisation du sevrage de la ventilation est également, comme pour le patient intubé, un enjeu important chez le patient trachéotomisé. Cependant, peu de données sont disponibles dans la littérature comparativement aux patients intubés. Le sevrage de la ventilation mécanique chez le patient trachéotomisé et le sevrage dans un deuxième temps de la canule de trachéotomie ne sont donc que peu codifiés. Au vu du manque de données disponibles, il est également difficile de prédire le devenir des patients trachéotomisés dans le cadre d'un sevrage difficile ou prolongé de la ventilation. Cette question de la prédiction du devenir est essentielle étant donné la morbidité et la mortalité élevées à moyen terme de ces patients.

L'objectif de ce travail de thèse était d'étudier divers aspects relatifs aux patients trachéotomisés aux soins intensifs dans le cadre d'un sevrage difficile ou prolongé. Ce travail a consisté en un volet rétrospectif et un volet prospectif.

Le volet rétrospectif a consisté en la création et l'analyse d'une base de données de patients trachéotomisés pour sevrage ventilatoire complexe aux soins intensifs du CHUV à Lausanne et deux études distinctes ont été réalisées depuis ces données. La première étude a recherché des facteurs prédicteurs du devenir des patients trachéotomisés et a fait l'objet d'une publication originale dans le journal peer-reviewed *Annals of Intensive Care* (version publiée à la *section 5*). La seconde a étudié les stratégies utilisées dans le sevrage ventilatoire et le sevrage de la canule de trachéostomie. Ce travail a été soumis au *Journal of Critical Care* (version soumise à la *section 6*).

Le volet prospectif a consisté en une étude physiologique dont l'objectif était d'étudier l'impact sur l'effort inspiratoire (mesuré invasivement au moyen d'une sonde de pression œsophagienne) de trois différents tests de déventilation couramment utilisés chez le patient trachéotomisé. Cette étude physiologique en crossover a permis de démontrer que les différents tests de déventilation avaient des effets différents sur le travail respiratoire. Les résultats de ce travail sont présentés dans le présent document et feront l'objet d'une publication ultérieure (*section 7*).

De manière générale, ce travail de thèse a permis d'acquérir des connaissances supplémentaires relatives à la prédiction du devenir des patients trachéotomisés. Il a également permis d'obtenir des informations complémentaires relativement aux stratégies de sevrage de la ventilation et de la canule de trachéotomie ainsi que des données physiologiques originales sur l'impact des tests de sevrage sur le travail ventilatoire.

Annals of Intensive Care

RESEARCH

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# Early prediction of hospital outcomes in patients tracheostomized for complex mechanical ventilation weaning

Davy Cabrio[1,2*], Timothée Vesin[2], Ermes Lupieri[1], Hélène Messet[3], Kishore Sandu[4] and Lise Piquilloud[1,2]

## Abstract

**Background:** Tracheostomy is often performed in the intensive care unit (ICU) when mechanical ventilation (MV) weaning is prolonged to facilitate daily care. Tracheostomized patients require important healthcare resources and have poor long-term prognosis after the ICU. However, data lacks regarding prediction of outcomes at hospital discharge. We looked for patients' characteristics, ventilation parameters, sedation and analgesia use (pre-tracheostomy) that are associated with favorable and poor outcomes (post-tracheostomy) using univariate and multivariate logistic regressions.

**Results:** Eighty tracheostomized patients were included (28.8% women, 60 [52–71] years). Twenty-three (28.8%) patients were intubated for neurological reasons. Time from intubation to tracheostomy was 14.7 [10–20] days. Thirty patients (37.5%) had poor outcome (19 patients deceased and 11 still tracheostomized at hospital discharge). All patients discharged with tracheostomy ($n=11$) were initially intubated for a neurological reason. In univariate logistic regressions, older age and higher body-mass index (BMI) were associated with poor outcome (OR 1.18 [1.07–1.32] and 1.04 [1.01–1.08], $p<0.001$ and $p=0.025$). No MV parameters were associated with poor outcome. In the multiple logistic regression model higher BMI and older age were also associated with poor outcome (OR 1.21 [1.09–1.36] and 1.04 [1.00–1.09], $p<0.001$ and $p=0.046$).

**Conclusions:** Hospital mortality of patients tracheostomized because of complex MV weaning was high. Patients intubated for neurological reasons were frequently discharged from the acute care hospital with tracheostomy in place. Both in univariate and multivariate logistic regressions, only BMI and older age were associated with poor outcome after tracheostomy for patients undergoing prolonged MV weaning.

**Keywords:** Mechanical ventilation, Prolonged weaning, Outcomes, Tracheostomy, Prediction

## Background

Weaning, the process of liberating the patient from mechanical ventilation, is crucial to improve critically ill patient's outcome [1]. Tracheostomy in the intensive care unit is a frequent intervention for patients who cannot be weaned from mechanical ventilation (MV) [2]. It was shown in a large multi-center prospective study [1] that 8.7% of patients invasively ventilated have prolonged weaning (defined as the persistent need for MV for 7 days after the first attempt at discontinuing MV) and 4.1% of ventilated patients require tracheostomy.

Among patients with prolonged weaning, we can describe two main groups who need tracheostomy: patients with inadequate airway protection due to neurological impairment and patients with persistent respiratory impairment. In patients suffering from neurological sequelae, tracheostomy helps protect the airway and reduce ventilator-associated pneumonias

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[3, 4], reduces days with MV [5], facilitates transfer to long-term care facilities [3], but does not reduce mortality [6]. For patients suffering from persistent respiratory impairment, tracheostomy decreases work of breathing [7], sedation needs [8], allows better mobilization and improves patients' comfort compared to orotracheal intubation [9]. In addition, tracheobronchial toilet is easier [8] and communication with care providers is improved [10]. Once MV is weaned off, oral feeding can often be reintroduced even with tracheostomy cannula still in place [10].

Despite the benefits listed above, tracheostomy can lead to complications, such as tracheal stenosis and stromal bleeding or infections [11]. Tracheostomized patients are also resources demanding. They stay for a long period of time in the ICU, hospital and long-term care facilities. Both patients tracheostomized for non-neurological and neurological problems have high mortality rates of at least 45% at 1 year [12, 13] and poor long-term outcomes [13, 14]. Even the impact of tracheostomy itself on the long-term outcome is poorly known and difficult to individualize from other healthcare and disease-related factors. Poor outcome of tracheostomized patients highlights the importance of further assessing the criteria that could be used to decide which patients are good candidates to benefit from tracheostomy. Recent French guidelines addressed this important question, also underlining that additional data is needed [15]. Only higher body weight [16], presence of comorbidities [17–19] and albuminemia levels [20] have previously been associated with worse outcome in tracheostomized patients. In practice, ICU clinicians use clinical judgment and the general health status of the patient to decide whether to perform tracheostomy. Among unanswered questions, the relationship between ventilator settings, sedation and analgesia administered before tracheostomy and outcome has also not been systematically studied in tracheostomized patients. In addition, no data is available regarding the impact on outcome of performing early and frequent attempts to discontinue MV (spontaneous breathing trial or SBT). Finally, data is also sparse regarding the correlation between MV weaning strategies after tracheostomy and outcome [21, 22]. We hypothesize that patients' and treatments-related characteristics could help predict outcomes in patients tracheostomized for complex MV weaning.

The main objective of this work was to study, in patients tracheostomized for MV weaning purposes, the association between patients' outcome at hospital discharge and patients' characteristics, tracheostomy technique, MV management and sedation and analgesia use before performing the tracheostomy.

## Methods

Retrospective single-center study conducted at the medico-surgical Adult Intensive Care Unit of the Lausanne University Hospital (CHUV), Lausanne, Switzerland. Data were collected from medical files and clinical information system. The present study was approved by the local ethics committee (Commission cantonale d'éthique de la recherche sur l'être humain, protocol number 2019-01403). Due to the nature of collected data, waiver of consent was obtained and only patients who explicitly refused the use of their clinical data for research purposes were excluded. The study was registered on clinicaltrials.org (NCT04987398).

Adult patients admitted to the Adult ICU of the Lausanne University Hospital between May 1st 2017 and November 30th 2018 who were mechanically ventilated for at least 72 h and tracheostomized were considered for inclusion. Exclusion criteria were: patients' refusal to participate to a research project, tracheostomy performed before ICU admission, tracheostomy performed for ear–nose–throat (ENT) reasons, burns' victim or pre-existing condition(s) prior to the ICU admission precluding ventilation weaning. For all the included patients weaning from mechanical ventilation and tracheostomy management and weaning were performed following the dedicated procedures available in the Lausanne University Hospital ICU.

Patients' characteristics at ICU admission and reason for ICU admission were collected. Reason for intubation was also recorded. Clinical frailty score, Nutrition risk screening (NRS) score, Simplified Acute Physiology Score II (SAPS II) and Sequential Organ Failure Assessment (SOFA) score were collected as well. Key dates during hospital stay (admission and discharge from ICU and hospital, intubation day, tracheostomy day and definitive cannula ablation day) were collected. Ventilator settings were collected once daily at 8 a.m. except the day of tracheostomy. Ventilatory mode used for the majority of time during each day was collected between intubation and the day before tracheostomy. The use or not of sedation, analgesia and neuromuscular blocking agents (NMBA) was collected every day between intubation and the day before tracheostomy. Dynamic plateau pressure was measured by the ventilator in volume-assist control (VAC), during a short tele-inspiratory pause set by default for each breath (set at 10–15% of the total inspiratory time). Driving pressure was calculated as the difference between dynamic plateau pressure and set PEEP. Data about medication are reported as the percentage of days with use of each medication before tracheostomy. Separation attempts from MV before tracheostomy were considered as either spontaneous breathing trials (SBT) or immediate extubation without previous SBT. They

were recorded until the day before tracheostomy. On the day of tracheostomy, ventilation mode and settings were collected every 30 min during the 2 h before intervention and were averaged. Maximal norepinephrine infusion rate administered during those 2 h was collected. SOFA score was also calculated and the worst $PaO_2/FiO_2$ ratio on the day of tracheostomy was recorded. Tracheostomy technique (surgical or percutaneous) and the type of cannula inserted were collected. As general hospital stay data, we collected ICU and hospital mortality, unexpected death vs death following withdrawal of life-sustaining treatments (WLST), ICU and hospital stay durations, days free from MV at days 30 and 60 after intubation, decannulation, time from intubation to decannulation and presence of ICU-acquired weakness when reported in the ICU discharge letters and defined either by a Medical Research Council (MRC) sum score of less than 48/60, a compatible electroneuromyography exam or high clinical suspicion in the absence of sufficient collaboration to perform MRC scale. More details on data collection are available in Additional file 1. Missing data were not imputed.

Favorable outcome was considered when the patient was alive and decannulated at hospital discharge. Contrarily, poor outcome was considered as in-hospital death or discharge with tracheostomy cannula in place. Patients were divided into two sub-groups depending on their outcome (favorable vs poor).

No statistical sample size calculation was performed a priori for this retrospective study. Sample size was equal to the number of patients treated during the study period who met inclusion criteria and did not meet exclusion criteria.

### Data analyses

Data was reported as median [interquartile range] or number (percentage). Normality was tested using Shapiro–Wilk test. Comparisons between outcome groups for continuous data were performed using *T* test or Mann–Whitney test as appropriate. Fisher's exact test was used for categorical data. Binary logistic regressions were used to evaluate the association of pre-tracheostomy variables and of tracheostomy technique with patients' outcome. These analyses were performed for both the global patients' population and the subgroup of patients intubated for non-neurological reasons. Respiratory rate was not included in the univariate analyses, because it represents both a ventilator setting (controlled ventilation) and the patient's own respiratory rate if present (assisted ventilation). A multivariate logistic regression model was constructed both for the global patients' population and for patients intubated for non-neurological reasons to identify variables independently associated with favorable or poor outcomes. Variable entered in the multivariate model were those with univariate $p$ value of $< 0.10$. Results for univariate and multivariate logistic regression models were reported as odds ratio (OR) and 95% confidence interval (CI). Parameters significantly associated with outcomes in the multivariate regressions model were compared between the patients intubated for neurological, respiratory and other reasons using ANOVA or Kruskal–Wallis test as appropriate. Statistical analyses were performed using GraphPad Prism version 9.1.0 for Windows (GraphPad Software, San Diego, CA, USA) except for Fisher's exact tests, which were performed using *R* version 1.4.2 (R Foundation for Statistical Computing, Vienna, Austria). All statistical tests were two-tailed and $p$ value $< 0.05$ was considered significant.

## Results

### Study population

A total of 80 patients were included. Twenty-three patients were intubated for neurological reasons. Twenty-eight were intubated for primary respiratory reasons and 29 for non-neurological and non-respiratory reasons. Those two last sub-groups had similar characteristics (see Additional file 2) and were analyzed as a single sub-group ($N = 57$). The study flowchart is displayed in Fig. 1. No complications related to the insertion procedure of tracheostomy (performed by an ENT specialist or a thoracic/abdominal surgeon) were observed. All the cannula used were Shiley (Covidien, Minneapolis MN, USA), size 6–10.

### Patients' characteristics and outcomes

Patients' characteristics, ICU admission data and reasons leading to intubation are included in Table 1 for the global study population and after separation in favorable and poor outcome. General characteristics and some comorbidities data are provided for both sub-groups of patients intubated for non-neurological and neurological reasons in Additional file 3 and Additional file 4, respectively.

In the global study population, 19 (23.8%) patients died during hospital stay, 9 in the ICU (ICU mortality of 11.3%) and 10 after ICU stay. One patient died of direct complication of tracheostomy-related adverse event (accidental decannulation). Among all deceased patients, 12 (63.2% of all deceased patients) died after WLST. Seven WLST were conducted in the ICU and 5 after the ICU stay. To note, no patients in the favourable outcome group had WLST during the hospital stay. For 10/61 (16.4%) patients alive at hospital discharge, a "do not resuscitate order in case of cardiac arrest" was found in the medical record.

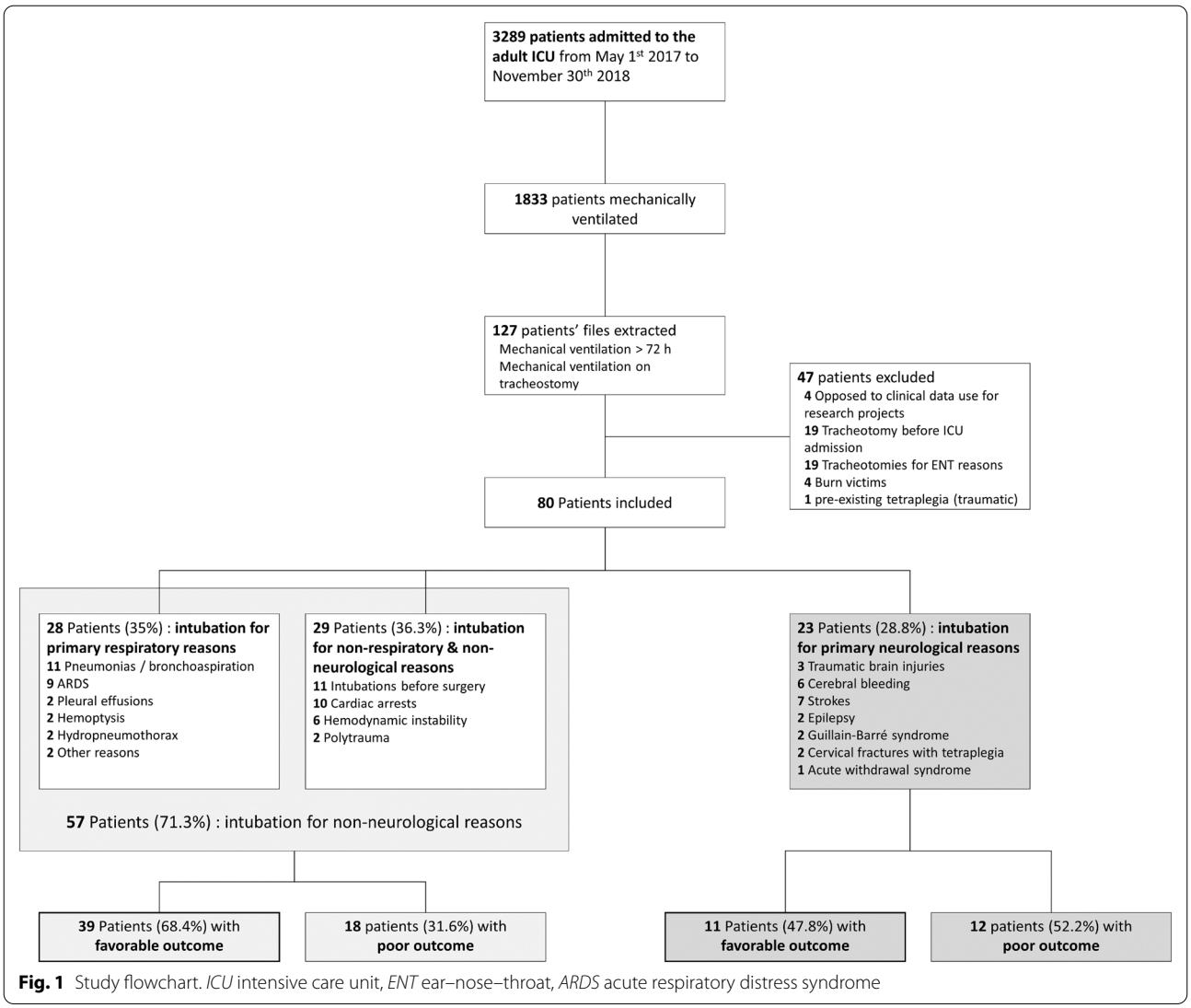


**Fig. 1** Study flowchart. *ICU* intensive care unit, *ENT* ear–nose–throat, *ARDS* acute respiratory distress syndrome

In patients intubated for neurological reasons, 3 out of 23 (13%) died during hospital stay, one in the ICU (WLST) and 2 after ICU stay (non-WLST). In patients intubated for non-neurological reasons, 16 out of 57 (28.1%) died during hospital stay, 8 in the ICU (6 WLST and 2 non-WLST) and 8 after ICU stay (5 WLST and 3 non-WLST). Hospital mortality tended to be lower in patients intubated for neurological reasons than for non-neurological reasons (13% vs 28.1%, $p = 0.245$) but the difference was not significant.

Among the global study population, 30 patients (37.5%), were classified as poor outcome, 19 because of death and 11, because tracheostomy cannula was not weaned during acute care hospital stay. Those 11 patients were all intubated for neurological reasons. General hospital data are displayed in Table 2 for the global population and in Additional file 3 and Additional file 4 both sub-groups.

### Data from intubation to tracheostomy

Main ventilator settings and monitored parameters, separation attempts, use of sedation, opioids and NMBA for the period from intubation to the day before tracheostomy are mentioned in Table 3 for the global population and for patients with favorable and poor outcomes. The same information is mentioned for the subgroups of patients intubated for non-neurological or neurological reasons in Additional file 3 and Additional file 4. SOFA score on the day of tracheostomy, the worst $PaO_2/FiO_2$ ratio on the day of tracheostomy, tracheostomy technique and time from intubation to tracheostomy are presented in Table 3 for the global

**Table 1** Patients' general characteristics, comorbidities and admission data

| | Study population *N* = 80* | Favourable outcome *N* = 50* | Poor outcome *N* = 30* | *p value*[#] |
|---|---|---|---|---|
| General characteristics | | | | |
| Age, year | 60 [52–71] | 59 [50–67] | 68.5 [55–76] | *0.03* |
| Women, *n* (%) | 23 (28.8%) | 16 (32%) | 7 (23.3%) | |
| BMI, kg/m$^2$ | 25.6 [21–30] | 24.2 [21–27] | 28.2 [24–32] | *< 0.01* |
| Comorbidities | | | | |
| Pulmonary comorbidities | | | | |
| Obstructive disease, *n*. (%) | 18 (22.5%) | 10 (20%) | 8 (26.7%) | *0.58* |
| Restrictive disease, *n*. (%) | 1 (1.3%) | 1 (2%) | 0 (0%) | *1* |
| OAS, *n*. (%) | 9 (11.3%) | 5 (10%) | 4 (13.3%) | *0.72* |
| Other pulmonary disease, *n*. (%) | 2 (2.5%) | 2 (4%) | 0 (0%) | *0.53* |
| Home $O_2$-therapy, *n*. (%) | 2 (2.5%) | 2 (4%) | 0 (0%) | *0.53* |
| Home NIV-therapy, *n*. (%) | 3 (3.8%) | 2 (4%) | 1 (3.3%) | *1* |
| Cardiac comorbidities | | | | |
| Coronary artery disease, *n*. (%) | 6 (7.5%) | 5 (10%) | 1 (3.3%) | *0.40* |
| Heart failure, *n*. (%) | 0 (0%) | 0 (0%) | 0 (0%) | *1* |
| Other comorbidities | | | | |
| Chronic kidney disease, *n*. (%) | 4 (5%) | 1 (2%) | 3 (10%) | *0.15* |
| Active neoplasia, *n*. (%) | 22 (27.5%) | 15 (30%) | 7 (23.3%) | *0.61* |
| Central neurological disease, *n*. (%) | 1 (1.3%) | 1 (2%) | 0 (0%) | *1* |
| Clinical Frailty Score | 3 [2–5] | 3 [2–5] | 4 [2–5] | *0.83* |
| NRS score at admission | 6 [3–6] | 6 [3–6] | 5.5 [4–6] | *0.37* |
| Admission data | | | | |
| Reason for ICU admission | | | | *0.31* |
| Cardiac arrest | 5 (6.3%) | 3 (6%) | 2 (6.7%) | |
| Oliguria/anuria/CRRT need | 2 (2.5%) | 1 (2%) | 1 (3.3%) | |
| Respiratory distress | 20 (25%) | 15 (30%) | 5 (16.7%) | |
| Shock | 9 (11.3%) | 5 (10%) | 4 (13.3%) | |
| Post-operative (planned) | 6 (7.5%) | 6 (12%) | 0 (0%) | |
| Post-operative (emergency surgery) | 11 (13.8%) | 4 (8%) | 7 (23.3%) | |
| Polytrauma | 6 (7.5%) | 4 (8%) | 2 (6. 7%) | |
| Other hospital transfer | 5 (6.3%) | 3 (6%) | 2 (6. 7%) | |
| Altered level of consciousness | 16 (20%) | 9 (18%) | 7 (23.3%) | |
| Type of ICU admission | | | | *1* |
| Medical, *n*. (%) | 28 (35%) | 18 (36%) | 10 (33.3%) | |
| Surgical, *n*. (%) | 52 (65%) | 32 (64%) | 20 (66. 7%) | |
| SAPS II at admission | 46.5 [39–62] | 44.5 [36–64] | 51.0 [43–61] | *0.33* |
| SOFA Score at admission | 9.0 [7–11] | 8.0 [7–11] | 9.0 [7–11] | *0.89* |
| Neurological reason for intubation | 23 (28.8%) | 11 (22%) | 12 (40%) | 0.13 |

*$N = 80$, except for NRS score at admission, where $N = 57$ ($N = 35$ for favourable outcome, $N = 22$ for poor outcome)

*BMI* body mass index, *OAS* obstructive apnea syndrome, *NIV* non-invasive ventilation, *NRS* nutrition risk screening, *ICU* intensive care unit, *CRRT* continuous renal replacement therapy, *SAPS II* Simplified Acute Physiology Score II, *SOFA score* Sequential Organ Failure Assessment score

[#] *p* value calculated using *t* test or Mann–Whitney test for continuous data and Fisher's exact test for categorical data

population and in Additional file 3 and Additional file 4 for the subgroups of patients intubated for non-neurological and neurological reasons.

Use of sedation and opioids the day before tracheostomy, ventilation data and norepinephrine infusion rate 2 h before tracheostomy are mentioned in Additional file 5.

Figure 2 illustrates the number of patients with favorable and poor outcome according to the number of separation attempts before tracheostomy.

**Table 2** General hospital data

| | | Study population | | Favourable outcome | | Poor outcome | |
|---|---|---|---|---|---|---|---|
| | *N* | | *N* | | *N* | | *p* value |
| ICU stay duration, days | 80 | 29.5 [20–44] | 50 | 28.5 [21–45] | 30 | 29.5 [20–43] | *0.82* |
| Tertiary hospital stay duration, days | 80 | 55 [43–78] | 50 | 57 [46–90] | 30 | 49 [37–64] | *0.02* |
| Days free of MV at day 30, days | 72 | 3.7 [0–12] | 47 | 5 [0–12] | 25 | 0.8 [0–12] | *0.71* |
| Days free of MV at day 60, days | 72 | 32.9 [20–41] | 47 | 35 [23–42] | 25 | 29.9 [1–37] | *0.11* |
| Intubation to cannula ablation during or after acute care hospital stay, days | 54 | 42 [35–58] | 49 | 40 [34–48] | 5 | 76 [61–144] | *< 0.01* |
| ICU-acquired weakness diagnosis, *n*. (%) | 80 | 20 (25%) | 50 | 13 (26%) | 30 | 7 (23. 3%) | *0.79* |
| With MRC score < 48/60, *n*. (%) | 80 | 17 (21.3%) | 50 | 11 (22%) | 30 | 6 (20%) | *1* |
| With EMNG/high clinical suspicion, *n*. (%) | 80 | 3 (3.8%) | 50 | 2 (4%) | 30 | 1 (3.3%) | *1* |
| MRC score value | 17 | 20 [0.5–32.5] | 11 | 20 [0–33] | 6 | 17.5 [5.3–35.5] | *0.9* |

*ICU* intensive care unit, *MV* mechanical ventilation, *MRC* medical research council sum score, *EMG* electromyography

[#] *p* value calculated using *T* test or Mann–Whitney test for continuous data and Fisher's exact test for categorical data

### Factors associated with outcome

Table 4 summarizes for the global population the results of univariate logistic regressions and multivariate analysis. In univariate logistic regressions, older age and higher BMI were associated with poor outcome, with OR of 1.18 [1.07–1.32] and 1.04 [1.01–1.08] (*p < 0.001* and *0.025*, respectively). As post-hoc analysis, a second multivariate model with duration from intubation to tracheostomy forced into the model because of its clinical relevance was performed. This model did not show different results (see Additional file 6). We also conducted univariate logistic regressions and multivariate analysis for the sub-group of patients intubated for non-neurological reasons. The univariate analyses revealed only age as a factor associated with poor outcome (OR of 1.054 [1.01–1.11] *(p = 0.0191)*). The multivariate model showed that BMI and age were associated with poor outcome in this sub-group of patients intubated for non-neurological reasons. Detailed results of the univariate and multivariate analyses are mentioned in Additional file 7.

## Discussion

We reviewed ventilation settings, sedation–analgesia and outcomes of patients ventilated for more than 72 h and tracheostomized during the ICU stay, both for neurological and non-neurological reasons. For the global patient group, in univariate logistic regressions, only older age and higher BMI were associated with poor outcome, defined as in-hospital death or hospital discharge without decannulation. This remained true in the multivariate logistic regression analysis. For the subgroup of patients intubated for non-neurological reasons, the multivariate analysis led to similar conclusions. In this study, we also confirmed high ICU-admission severity scores, high hospital mortality and long ICU and hospital length of stay in tracheostomized patients [1].

Patients intubated and ventilated for all causes and tracheostomized for difficult weaning have high mortality [14, 23]. For example, in the population of patients ventilated for more than 10 days and tracheostomized following acute respiratory distress syndrome, high 28-day and 90-day mortality was reported (30.8% and 45.2%, respectively [12]). Our study population has the characteristics of a general ICU population, including both medical and surgical patients and patients intubated both for neurological and non-neurological reasons. We found relatively low ICU mortality for tracheostomized patients initially intubated for neurological reasons compared to other studies [24, 25] but a high hospital mortality in line with the literature for the global group of patients [1]. The high hospital mortality observed in our population was expected, considering the high severity scores at admission. Death after withdrawal of life-sustaining therapy concerned 63.2% of patients, suggesting frequent poor evolution after tracheostomy, underlining the difficulty of predicting global evolution at the time of tracheostomy.

In the literature, ICU and hospital length of stay differ in tracheostomized patients depending on the series of patients. Hospital length of stay in our population was higher compared to most available data. This could be related to differences in health care policies. Indeed, long-term weaning facilities are not available in Switzerland. In addition, most long-term care facilities do not manage mechanical ventilation in tracheostomized patients and home discharges with home ventilation on tracheostomy is unusual in Switzerland. Those factors could explain the prolonged length of stay in acute-settings hospital. Local practices regarding late or early

**Table 3** Ventilation data, sedation, opioids, NMBA use and tracheostomy data

| | **Study population** ***N*** **= 80*** | **Favourable outcome** ***N*** **= 50*** | **Poor outcome** ***N*** **= 30*** | ***p value#*** |
|---|---|---|---|---|
| Ventilation data between intubation and tracheostomy | | | | |
| Percentage of mechanical ventilation days with more than 12 h with: | | | | |
| VAC, *n*. (%) | 33.3% [18–59%] | 39.3% [22–60%] | 28.7% [10–48%] | *0.16* |
| PAC, *n*. (%) | 0% [0–0%] | 0% [0–0%] | 0% [0–0%] | *0.85* |
| PSV, *n*. (%) | 61.1% [40–79%] | 57.7% [40–74%] | 66.7% [46–86%] | *0.22* |
| Other, *n*. (%) | 0% [0–0%] | 0% [0–0%] | 0% [0–0%] | *0.55* |
| $V_T$, mL | 454.6 [414–530] | 441.2 [403–532] | 469.5 [424–533] | *0.29* |
| $V_T$/PBW, mL/kg | 7 [6–8] | 7 [6–8] | 7 [6–8] | *0.57* |
| PEEP, $cmH_2O$ | 6.9 [6–8] | 6.8 [6–8] | 7.1 [6–8] | *0.10* |
| RR, cycle/min | 21.8 [20–25] | 22.6 [20–25] | 21.5 [18–26] | *0.94* |
| Dynamic $P_{plat}$, $cmH_2O$ | 20.3 [18–24] | 21.7 [18–25] | 20 [17–22] | *0.10* |
| Driving pressure, $cmH_2O$ | 13.4 [11–15] | 13.9 [12–17] | 12.2 [10–14] | *0.04* |
| Separation attempts | | | | *0.57* |
| *0* | 21 (26.3%) | 11 (22%) | 10 (33.3%) | |
| *1* | 11 (13.8%) | 8 (16%) | 3 (10%) | |
| *2* | 11 (13.8%) | 6 (12%) | 5 (16.7%) | |
| *> 2* | 37 (46.3%) | 25 (50%) | 12 (40%) | |
| Percentage of days with sedation use | | | | |
| Any sedation, % | 93.5% [76–100%] | 100% [79–100%] | 89.3% [66–100%] | *0.09* |
| Propofol, % | 74.3% [50–91%] | 77.8% [55–95%] | 69% [49–86%] | *0.29* |
| Midazolam, % | 19.1% [0–53%] | 33.3% [9–54%] | 12.9% [0–34%] | *0.06* |
| Dexmedetomidine, % | 0% [0–21%] | 9.8% [0–25%] | 0% [0–13%] | *0.11* |
| Percentage of days with opioids use | | | | |
| Opioids, % | 100% [87–100%] | 100% [89–100%] | 100% [77–100%] | *0.77* |
| Morphine, % | 0% [0–0%] | 0% [0–0%] | 0% [0–2%] | *0.30* |
| Fentanyl, % | 94.2% [67–100%] | 93.8% [72–100%] | 96.1% [53–100%] | *0.88* |
| Other opioids, % | 0% [0–0%] | 0% [0–0%] | 0% [0–0%] | *0.80* |
| Percentage of days with NMBA use | | | | |
| NMBA, % | 12.5% [0–30%] | 14.4% [4–31%] | 10.4% [0–28%] | *0.40* |
| Proportion of patients receiving sedation or opioids the day before tracheostomy | | | | |
| Sedation, *n* (%) | 60 (75.0%) | 38 (76%) | 22 (73.3%) | *0.80* |
| Opioids *n* (%) | 67 (83.75%) | 43 (86%) | 24 (80%) | *0.54* |
| Tracheostomy data | | | | |
| Worst $PaO_2/FiO_2$ ratio on the day of tracheostomy | | | | *0.50* |
| ≥ 400 mmHg | 2 (2.5%) | 1 (2%) | 1 (3.3%) | |
| < 400 mmHg | 12 (15%) | 5 (10%) | 7 (23.3%) | |
| < 300 mmHg | 18 (22.5%) | 13 (26%) | 5 (16.7%) | |
| < 200 mmHg | 43 (53.8%) | 28 (56%) | 15 (50%) | |
| < 100 mmHg | 5 (6.3%) | 3 (6%) | 2 (6.7%) | |
| Type of tracheostomy | | | | *0.76* |
| Percutaneous, *n* (%) | 13 (16.25%) | 9 (18%) | 4 (13. 3%) | |
| Surgical, *n* (%) | 67 (83.75%) | 41 (82%) | 26 (86. 7%) | |
| Time from intubation to tracheostomy, days | 14.7 [10–20] | 14.6 [10–20] | 14.8 [10–22] | *0.92* |

*N* = 80 except for dynamic $P_{plat}$ and driving pressure, where *N* = 70 (*N* = 45 for favourable outcome and N = 25 for poor outcome)

*VAC* volume assist-control, *PSV* pressure-support ventilation, *PAC* pressure assist-control ventilation, *VT* tidal volume, *PBW* predicted body-weight, *PEEP* positive end-expiratory pressure, *RR* respiratory rate, $P_{plat}$ plateau pressure, *NMBA* neuromuscular blocking agents, $V_T$, $V_T$/PBW, PEEP, RR and Dynamic $P_{plat}$ were recorded once a day at 8 am

# *p* value calculated using *T* test or Mann–Whitney test for continuous data and Fisher's exact test for categorical data

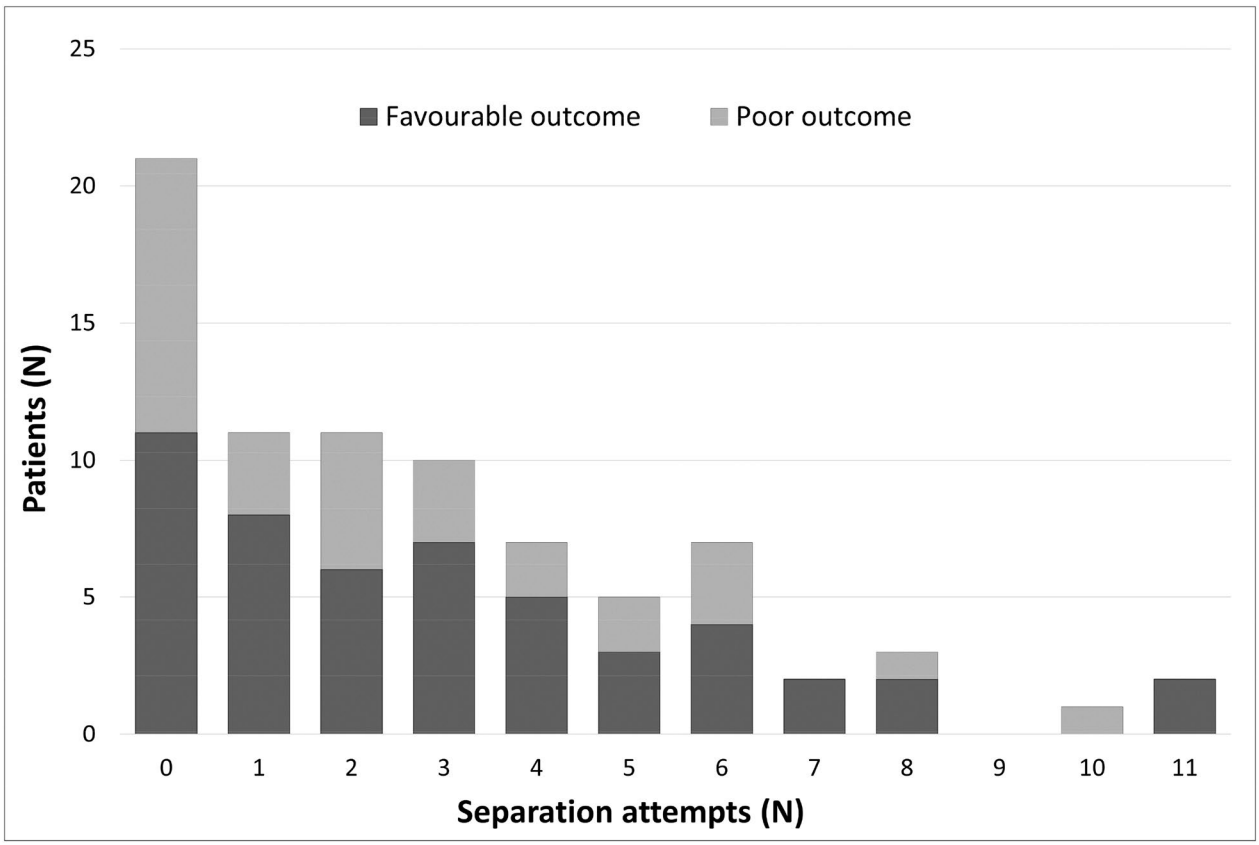


**Fig. 2** Separation attempts before tracheostomy. Number of separation attempts by patients for each group of outcome

withdrawal of life-sustaining treatment could also impact hospital length of stay and this can differ between countries, hospitals and even health-care practitioners [26]. Our high percentage of WLST combined with high length of hospital stay, when compared to other countries in Europe and in the world [27] underline the fact that WLST only takes place relatively late in our hospital in tracheostomized patients. This emphasizes the fact that predicting outcomes of tracheostomized patients takes time and requires, at least in Switzerland, a multi-disciplinary consensus, which is sometimes difficult to reach. Such a consensus can sometimes even be difficult to find within the team in charge of the patient because of different individual perceptions of the clinical situation. This is true not only at time of tracheostomy, but also after ICU discharge.

In addition to common ICU parameters to predict outcomes, our study specifically assessed the relationship between outcome and ventilation, sedation, opioid and NMBA use before tracheostomy. No ventilation parameters showed any association with poor outcome. To note, our data also showed good compliance with international ventilation guidelines [28]. Sedation, opioids and NMBA use before tracheostomy did not show any association with outcome. This remained true for tracheostomized patients who intubated for neurological and non-neurological reasons.

This study adds a new perspective on the prediction of unfavorable outcome in tracheostomized patients by demonstrating that ventilation data prior to the tracheostomy did not help predict outcome. Indeed, only higher BMI and older age were associated with poor outcome. This highlights yet the fact that decision to undergo tracheostomy can only be based on general clinical judgment and that more or less severe respiratory status and worse ventilation parameters cannot be used to select patients who could benefit from tracheostomy.

Separation attempts were performed in 73.4% of patients before tracheostomy, which is similar to numbers reported in the recent WIND study collective [1]. The number of separation attempts before tracheostomy was not associated with better or worse outcome. We initially hypothesized that the relationship between mortality and the number of SBT takes the form of a U-shaped curve, with worse outcomes in patients with no SBT (i.e., because of persistent organ failure) and in patients with

**Table 4** Univariate analyses and multivariate logistic regression model for factors potentially associated with bad outcome

| | Univariate regression | | Multivariate model | | |
|---|---|---|---|---|---|
| | **OR (CI 95%)** | ***p* value** | **OR (CI 95%)** | **VIF** | ***p* value** |
| BMI | 1.181 (1.07–1.32) | 0.0009 | 1.205 (1.09–1.36) | 1.003 | 0.0008 |
| Age | 1.038 (1.01–1.08) | 0.0253 | 1.044 (1.00–1.09) | 1.037 | 0.0463 |
| Sex | 2.061 (0.73–6.42) | 0.2967 | | | |
| Number of comorbidities | 1.248 (0.73–2.15) | 0.4471 | | | |
| Clinical Frailty Score | 0.986 (0.76–1.27) | 0.8269 | | | |
| NRS score at ICU admission | 1.129 (0.88–1.48) | 0.385 | | | |
| SAPS II at ICU admission | 1.011 (0.99–1.04) | 0.3227 | | | |
| SOFA score at ICU admission | 1.010 (0.87–1.17) | 0.8776 | | | |
| Type of ICU admission (medical/surgical) | 0.560 (0.22–1.44) | 0.3203 | | | |
| Neurological cause for intubation | 0.849 (0.30–2.30) | 0.8038 | | | |
| $V_T$/PBW | 1.160 (0.81–1.68) | 0.5643 | | | |
| PEEP | 1.026 (0.79–1.34) | 0.996 | | | |
| Dynamic plateau pressure | 0.898 (0.78–1.02) | 0.1097 | | | |
| Percentage of days with sedation use | 0.213 (0.03–1.26) | 0.1011 | 0.208 (0.02–1.57) | 1.035 | 0.14 |
| Percentage of days with opioids use | 0.293 (0.02–5.01) | 0.7923 | | | |
| Percentage of days with NMBA use | 0.592 (0.07–4.19) | 0.401 | | | |
| Control ventilation before tracheostomy | 0.383 (0.07–1.97) | 0.1597 | | | |
| 1st separation attempt | 1.062 (0.95–1.19) | 0.2298 | | | |
| Any separation attempt | 0.564 (0.20–1.57) | 0.3983 | | | |
| Sedation use (day before tracheostomy) | 1.556 (0.54–4.91) | 0.551 | | | |
| Opioids use (day before tracheostomy) | 3.949 (0.96–26.82) | 0.2531 | | | |
| Tracheostomy technique (percutaneous vs surgical) | 1.427 (0.42–5.70) | 0.728 | | | |
| Time from intubation to tracheostomy | 1.006 (0.95–1.07) | 0.921 | | | |

*BMI* body mass index, *NRS* nutrition risk screening, *ICU* intensive care unit, *SAPS II* Simplified Acute Physiology Score II, *SOFA score* Sequential Organ Failure Assessment score, $V_T$*/PBW* tidal volume divided by predicted body weight, *PEEP* positive end-expiratory pressure, *NMBA* neuromuscular blocking agents

Left *p* values calculated using univariate logistic regression for each variable. Right *p* values calculated with multiple logistic regression model, which included BMI, age and sedation use

many SBT (i.e., very prolonged weaning). Therefore, we looked in our data but found no pattern to corroborate this hypothesis. To note, this study did not address the subject of MV weaning strategies after tracheostomy.

As limitations for this study, we must mention that, in this retrospective study, mechanical ventilation data were collected at arbitrary time-points and do not always accurately represent 24-h data. However, as data were collected daily, the ventilation parameters reflect the whole duration of mechanical ventilation before tracheostomy. Second, regarding patients sub-groups, it can be argued that patients intubated because of cardiac arrest could have been classified as patients with neurological impairment. However, eight of them were tracheostomized because of difficult weaning and one because of difficult secretion management. Only one patient was tracheostomized because of persistent neurological impairment. Thirdly, no comparison with a control group without tracheostomy was performed. Even if this comparison would be interesting to assess the impact of tracheostomy on patients' outcome, we could not do it. Tracheostomy is part of the protocolized management of prolonged weaning in our ICU in the absence of poor prognosis regarding recovery potential. Patients with prolonged weaning who are not tracheostomized have thus different characteristics compared to the tracheostomized patients and cannot be used as a control group. Fourthly, because of the monocentric nature of this study and very different practices regarding tracheostomy between different centers due to the lack of unifying guidelines for tracheostomy indications, our conclusions can probably not be generalized to all other ICUs. Health-care policies and organizational differences concerning the transfer from the ICU to a step-down unit (or other health-care facilities) can also limit the applicability of our results to other hospitals. Finally, in the absence of sample size calculation, our study could potentially have been underpowered to evaluate the association between some factors and outcome. However, tracheostomies for prolonged weaning in the ICU is relatively rare, and monocentric studies rarely have much larger collectives.

## Conclusions

This study showed high mortality and long duration of hospital stay in a medico-surgical population of patients tracheostomized in the ICU in part of the process of MV weaning. In univariate logistic regressions, older age and higher BMI were associated with poor outcome, defined as in-hospital death or hospital discharge without decannulation. This remained true in the multivariate logistic regression analysis. The same factors associated with outcome were identified when the multivariate analysis was performed in the subgroup of patients intubated for non-neurological reasons. We found no association between ventilatory data before tracheostomy and outcome, neither for the global patient population nor for the patients intubated for non-neurological reasons. This was also true for sedation, analgesics and NMBA use up to the day before tracheostomy. Separation attempts were frequent before tracheostomy but the number of attempts was not associated with outcome.

#### Abbreviations

ICU: Intensive care unit; MV: Mechanical ventilation; ENT: Ear–nose–throat; BMI: Body-mass index; CHUV: Centre Hospitalier Universitaire Vaudois; NRS: Nutrition Risk Screening; SAPS II: Simplified Acute Physiology Score II; SOFA: Sequential Organ Failure Assessment; NMBA: Neuromuscular blocking agent; SBT: Spontaneous breathing trial; WLST: Withdrawal of life-sustaining treatment; OR: Odds ratio; CI: Confidence interval; ESM: Electronic supplemental materials.

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13613-022-01047-z.

**Additional file 1.** Data collection details.

**Additional file 2.** Patients' general characteristics, comorbidities and admission data for study population andseparated by cause for intubation.

**Additional file 3.** General characteristics & comorbidities, admission data, ventilation data, sedation, opioids, NMBA use, tracheostomy data and outcomes data for patients intubated for non-neurological reasons.

**Additional file 4.** General characteristics & comorbidities, admission data, ventilation data, sedation, opioids, NMBA use, tracheostomy data and outcomes data with patients intubated for neurological reasons only.

**Additional file 5.** Ventilation and norepinephrine use 2-hours before tracheostomy.

**Additional file 6.** Univariate and multivariate logistic regression models for factors potentially associated with poor outcome.

**Additional file 7.** Univariate analyses and multivariate logistic regression model for factors potentially associated with poor outcome for patients intubated for non-neurological reasons only.

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Not applicable.

#### Author contributions

DC and LP designed the study, DC and TV collected the data. DC, TV and LP designed the analysis plan. DC, TV, LP, EL, HM and KS contributed to data analysis and interpretation. DC and TV wrote the first draft of the manuscript. All the authors contributed substantially to the writing of the manuscript and critically reviewed the final version. All authors read and approved the final manuscript.

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#### Availability of data and materials

The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

#### Ethics approval and consent to participate

This study was approved by the local ethics committee (Commission cantonale d'éthique de la recherche sur l'être humain, CER-VD) on December 23rd 2020 (protocol number 2019-01403). Waiver of consent was granted for use of data and only patients who had explicitly refused the use of their clinical data for research purposes were excluded. This study was conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH–GCP as well as other locally relevant legal and regulatory requirements. This study was registered on clinicaltrials.org (NCT04987398).

#### Notation of prior abstract publication/presentation

This study was presented as an abstract and poster at the Swiss Society of Intensive Medicine (SSMI) on September 22nd 2021 (Interlaken, Switzerland).

#### Consent for publication

Not applicable.

#### Competing interests

The authors declare that they have no competing interests.

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## Publisher's Note

# 1. TABLE OF CONTENT

# 2. INTRODUCTION

In the intensive care unit (ICU), mechanical ventilation (MV) is challenging to wean in approximately 19% of patients. Both difficult (10.1%) and prolonged (8.7%) weaning (1, 2) contribute to longer duration of ICU stay and increased mortality and morbidity (1-6). For this reason, as recommended in the last consensus conference on the topic (7), MV weaning should be an active process centred on the research of weaning readiness criteria, the execution of spontaneous breathing trials (SBT) and prompt extubation after successful SBT (8, 9). The goal of SBT is to assess the ability to breath without the assistance of the ventilator and therefore detect patients who are ready to be extubated. The most frequently used SBT are either decrease of pressure support (PS) and/or positive end-expiratory pressure (PEEP) to varying levels, or disconnection from the ventilator and breathing through a T-tube for $O_2$ delivery. SBT are well studied in intubated patients (7, 10, 11), including their effect on patients' work of breathing. A recent meta-analysis (11) compared, in orally intubated patients, work of breathing (WOB) and oesophageal pressure-time product (PTPes, a reflection of global inspiratory muscle strength) during different types of SBT and after extubation. Compared with the situation after extubation, the SBT with PS were associated with a reduction in WOB and PTPes. In contrast, WOB during the T-piece trial was close to WOB measured after extubation, suggesting that this test better reflected the physiological conditions of the post-extubation period. However, it has been shown that using the T-tube trial as the default weaning test in intubated patients can unnecessarily prolong the duration of ventilation because it sometimes fails to detect patients who are ready for extubation. SBT in PS can identify a patient ready to be extubated earlier without increasing the risk of re-intubation, even in the subgroup of patients at risk of extubation failure (12, 13).

For patients who are unable to be weaned, tracheostomy is often required, even if it is an invasive surgical procedure. It may reduce work of breathing, sedation need (14) and it facilitate patients' care (15, 16). It also allows phonation (17, 18) and sometimes oral feeding (19), even if MV is still intermittently necessary. Some aspects of tracheostomy are well studied, such as the timing of the procedure (16, 20, 21) and the tracheostomy technique (22, 23). Other aspects, such as MV weaning, are not well codified in tracheostomized patients and strategies vary depending on centres (24-27). This is due to the lack of data in the literature for this specific situation and to the fact that data available in intubated patients cannot be translated to tracheostomized patients because of the different characteristics of tracheostomy cannula and endotracheal tube, especially in term of resistance of the device. As a consequence, concerning MV weaning, the potential advantages of disconnecting the patients from the ventilator compared to a progressive reduction of PS remains debated. Jubran et al. (28) showed in 2013 that disconnection from the ventilator and breathing through the tracheostomy collar allowed for quicker MV weaning than progressive reduction in pressure support (PS) but without any impact on mortality. Importantly, this study was conducted in a small number of patients and provided no data on the effect on patients' work of breathing between both strategies.

Regarding tracheostomy cannula weaning, several strategies coexist (29). For example, intermittent and

iterative cuff deflation (26) allows upper airway air flow, stimulates larynx re-afferentation and decreases the risk of micro-aspirations (30) and pneumonia (31). It can be started either during continuous or during intermittent MV support. Progressive reduction of cannula diameter (downsizing) is used in some centres to increase air flow in the upper airways when the cannula cuff is deflated and to start stoma cicatrisation. Both regular cuff deflation and downsizing decrease pressure on tracheal mucosa. The use of fenestrated cannula is an alternative to allow speaking (32, 33) and upper airway air flow when the patient is disconnected from the ventilator (34). Talking valves on tracheostomy cannula are sometimes used as a step toward tracheostomy cannula weaning (18, 35-37). They are most often used in patients who no longer need continuous ventilatory support. However, in some patients, dedicated talking valves can also be placed in-line in the ventilator circuit during MV (with deflated cuff and intentional air leaks) (38). This approach improves communication and airway protection, without leading to lung de-recruitment (36). Finally, cannula capping is sometimes used as a last step before cannula ablation (24, 39), even if few data is available regarding this practice (40). All those strategies are used in different combinations in different ICU but without much literature support.

To optimise the care of tracheostomized patients, it is first important to better understand which patients will really benefit from tracheostomy. Additional data on SBT in tracheostomized patients are needed to expedite the weaning process. Finally, more data on the weaning strategies of MV and tracheostomy cannula could help design clinical protocols to improve tracheostomized patients' outcome.

# 3. OBJECTIVES

This work aimed to answer to three different questions regarding the outcome prediction and management of patients tracheostomized in the ICU because of difficult or prolonged weaning. To that purpose, this work was separated into two parts with separate objectives: one retrospective data analysis comprising two studies and one physiological prospective study.

The main objective of the first retrospective analysis was to study the association between tracheostomized patients' outcomes at hospital discharge and patients' characteristics, tracheostomy technique, MV management and sedation/analgesia use before tracheostomy.

The main objective of the second retrospective analysis was to describe MV and cannula weaning process in tracheostomized patients. The additional objective of this second retrospective study was to look for an association between patients' outcome and both MV weaning after tracheostomy and tracheostomy weaning strategies used.

The main objective of the prospective physiological study was to study the effect of three different spontaneous breathing trials performed in tracheostomized patients on esophageal pressure-time product, a parameter of global inspiratory strength. We also aimed to describe respiratory profiles during those three different spontaneous breathing trials.

# 4. EARLY PREDICTION OF HOSPITAL OUTCOMES IN PATIENTS TRACHEOSTOMIZED FOR COMPLEX MECHANICAL VENTILATION WEANING

## 4.1. Aim

The aim of this study was to analyze the association of tracheostomized patients' outcomes at hospital discharge with patients' characteristics, tracheostomy technique, MV management and sedation/analgesia use before tracheostomy.

## 4.2. Methods

Retrospective single-center study. Adult patients mechanically ventilated for at least 72 hours and tracheostomized were considered for inclusion. Patients who had a tracheostomy before ICU admission or performed for ear-nose-throat reasons were excluded. Conditions precluding MV weaning and burn victims were also excluded from the study. Data were collected from medical files and clinical information system. Patients' characteristics, risk score, comorbidities were collected. Key dates from the whole hospital stay were collected. Ventilator settings, sedation and analgesics use before tracheostomy were compiled. Tracheostomy technique used was collected. Finally, general hospital data and outcome data were sampled. Favorable outcome was defined as being alive and decannulated at hospital discharge. Comparisons between outcome groups were performed using T-test, Mann-Whitney test and Fischer's exact test as appropriate. Binary and multivariate logistic regressions were used to evaluate the association of pre-tracheostomy variables with patients' outcome.

## 4.3. Main results

80 patients were included (28.8% women) with a median age of 60 [52-71] years old. Twenty-three (28.8%) patients were intubated for neurological reasons. Time from intubation to tracheostomy was 14.7 [10-20] days. Thirty patients (37.5%) had poor outcome (19 patients deceased and 11 were still tracheostomized at hospital discharge). Characteristics of patients were similar between both subgroups, except for age and BMI (favorable outcome group was younger and had lower BMI). In the univariate logistic regressions, older age and higher body-mass index (BMI) were associated with poor outcome. No mechanical ventilation parameters were associated with poor or favorable outcome. In the multiple logistic regression model higher BMI and older age were also associated with poor outcome.

## 4.4. Conclusion

This population of patients suffers from high mortality and long hospital stay durations. Only younger age and lower BMI were associated with favorable outcome at hospital discharge. No variable from the mechanical ventilation data or tracheostomy timing or technique were associated with outcome.

## 4.5. Study details

This study was published in *Annals of Intensive Care* on August 8$^{th}$, 2022.

# 5. MECHANICAL VENTILATION AND TRACHEOSTOMY CANNULA WEANING STEPS AND TIMING IN ICU PATIENTS TRACHEOSTOMIZED FOR DIFFICULT WEANING

## 5.1. Background

Invasive mechanical ventilation (MV) may sometimes be difficult to wean (1-3). Approximately 19% of invasively ventilated patients in the ICU experience difficult (10.1%) or prolonged (8.7%) weaning (1, 2), with both conditions contributing to longer duration of ICU stay and increased mortality and morbidity (1, 2, 4, 5). All strategies that could help separating the patient from the ventilator are thus of interest. Tracheostomy is often considered in case of prolonged weaning as it may reduce work of breathing, decrease sedation need (14) and facilitate patients' care (27). It also allows phonation (17, 18) and sometimes oral feeding while MV is still intermittently necessary. However, on the other hand, the placement of a tracheostomy cannula is also associated with significant local complications (41, 42) that become more frequent the longer it remains in place (43).

MV weaning of tracheostomized patients is not well codified and strategies vary depending on centres (25). This includes the strategy used to reduce the ventilator support, the assessment of the readiness to wean status and the steps to go through before ablating the tracheostomy cannula. Regarding the strategy used for reducing the support delivered by the ventilator, progressive step-by-step decrease in pressure support or disconnection from the ventilator are two different options. These two methods have been compared in a small study with an advantage in favor of the disconnection that was associated with a shorter duration of MV (28).

Regarding tracheostomy cannula weaning, several strategies also coexist (29). For example, intermittent and iterative cuff deflation (26) allows upper airway airflow, which stimulates larynx afferentation and contributes to decrease the risk of micro-aspirations (30) and nosocomial pneumonia (31). It can be used on a daily basis, starting with short periods of deflation in patients who still need intermittent MV or who still are under continuous ventilatory support. Progressive reduction of cannula diameter (downsizing) is used in some centres to increase air flow in the upper airways when the cannula cuff is deflated and to enable phonation if MV is not continuous. Both regular cuff deflation and downsizing decrease pressure on tracheal mucosa. The use of fenestrated cannula is an alternative to allow speaking (32) and upper airway airflow when the patient is disconnected from the ventilator (34). Talking valves on tracheostomy cannula are also sometimes used as a step toward tracheostomy cannula weaning (18, 35, 37). They are most often used in patients who no longer need continuous ventilatory support. However, in some patients, they can also be placed in-line in the ventilator circuit during MV (with deflated cuff and intentional air leaks) (38). This approach improves communication and airway protection, without leading to lung de-recruitment (36). Finally, cannula capping is sometimes used as a last step before cannula ablation (24, 39), even if few data is available regarding this practice (40).

Our objective was to describe the MV and cannula weaning process (steps and timing) used in patients intubated for non-neurological and non-"ear-nose-throat" (ENT) reasons in our tertiary centre medico-surgical adult ICU. Our secondary objective was to look for an association between the MV and tracheostomy weaning steps used in our ICU and patients' outcome. The patients included in this study were part of a bigger cohort of patients intubated either for neurological and non-neurological reasons previously used to analyse the relationship between, patients' characteristics, pre-tracheostomy management and patients' outcomes (27).

## 5.2. Methods

### 5.2.1. Study design and ethics considerations

We conducted a retrospective single-centre study in the medico-surgical Adult Intensive Care Unit of the Lausanne University Hospital (CHUV), Switzerland. Source data were medical files and clinical information system. This study was approved by the local ethics committee (Commission cantonale d'éthique de la recherche sur l'être humain, protocol number 2019-01403). Waiver of consent was obtained, except for patients who explicitly refused the use of their clinical data for research purposes, who were excluded.

### 5.2.2. Inclusion and exclusion criteria

Patients admitted to the Adult ICU between May 1$^{st}$ 2017 and November 30$^{th}$ 2018 and who were tracheostomized after at least 72 hours of MV were screened for inclusion. Exclusion criteria were: explicit refusal to the use of data for research purposes, intubation for neurological or for ENT reasons, tracheostomy performed before ICU admission, ICU hospitalization because of burns and pre-existing conditions (prior to ICU admission) precluding ventilation weaning.

### 5.2.3. Data collection and definitions

Patients' characteristics at ICU admission, reason for ICU admission, data regarding MV weaning before tracheostomy, Clinical frailty scale (CFS), Nutrition risk screening (NRS) score, Simplified Acute Physiology Score II (SAPS II) and Sequential Organ Failure Assessment (SOFA) scores on the day of admission were collected. MV separation attempts (SA) before tracheostomy were defined, according to our protocol as either a Spontaneous breathing trial (SBT) or extubation with no prior SBT (2). A SBT was defined as either a mention of T-tube SBT or as pressure support (PS) ventilation with a PS level of maximum 8 $cmH_2O$ and a maximal concomitant level of positive end-expiratory pressure (PEEP) of 5 $cmH_2O$.

Tracheostomy technique (surgical or percutaneous), the type and size of the first cannula inserted and SOFA score on the day of tracheostomy were recorded. Data concerning the MV weaning process after tracheostomy were collected. Arbitrarily, MV was considered as weaned in a tracheostomized patient when there were at least three consecutive days with less than 12 hours of MV per day. The day of the first weaning in a tracheostomized patient was recorded as the first of these three days. In case of reconnection to the ventilator after the first MV weaning, the number of reconnections and the number of hours per day of MV were collected until decannulation or ICU discharge (whichever came first).

We recorded time from tracheostomy to the first MV separation attempt, the total number of SA and time from tracheostomy to MV weaning. We also collected the minimal and maximal PS and PEEP levels daily during that time.

Data on transcannulations and use of deflated cannula cuff, speaking valve and hermetic cap toward tracheostomy cannula ablation or ICU discharge (whichever comes first) were also collected. The time from tracheostomy to the first of each event, as well as the number of occurrences per patient per week were recorded. Physical therapy (PT) sessions (active mobilization only) were also recorded each day between tracheostomy and decannulation or ICU discharge (whichever comes first).

As outcome data, we collected ICU and hospital mortality, ICU and hospital stay durations, time from tracheostomy to ICU discharge, presence of ICU-acquired weakness documented in the ICU discharge letter and defined either by a Medical Research Council (MRC) sum score of less than 48/60, a compatible electroneuromyography exam or high clinical suspicion in the absence of sufficient collaboration to perform the MRC score. We also recorded the number of patients alive at hospital discharge who were transferred to an in-patient rehabilitation facility.

Favorable outcome was considered when the patient was weaned of tracheostomy cannula within 30 days of the tracheostomy procedure and alive at hospital discharge. Poor outcome was considered when a patient either died during hospital stay or was not weaned from tracheostomy cannula within 30 days after the tracheostomy procedure.

### 5.2.4. Data analysis

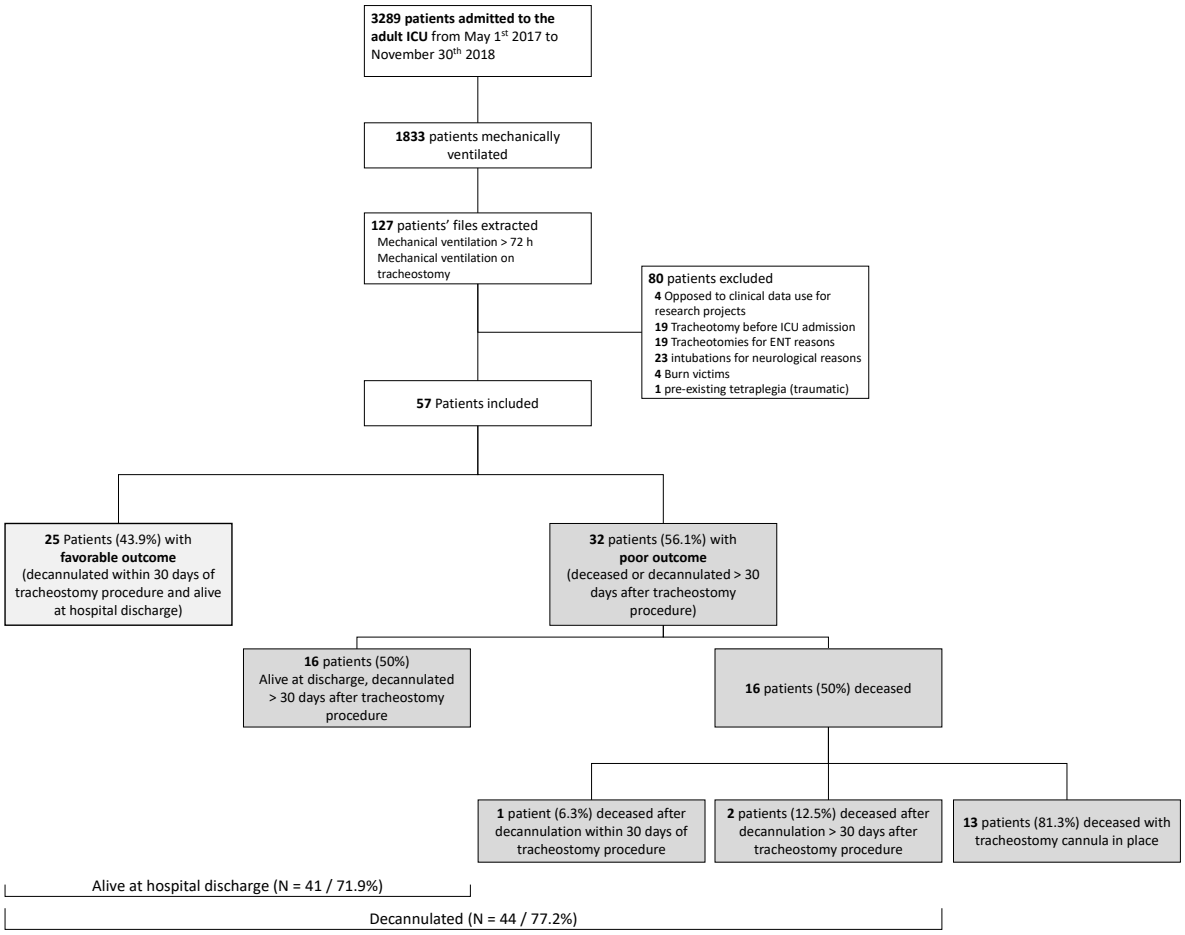
No statistical sample size calculation was performed for this retrospective study. Sample size equalled to the number of patients who could be included and were treated during the study period. Missing data were not imputed. Data was reported as number and percentage for proportions and as median [25th and 75th percentile] for continuous data. Normality was tested using the Shapiro-Wilk test. Comparisons between favorable and poor outcome sub-groups for continuous data were performed using T-tests or Mann-Whitney tests as appropriate. Fisher's exact test was used for categorical data. Univariate binary logistic regressions were used to evaluate the association between the parameters of interest related to the MV and tracheostomy weaning process and patients' outcome. Results for univariate logistic regressions were reported as odds ratio (OR) with 95% confidence interval (CI). Statistical analyses were performed using GraphPad Prism version 9.1.0 for Windows (GraphPad Software, San Diego, California USA) except for Fisher's exact tests, which were performed using R version 1.4.2 (R Foundation for Statistical Computing, Vienna, Austria). All statistical tests were two-tailed and p-value $< 0.05$ was considered significant.

## 5.3. Results

A total of 57 patients who were intubated for non-neurological and non-ENT reasons were included. Among them, 25 (43.9%) were decannulated within 30 days of the tracheostomy procedure and discharged alive from hospital (favorable outcome). The remaining 32 (56.1%) patients were classified as poor outcome

because they either died in the hospital (N = 16, 28.1%) or were decannulated after more than 30 days even if discharged alive from the hospital (N = 16, 28.1%). Among the 16 deceased patients, 3 were decannulated before death, 1 within 30 days of the tracheostomy procedure and 2 after more than 30 days. The study flowchart is displayed in **Figure 1**. Among patients weaned from tracheostomy (N = 44), 18 (41%) patients were decannulated in the ICU and 26 (59%) later during the hospital stay. None were decannulated after hospital discharge.

**Figure 1**. Study flowchart




ICU = intensive care unit, ENT = ear-nose-throat

General patients' data, CFS, NRS, comorbidities, admission data and pre-tracheostomy weaning data are mentioned in **Table 1**, both for the total population and for the favorable and poor outcome sub-groups (with p-value for sub-groups comparisons).

**Table 1**. Patients' characteristics and pre-tracheostomy MV weaning data

| | **Total population** N = 57* | **Favorable outcome** N = 25* | **Poor outcome** N = 32* | *p-value#* |
|---|---|---|---|---|
| **General data** | | | | |
| Age - yr | 60 [52 - 73] | 56 [48 - 65.5] | 65.5 [56.5 - 76.8] | *0.014* |
| Women – n. (%) | 15 (26.3%) | 6 (24%) | 9 (28.1%) | *1* |
| BMI - kg/m$^2$ | 24.5 [20.9 - 28.8] | 23.7 [20.3 - 26.4] | 26.6 [21.3 - 30.6] | *0.077* |
| Clinical Frailty Scale | 4 [3 - 5.5] | 3 [2 - 5.5] | 4 [3 - 5.8] | *0.195* |
| NRS score | 6 [3 - 6] | 6 [3 - 6] | 6 [3 - 7] | *0.495* |
| **Comorbidities** | | | | |
| Pulmonary comorbidities – n. (%) | | | | |
| *Obstructive disease* | 16 (28.1%) | 6 (24%) | 10 (31.3%) | *0.378* |
| *Restrictive disease* | 1 (1.8%) | 0 (0%) | 1 (3.1%) | *1* |
| *OSA* | 8 (14%) | 4 (16%) | 4 (12.5%) | *0.709* |
| *Other pulmonary disease* | 2 (3.5%) | 1 (4%) | 1 (3.1%) | *1* |
| *Home $O_2$ -therapy* | 2 (3.5%) | 2 (8%) | 0 (0%) | *0.1733* |
| *Home CPAP or NIV therapy* | 2 (3.5%) | 2 (8%) | 0 (0%) | *0.173* |
| Cardiac comorbidities – n. (%) – n. (%) | | | | |
| *Coronary artery disease* | 6 (10.5%) | 4 (16%) | 2 (6.3%) | *0.2275* |
| *Heart failure* | 13 (22.8%) | 5 (20%) | 8 (25%) | *1* |
| Other comorbidities – n. (%) | | | | |
| *Chronic kidney disease* | 4 (7%) | 1 (4%) | 3 (9.4%) | *0.631* |
| *Active neoplasia* | 19 (33.3%) | 6 (24%) | 13 (40.6%) | *0.154* |
| Peripheral neurological disease – n. (%) | | | | *0.383* |
| *Parkinson disease* | 1 (1.8%) | 1 (4%) | 0 (0%) | |
| *Myasthenia as passive comorbidity* | 3 (5.3%) | 2 (8%) | 1 (3.1%) | |
| **Admission data** | | | | |
| Type of ICU admission – n. (%) | | | | *0.172* |
| *Medical* | 22 (38.6%) | 12 (48%) | 10 (31.3%) | |
| *Surgical* | 35 (61.4%) | 13 (52%) | 22 (68.8%) | |
| Reason for ICU admission – n. (%) | | | | *0.761* |
| *Cardiac arrest* | 5 (8.8%) | 3 (12%) | 2 (6.3%) | |
| *Acute kidney injury* | 2 (3.5%) | 1 (4%) | 1 (3.1%) | |
| *Respiratory distress* | 22 (38.6%) | 10 (40%) | 12 (37.5%) | |
| *Shock* | 12 (21.1%) | 6 (24%) | 6 (18.8%) | |
| *Post-operative (elective surgery)* | 6 (10.5%) | 3 (12%) | 3 (9.4%) | |
| *Post-operative (emergency surgery)* | 5 (8.8%) | 1 (4%) | 4 (12.5%) | |
| *Polytrauma* | 2 (3.5%) | 1 (4%) | 1 (3.1%) | |
| *Other hospital transfer* | 3 (5.3%) | 0 (0%) | 3 (9.4%) | |
| SAPS II | 47 [39 - 65] | 45 [35.5 - 64] | 48 [41.3 - 67.3] | *0.572* |
| SOFA at admission | 9 [7 - 11.5] | 10 [8 - 11.5] | 9 [7 - 11.75] | *0.758* |
| **Pre-tracheostomy weaning data** | | | | |
| Patients with at least 1 SA (SBT and/or extubation) – n. (%) | 41 (71.9%) | 17 (68%) | 24 (75%) | *0.57* |
| SBT | 38 (66.7%) | 14 (56%) | 24 (75%) | *0.163* |
| Extubation | 19 (33.3%) | 8 (32%) | 11 (34.4%) | *1* |
| Time to first SA (SBT and/or extubation) - days | 6 [1 - 10] | 3 [1 - 10.5] | 6.5 [1 - 9.5] | *0.507* |
| SBT | 6 [1 - 10] | 3.5 [1 - 12] | 6.5 [1.8 - 9.5] | *0.559* |
| extubation | 6 [4 - 11] | 6.5 [1.8 - 10.8] | 6 [4 - 11] | *0.634* |
| Total number of SA per patient (SBT and/or extubation) – n. | 2 [0 - 4.5] | 1 [0 - 3] | 2.5 [0.25 - 5] | *0.172* |
| SBT | 1 [0 - 4] | 1 [0 - 3] | 2 [0.25 - 5] | *0.147* |
| Extubation | 0 [0 – 1] | 0 [0 – 1] | 0 [0 – 1] | *0.644* |

* N = 57, except for NRS score where N = 38 (N = 16 for favorable outcome, N = 22 for poor outcome), for First separation attempt where N = 41 (N = 17 for favorable outcome, N = 24 for poor outcome), for First SBT where N = 38 (N = 14 for favorable outcome, N = 24 for poor outcome) and for First extubation where N = 19 (N = 8 for favorable outcome, N = 11 for poor outcome). BMI = body mass index, NRS = nutrition risk screening, OSA = obstructive sleep apnea, CPAP = continuous positive airway pressure, NIV = non-invasive ventilation, ICU = intensive care unit, SAPS II = Simplified Acute Physiology Score II, SOFA score = Sequential Organ Failure Assessment score, SA = separation attempts, SBT = spontaneous breathing trial. # P-value calculated using T-test or Mann-Whitney test for continuous data and Fisher's exact test for categorical data.

Tracheostomy data, post-tracheostomy MV weaning data until the first successful weaning as well as the number and duration of reconnections to the ventilator after successful MV weaning up to ICU discharge or decannulation (whichever comes first) are mentioned in **Table 2** for the total population and for patients

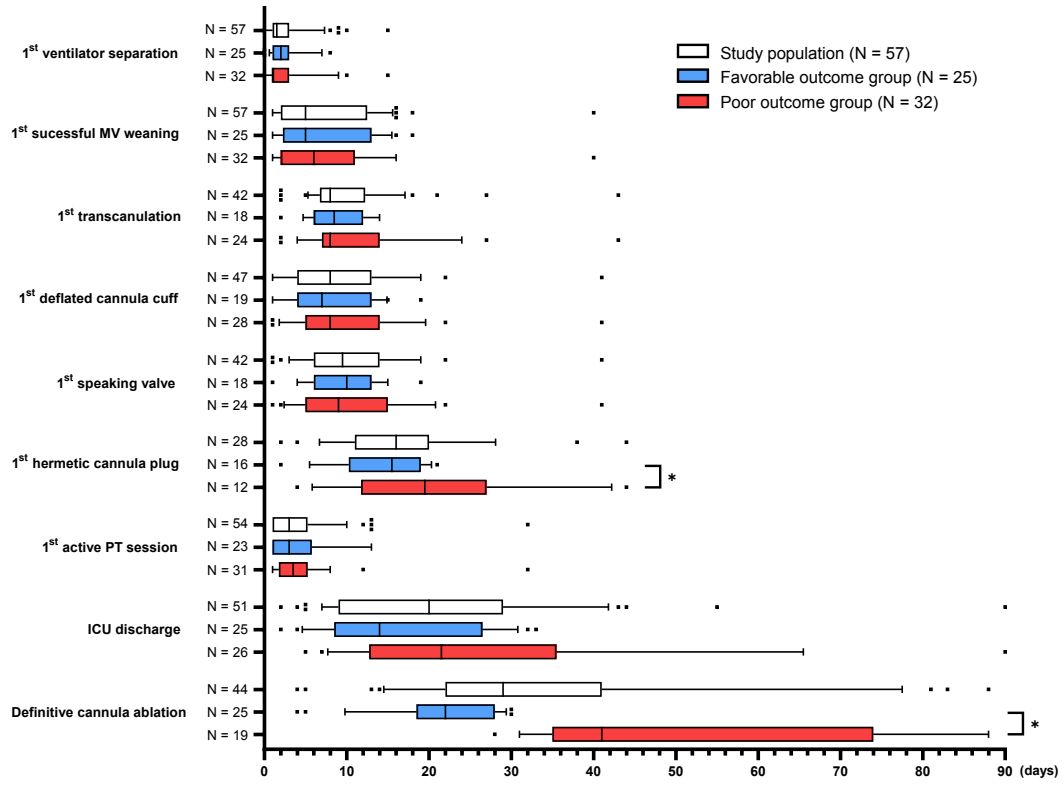
with favorable and poor outcomes (with p-value for sub-groups comparisons). Of note, 50% [0-100%] of the time with a tracheostomy in place was spent with a cannula Shiley size 8. Size 6 was the second most used size with 17.9% [0 – 94.2%] of the time. ICU-acquired weakness diagnosis at ICU discharge and tracheostomy weaning data are mentioned in **Table 2**. Data related to timings of the MV and cannula weaning steps are displayed in **Figure 2** for the total population and for the patients with favorable and poor outcome. Comparisons between sub-groups are mentioned in **Table 2** and **Figure 2** with corresponding p-values.

**Table 2** – Tracheostomy and MV weaning data

| | N | Study population | N | Favorable outcome | N | Poor outcome | *p-value** |
|---|---|---|---|---|---|---|---|
| **Tracheostomy data** | | | | | | | |
| Time from intubation to tracheostomy - days | 57 | 15.4 [11 - 21.1] | 25 | 13.3 [10 - 19.9] | 32 | 16 [11.9 - 22.5] | 0.535 |
| SOFA on day of tracheostomy | 57 | 9 [7 - 11] | 25 | 9 [6.5 - 12] | 32 | 9 [7 - 11] | 0.914 |
| Tracheostomy technique – n. (%) | 57 | | 25 | | 32 | | 0.151 |
| *Percutaneous* | | 5 (8.8%) | | 4 (16%) | | 1 (3.1%) | |
| *Surgical* | | 52 (91.2%) | | 21 (84%) | | 31 (96.9%) | |
| Size of the 1st cannula put in place – n. (%) | 57 | | 25 | | 32 | | 0.622 |
| *Shiley n°6* | | 21 (36.8%) | | 10 (40%) | | 11 (34.4%) | |
| *Shiley n°7* | | 33 (57.9%) | | 13 (52%) | | 20 (62.5%) | |
| *Shiley n°8* | | 1 (1.8%) | | 1 (4%) | | 0 (0%) | |
| *Shiley n°10* | | 2 (3.5%) | | 1 (4%) | | 1 (3.1%) | |
| **Post-tracheostomy MV data until first successful MV weaning** | | | | | | | |
| Time from tracheostomy to 1st separation from the ventilator - days | 56 | 1.5 [1 - 3] | 25 | 2 [1 - 3] | 31 | 1 [1 - 3] | 0.725 |
| Number of patients weaned – n (%) | 57 | 53 (93%) | 25 | 24 (96%) | 32 | 29 (90.6%) | 0.623 |
| Time from tracheostomy to MV weaning - days | 53 | 5 [2 – 12.5] | 24 | 5 [2.3 - 13] | 29 | 6 [2 – 11] | 0.807 |
| Patients weaned on the 1st day after tracheostomy procedure | 57 | 7 (12.3%) | 25 | 3 (12%) | 32 | 4 (12.5%) | 1 |
| MV hours per day - hours | 50 | 19.8 [17.4 - 22.4] | | 19.8 [16.5 - 21.6] | | 19.9 [17.6 - 22.8] | 0.369 |
| Minimal PS level – $cmH_2O$ | 50 | 7.5 [5.8 - 9.6] | | 7.2 [5.7 - 9.3] | | 7.8 [5.7 - 10.8] | 0.349 |
| Maximal PS level – $cmH_2O$ | 50 | 11.5 [9 - 14.4] | | 11.6 [9 - 14.1] | | 11.5 [8.7 - 14.4] | 0.764 |
| Minimal PEEP level – $cmH_2O$ | 50 | 6 [5.4 - 7] | | 6 [5.8 - 7] | | 5.8 [5 - 7.1] | 0.26 |
| Maximal PEEP level – $cmH_2O$ | 50 | 7 [6 - 8.3] | | 7.3 [6.1 - 7.9] | | 6.6 [5.6 - 8.5] | 0.586 |
| **Use of MV after first successful weaning** | | | | | | | |
| Patients never reconnected to MV after first successful MV weaning | 57 | 7 (12.3%) | 25 | 4 (16%) | 32 | 3 (9.4%) | 0.687 |
| MV sessions (reconnections) per day – n. (%) | | 0.7 [0.3 - 1.2] | | 0.7 [0.4 - 0.9] | | 0.8 [0.3 - 1.5] | 0.455 |
| Duration of MV sessions - hours | | 3.8 [2.6 - 7.3] | | 4.3 [2.5 - 5.6] | | 3.6 [2.6 - 7.7] | 0.7 |
| MV hours per day - hours | | 3.1 [1.4 - 4.8] | | 3.3 [1.4 - 4] | | 3 [1.3 - 6.8] | 0.48 |
| Minimal PS level – $cmH_2O$ | | 7.8 [6 - 9] | | 7.7 [5.8 - 8.4] | | 8.3 [6.5 - 9.3] | 0.288 |
| Maximal PS level – $cmH_2O$ | | 9.8 [7.9 - 11.5] | | 9 [7.6 - 10.4] | | 10 [8.2 - 11.8] | 0.489 |
| Minimal PEEP level – $cmH_2O$ | | 6 [5 - 6.5] | | 5.8 [5 - 6.7] | | 6 [5 - 6.5] | 0.491 |
| Maximal PEEP level – $cmH_2O$ | | 6.6 [5.6 - 7.5] | | 7 [5.7 - 7.6] | | 6.5 [5 - 7.6] | 0.624 |
| **Tracheostomy weaning data** | | | | | | | |
| Number of transcannulations – n. (%) | 57 | | 25 | | 32 | | 0.613 |
| *0* | | 14 (24.6%) | | 6 (24%) | | 8 (25%) | |
| *1* | | 29 (50.9%) | | 14 (56%) | | 15 (46.9%) | |
| *2* | | 11 (19.3%) | | 5 (20%) | | 6 (18.8%) | |
| *more than 2* | | 3 (5.3%) | | 0 (0%) | | 3 (9.4%) | |
| Downsizing – n. (%) | 57 | | 25 | | 32 | | 0.131 |
| *0* | | 52 (91.2%) | | 25 (100%) | | 27 (84.4%) | |
| *1* | | 4 (7%) | | 0 (0%) | | 4 (12.5%) | |
| *2* | | 1 (1.8%) | | 0 (0%) | | 1 (3.1%) | |
| **ICU-acquired weakness data** | | | | | | | |
| ICU-acquired weakness | | | | | | | |
| *ICU-acquired weakness diagnosis – n. (%)* | | 19 (33.3%) | | 14 (43.8%) | | 5 (20%) | |
| *With MRC score < 48/60 – n. (%)* | | 16 (28.1%) | | 12 (37.5%) | | 4 (16%) | |
| *With EMNG / high clinical suspicion – n. (%)* | | 3 (5.2%) | | 2 (6.3%) | | 1 (4%) | |
| *MRC score value* | | 21.5 [5.5 - 32.3] | | 8.5 [0.8 - 19.5] | | 26.5 [10.8 - 33.8] | 0.221 |

SOFA = Sequential Organ Failure Assessment score, MV = mechanical ventilation, PS = pressure support, PEEP = positive end-expiratory pressure, ICU = intensive care unit, PT = physical therapy, MRC = medical research council score, EMNG = electromyo-neurography. * p-value calculated using T-test or Mann-Whitney test for continuous data and Fisher's exact test for categorical data.

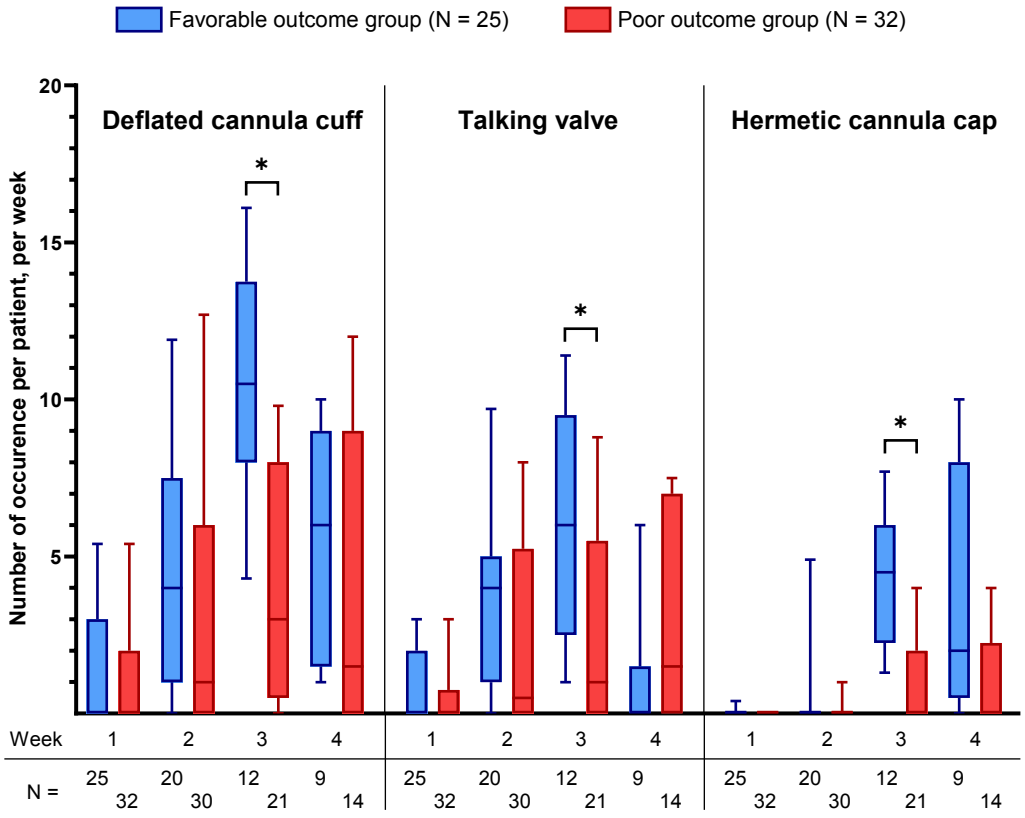
**Figure 2** – Timings of mechanical ventilation and tracheostomy weaning.




MV = mechanical ventilation, PT = physical therapy, ICU = intensive care unit. * p-value < 0.05.

**Figure 3** shows the number of sessions per patient during one week (for week 1-4 after the tracheostomy procedure) with deflated tracheostomy cannula cuff, talking valve and hermetic cap for favorable and poor outcome groups respectively (with p-values for comparisons between both sub-groups). Data were censored at four weeks, ICU discharge or tracheostomy cannula ablation (whichever came first).

**Figure 3** – Main tracheostomy weaning strategies use, per week, per patient and per outcome group




For each week, the number of patients taken into account was counted as the number of patients who spent at least one day in the ICU during this particular week before ICU discharge, death or decannulation. * p-value < 0.05.

**Table 3** provides outcome data for all the patients and for the sub-groups of favorable and poor outcomes.

**Table 3** – Patients' duration of stay and destination at hospital discharge

| | N | Total population | N | Favorable outcome | N | Poor outcome | *p-value** |
|---|---|---|---|---|---|---|---|
| ICU duration stay - days | 57 | 39 [24 - 46.5] | 25 | 36 [20 - 45] | 32 | 42 [26.8 - 48] | 0.087 |
| Hospital stay duration (included ICU stay) - days | 57 | 57 [45.5 - 89] | 25 | 56 [46 - 93] | 32 | 63.5 [45.3 - 89.5] | 0.82 |
| Discharged to in-patient rehabilitation centre – n. (%) | 41 | | 25 | | 16 | | 0.135 |
| *Yes* | | 25 (61%) | | 12 (48%) | | 13 (81.3%) | |
| *No* | | 14 (34.1%) | | 11 (44%) | | 3 (18.8%) | |
| *Unknown* | | 2 (4.9%) | | 2 (8%) | | 0 (0%) | |

ICU = intensive care unit. * p-value calculated using T-test or Mann-Whitney test for continuous data and Fisher's exact test for categorical data.

The association between patients' outcome and use of MV between the tracheostomy procedure and MV weaning, tracheostomy cannula weaning strategies and active PT performed are summarized in **Table 4** for univariate logistics regressions. Only the number of active PT sessions per week (OR = 1.20 [1.04 – 1.43]) and the number of times a hermetic cannula cap was used per week (OR = 1.42 [0.95 – 2.17]) were associated with favorable outcome.

**Table 4** – Univariate and multivariate logistic regressions

| | Univariate regression | | |
|---|---|---|---|
| | **N** | **OR (CI 95%)** | ***p-value*** |
| **From tracheostomy to first successful MV weaning** | | | |
| Time from tracheostomy to MV weaning | 53 | 0.993 (0.91 - 1.08) | 0.8025 |
| Time from tracheostomy to first ventilator separation | 56 | 0.951 (0.77 - 1.14) | 0.7293 |
| MV hours per day | 50 | 0.95 (0.81 - 1.12) | 0.3635 |
| **After first successful MV weaning** | | | |
| Patients never reconnected to MV after first successful MV weaning | 57 | 0.61 (0.37 – 10.2) | 0.67 |
| MV sessions (reconnections) per day | 50 | 0.537 (0.19 – 1.28) | 0.4492 |
| Duration of MV sessions | 50 | 0.947 (0.78 – 1.14) | 0.6942 |
| MV hours per day | 50 | 0.891 (0.72 – 1.06) | 0.4731 |
| **Cannula weaning strategies** | | | |
| Time to 1st transcannulation | 42 | 0.930 (0.80 - 1.03) | 0.4016 |
| Time to 1st deflated cuff | 47 | 0.954 (0.86 - 1.04) | 0.4777 |
| Time to 1st talking valve | 42 | 0.969 (0.87 - 1.06) | 0.8895 |
| Time to 1st hermetic cap | 28 | 0.908 (0.79 - 1.00) | 0.1501 |
| Number of times with deflated cuff per week | 57 | 1.154 (0.98 - 1.38) | 0.1412 |
| Number of uses of speaking valve per week | 57 | 1.125 (0.89 - 1.45) | 0.4792 |
| Number of uses of hermetic cap per week | 57 | 1.520 (1.05 - 2.29) | 0.0453 |
| **Physical therapy (PT)** | | | |
| 1st active PT session | 54 | 0.982 (0.86 - 1.10) | 0.6634 |
| Number of active PT sessions per week | 57 | 1.222 (1.06 - 1.45) | 0.0118 |

MV = mechanical ventilation, PT = physical therapy.

## 5.4. Discussion

In our study, in patients tracheostomized during the phase of liberation from MV, less than half of the patients (43.9%) were both decannulated within 30 days of the tracheostomy procedure and were also discharged alive from hospital. The majority of patients either died (N = 16, 28.1%) or were decannulated after more than 30 days of tracheostomy (N = 16, 28.1%). In our population, the only significant difference in characteristics and ICU admission data between outcome groups was age, with patients in the poor outcome group being older. Time from intubation to tracheostomy was 15.4 [11 – 21.1] days, with no significant difference between outcome groups. Time from tracheostomy to MV weaning and decannulation was 5 [1 - 12] and 29 [22 - 41] days respectively. No differences were found between outcome groups during the phase of MV weaning after tracheostomy. Concerning tracheostomy cannula weaning, the time until the first use of cannula hermetic cap was significantly shorter in favorable outcome group. The use of the different cannula weaning strategies was also different during the third week after tracheostomy in this group when comparing both sub-groups. When looking for potential predictors of outcome, in the univariate regression analysis, only the number of times tracheostomy cannula hermetic cap were used and the number of physical therapy (PT) sessions per week were associated with favorable outcome.

Interestingly, our patients were rapidly weaned off from MV (5 [1 – 12] days) after tracheostomy and overall were reconnected to the ventilator only a few times afterwards and for short periods of time, mainly for atelectasis prophylaxis in our ICU. We found that patients in the favorable outcome group were reconnected

for shorter periods and for fewer hours per day. In some patients, weaning of tracheostomy cannula was long (29 [22 - 41] days), not because of insufficient work of breathing, but because of reactive airways and their inability to manage excessive secretions. This hypothesis could be supported by the fact that ICU-acquired weakness was rather prevalent in our study population. Another hypothesis could be that our strategy to wean tracheostomy cannula is conservative and that proactivity towards tracheostomy cannula removal could expedite the process. This hypothesis is supported by recent data showing shorter duration between tracheostomy and cannula weaning (40). However, there is no data on mortality in this literature review, rendering comparison with our study population more difficult. The impact on patient-centered outcome of conservative versus pro-active tracheostomy cannula weaning strategy is unfortunately not known yet; the balance between risks of weaning the tracheostomy cannula too quickly compared to the complications of longer time with cannula in place lacks clarity. Complications related to early or late decannulations are different (41, 43) and have potentially different influence on mortality and morbidity. A recent promising approach used the number of suctioning needed as an indicator of readiness to remove cannula, with promising results (44).

Hermetic cannula cap was used more often in the favorable outcome group and this was particularly evident when tracheostomy cannula remained in place for a longer period of time (during week 3 and 4 after tracheostomy procedure). Because of the retrospective nature of the data, we cannot conclude whether the use of the technique itself resulted in better outcome or if this technique was simply used more often in the patients who stayed alive but could not be weaned rapidly from tracheostomy cannula. This area of tracheostomy weaning seems to be even less studied than other aspects, with little prospective studies (45, 46). Stelfox et al. carried a cross-sectional survey of specialists implicated in the management of tracheostomies that showed the perception that hermetic cap is a necessary step to wean tracheostomy cannula (46).

Weaning practices for MV and tracheostomy itself in tracheostomized patients are highly variable and based on low-quality evidence (40); this could explain that most centers develop their own protocols based on personal experiences and opinions (25, 47). In our mixed ICU (medical and surgical), protocolized strategies to wean tracheostomy include proactive early separation from the ventilator (disconnection as soon as possible and as long as clinically tolerated). Regarding cannula weaning, cannula cuff is usually deflated first (when separated from ventilator) in the absence of risk of bronchoaspiration. Cannula is changed for a fenestrated model (after 7 and 10 days following tracheostomy for surgical and percutaneous procedures respectively). Then, a speaking valve is places (only in non-ventilated patients in our ICU). Alternatively, when air leaks are sufficient when cannula cuff is deflated, a speaking valve can be put in place even on non-fenestrated cannula. The last step is usually the use of a hermetic cap before cannula is taken off definitely. Our practice does not routinely include downsizing and deflation of cannula cuff during MV. Our data shows the timing of each step and also that those steps were usually executed in this way. The standardization of these processes based on more substantial data could probably lead to improvement of the outcome of those

patients. Clearly, because those patients have high hospital mortality (27) and consume many resources, this is a major healthcare issue.

Our data are original because they describe real-life practices of MV and tracheostomy cannula weaning and their relationship with patients' outcome. This kind of data could help designing useful and efficient prospective studies needed to improve MV and tracheostomy weaning processes.

As study limitations, firstly, the retrospective nature of the study limits our conclusions to studying associations between weaning strategies and patients' outcomes. Also due to the retrospective nature of the study, some data could only be defined ad-hoc. In particular, SBT were counted using arbitrarily defined ventilator settings based on the data automatically recorded to the clinical data management system and not based on explicitly marked SBT by the clinicians. Patients were also classified as favorable and poor outcome on chosen criteria in the absence of consensual definition in the literature. Nevertheless, this type of retrospective data are essential to build hypothesis and future prospective studies addressing clinically relevant questions. Secondly, in an area where practice are so variable, the monocentric nature of this study shows a limited part of the management of those complicated patients and we think that protocols from other centers would lead to different associations and conclusions. Thirdly, the number of patients included is relatively low and could have limited the associations found between outcomes and collected data. Of note, patients intubated for neurological reasons were excluded from this study. Therefore, our conclusions cannot be extended to this specific patient population, which exhibit very different patterns of ventilation and mortality (27, 48, 49).

## 5.5. Conclusion

Patients who were tracheostomized for non-neurological and non-ear-nose-throat causes were weaned early from MV but decannulated much later. The use of hermetic cap was more frequent and occurred earlier in the favorable outcome group. Successful and earlier use of the tracheostomy cannula hermetic cap and the number of physical therapy sessions per week were the potential predictors of a favorable outcome.

## 5.6. Study details

This study has been submitted for publication in *Journal of Critical Care* on July 15$^{th}$, 2023.

# 6. IMPACT OF THREE DIFFERENT SPONTANEOUS BREATHING TRIALS ON INSPIRATORY EFFORT IN CRITICALLY ILL TRACHEOSTOMIZED PATIENTS

## 6.1. Introduction

During their intensive care unit (ICU) stay, some patients require invasive mechanical ventilation (MV), either through an endotracheal tube or a tracheostomy cannula. Weaning from MV is an important challenge because the duration of invasive ventilation should stay as short as possible. Delay in MV weaning is associated with increased rate of ventilator-associated pneumonia (31, 50), ICU-acquired weakness (51), longer ICU stay and increased mortality (1, 2, 4, 5, 52).

To assess if a patient is ready to be extubated, spontaneous breathing trials (SBT) are performed. Different SBT modalities are used in daily clinical practice (1, 7, 8, 10, 53). A recent meta-analysis compared, in intubated patients (tracheostomized patients excluded), work of breathing (WOB) and pressure-time product of esophageal pressure (PTPes) during different types of SBT and after extubation (11). SBT in pressure support (PS) were associated with reduced WOB and PTPes compared to post-extubation WOB and PTPes. In the contrary, WOB and PTPes during T-piece (disconnection from the ventilator) SBT were nearly similar to the post-extubation period, which would suggest that T-piece SBT better reflected physiological breathing after extubation. Using this modality by default could however delay extubation because more patients will fail T-piece SBT and will not be immediately extubated. SBT in PS have shown to increase extubation rate without increasing re-intubation (12).

When weaning is prolonged, patients are often tracheostomized because of the potential benefits of tracheostomy to reduce work of breathing (54, 55), decrease sedation use (14) and to improve communication (17, 18) and patients' comfort. However, data on MV weaning with the tracheostomy cannula in place is limited. In particular, the potential advantages of a disconnection strategy compared to a progressive reduction of PS remains a matter of debate. The study from Jubran et al. (28) in 2013 did show that disconnection from the ventilator and breathing through the tracheostomy collar allowed for quicker MV weaning than progressive reduction in PS but no difference in mortality was observed. However, this small study remains the only one in this field and no other data is available on the impact on work of breathing of the different SBTs that can be used in tracheostomized patients.

The effect of SBT on the respiratory physiology of tracheostomized patients cannot be easily translated from the studies done in patients intubated orotracheally because the characteristics of tracheostomy cannula and endotracheal tube are different, especially in term of resistance of the devices. Recently, reports of the use of high-flow $O_2$ for tracheostomy patients during disconnection have been published (56-58) but the impact of this strategy on inspiratory effort is unknown.

Our primary objective was to compare the pressure-time product (PTPes) of oesophageal pressure (as inspiratory effort intensity measurement) during three different sequential SBT in tracheostomized patients. The three different SBT were: low PS of 5 $cmH_2O$ and PEEP at 5 $cmH_2O$, disconnection from the ventilator

with low-flow $O_2$ and disconnection from the ventilator with high-flow $O_2$ (20 L/min) delivery through a dedicated interface. Our secondary objectives were to compare the respiratory pattern and work of breathing during the three different SBT modalities.

## 6.2. Method

### 6.2.1. Design

This study was a physiological crossover study. It took place in the adult medico-surgical ICU of the Lausanne University Hospital, between April 2019 and September 2021. Patients included were ICU patients who underwent tracheostomy for difficult or prolonged MV weaning. The protocol of the study was approved by the local Ethics Committee (Commission cantonale d'éthique de la recherche sur l'être humain, n° 2019-00190) and was registered on Clinicaltrials.gov (NCT03856424). Patients or their next-of-kin gave consent prior to their inclusion or were included based on an emergency inclusion procedure. In this case, consent was pursued afterwards.

### 6.2.2. Patients included and randomization procedure

Patients were considered for inclusion if MV was ongoing (for more than 72 hours) and a tracheostomy was planned as part of the clinical management. Exclusion criteria were: patient < 18 years old, pregnancy, patient with primary central neurological pathology or injury precluding MV weaning, patients tracheostomized for ear-nose-throat (ENT) reasons, patients with cardiac assist device, patient tracheostomized before current hospital stay, patient with contra-indication to nasogastric (NG) probe insertion (severe coagulopathy, skull fracture, facial trauma and oesophageal varices) and patients with withholding of life-sustaining therapies.

Three different SBT were sequentially performed in a randomized order with 30-minute washout periods in between. During the washout periods, the patients was reconnected to the ventilator with the same settings as before the first SBT. Standard monitoring, including pulse oximeter to measure transcutaneous pulse oximetry ($SpO_2$), were used.

The three SBT performed were:

1. Pressure support SBT with PS and PEEP both set at 5 $cmH_2O$
2. Disconnection from the ventilator and delivery of $O_2$ through a collar piece, with $O_2$ flow ranging from 1 to 8 L/min to target $SpO_2$ > 92% (or 88-92% for patients with known obstructive respiratory disease)
3. Disconnection from the ventilator and delivery of high-flow mixture of air/$O_2$ at a flow of 20 L/min delivered through a dedicated system connected to the tracheostomy cannula. $FiO_2$ was titrated to target $SpO_2$ > 92% (or 88-92% for patients with known obstructive respiratory disease).

### 6.2.3. Study protocol

After tracheostomy procedure took place, the following steps were followed:

1. A specific NG probe equipped with an esophageal balloon was inserted (Nutrivent®, SIDAM S.R.L., Mirandola, Italy). Adequate placement was ensured using a standard chest x-ray.

2. Each day, patients' readiness to undergo SBT was assessed by the clinician in charge. If the patient was haemodynamically stable, $SpO_2$ was > 92% with < 40% inspired fraction of $O_2$ ($FiO_2$), PEEP was ≤ 8 $cmH_2O$ and had RASS score (Richmond agitation-sedation scale) between -1 and 1 (alert and awake), a SBT was planned as in usual clinical practice (readiness to wean criteria met).
3. The dedicated NG probe was connected to a recording device (FluxMed®, MBMED, Martinez, Argentina) allowing esophageal recording. A dedicated airflow sensor was placed as close as possible to the tracheostomy cannula and connected to the recording device to record airway pressure and flow. A mainstream capnography measurement device was connected to the flow sensor and was also connected to the recording system.
4. Before the start of the recordings, the head of the bed was set at a 30 to 45° angle. An occlusion test was then performed as previously described (59). Correct balloon placement and correct amount of air in the balloon was confirmed by a ratio between delta airway pressure and delta esophageal pressure comprised between 0.8 and 1.2 during the occlusion test. If the ratio was not in this interval, balloon air volume was adjusted incrementally by 0.5 mL upwards. If a 1 mL variation was not sufficient to obtain desired ratio value, NG probe was moved by 1-2 cm before performing a new calibration attempt.
5. Baseline oesophageal pressure and respiratory profile were recorded during 15 minutes. The three SBT were then sequentially performed in a randomized order with 30-minute washout periods in-between.

In case of SBT intolerance, the trial was interrupted and ventilator settings were reset to pre-testing parameters. Intolerance criteria included new onset of respiratory distress signs (tachypnoea, $SpO_2$ drop, $FiO_2$ increase), haemodynamic instability (tachycardia, hypo- or hypertension, changes in vasopressor or anti-hypertension intravenous therapy), agitation, diaphoresis or stupor.

If either sequence was stopped because of intolerance, patients' readiness to undergo another SBT was assessed on the next day and then every day. The SBT sequence was then re-tried as soon as the readiness to wean criteria were met again. All sequences were repeated until the patient completed all three sequences during the same session.

### 6.2.4. Measurements and outcomes

Patients' general characteristics, comorbidities, timing of ICU admission, intubation and tracheostomy were all recorded from the clinical information system. During the SBT sequences, airway flow, airway pressure, oesophageal pressure and expired $CO_2$ were continuously recorded using the FluxMed® device. All respiratory variables used for analyses were derived from the files provided by the FluxMed® device. The FluxMed® automatically split the recordings into breathing cycles and measured esophageal pressure swing, PTPes and WOB per breath. To exclude cycles that were not correctly analysed by the FluxMed® device, cycles with negative total PTPes and/or inspiratory time (Ti) of > 2 seconds were excluded from the analysis. For each sequence, the first 3 minutes of the recording were also cut to ensure that no major artefact from the

ventilator and ventilator-patient circuit manipulation were present in the analysed cycles. The period analysed was 25 minutes long, with the remainder of the file cut from analysis.

### 6.2.5. Statistical analyses

No sample size was calculated for this physiological study. Data reported as number and percentage for proportions and as median [25th and 75th percentile] for continuous data. All statistical tests used were non-parametric because of the small number of patients. Respiratory profile, effort and $CO_2$ monitoring between the different SBT were compared using ANOVA test and Tukey post-hoc test for multiple comparisons. Paired comparisons with median value of selected parameters were analysed with Friedmann test. Statistical analyses were performed using GraphPad Prism version 9.1.0 for Windows (GraphPad Software, San Diego, California USA). All statistical tests were two-tailed and p-value < 0.05 was considered significant.

## 6.3. Results

A total of eight patients were included. General characteristics, ICU admission reason and timings related to intubation, tracheostomy and SBT are shown in **Table 1**. Of the 8 patients included, one was excluded because the NG probe could not be inserted. In the 7 other patients, all SBT sequences could be completed. Median age of patients was 72 [61 – 76] years. Median time from intubation until tracheostomy procedure was 14.1 [13.1 – 14.8] days.

**Table 1** – Patients' characteristics

| Patient | Sex | Age (years) | BMI ($kg/m^2$) | Reason for ICU admission reason | Department before ICU admission | Time between ICU admission and intubation | Time from intubation to tracheostomy | Time from tracheostomy to first SBT | Relevant comorbidities | Pre-SBT PEEP ($cmH_2O$) | Pre-SBT PS ($cmH_2O$) | Pre-SBT $FiO_2$ (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | F | 57 | 27.9 | Acute on chronic respiratory failure | Ward | -5 h | 13 days 2 h | 1 day 2 h | COPD | 7 | 7 | 25 |
| **3** | M | 72 | 22.8 | Post-surgery (cardio-vascular) | Ward | -4 h | 14 days 2 h | 4 days 2 h | - | 7 | 7 | 40 |
| **4** | M | 76 | 29.1 | Acute respiratory failure | Intermediate care unit | 1 h | 13 days 8 h | 1 day 1 h | COPD, OSA Heart failure | 7 | 7 | 30 |
| **5** | M | 61 | 31.6 | Shock | Other ICU | -4 days | 18 days 20 h | 2 days 4 h | - | 8 | 10 | 30 |
| **6** | M | 82 | 24.2 | Acute respiratory failure | Ward | 3 days 7 h | 14 days 11 h | 1 day 5 h | Heart failure | 5 | 5 | 28 |
| **7** | M | 73 | 34.6 | Polytrauma | Emergency room | -2 h | 14 days 20 h | 1 day 2 h | OSA | 8 | 9 | 25 |
| **8** | M | 70 | 37.4 | Acute respiratory failure | Emergency room | -3 h | 11 days 23 h | 1 day 19 h | OSA | 6 | 7 | 35 |

BMI = body-mass index, ICU = intensive care unit, SBT = spontaneous breathing trial, PEEP = positive end-expiratory pressure, PS = pressure support, $FiO_2$ = inspired fraction of $O_2$

Four patients (57.1%) completed all three SBT sequences on the first try. Three patients (42.9%) failed one sequence and required another recording. For patient 3 and patient 7, the SBT sequences were successful on the second try, respectively 3 and 5 days later. Patient 5 (14.3%) successfully completed the three SBT the third time. The second and third try occurred 1 and 5 days after the first.

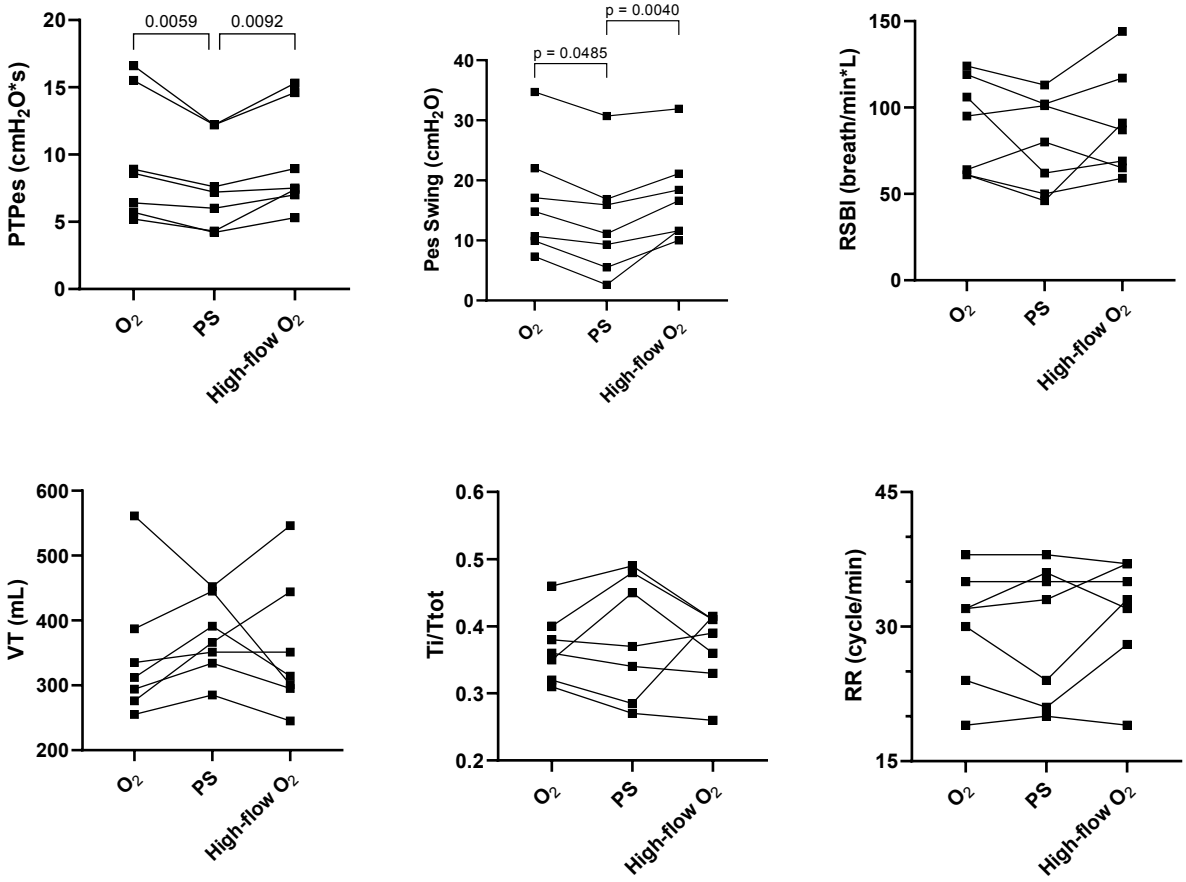
**Table 2** compares physiological and ventilation monitoring data from all successful sequences. **Figure 1** show the Friedman paired analysis between successful sequences for relevant invasive monitoring parameters and respiratory profile.

**Table 2** – Respiratory profile, effort monitoring and $O_2$ profile

| Patient | Sequence | RR | RSBI | VT | Ti | Ti/Ttot | Pes Swing | PTPes | $EtCO_2$ | VDalv/VT |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $O_2$ | 19 [18 - 21]* | 61 [54 - 70]* | 312 [292 - 330]* | 0.95 [0.9 - 1.1]* | 0.31 [0.3 - 0.4]* | 22 [20.8 - 23.6]* | 16.6 [14.6 - 18.9]* | 39 [38.2 - 39.8]* | 0.44 [0.4 - 0.5]* |
| | $HFO_2$ | 19 [18 - 20] | 59 [55 - 63] | 314 [300 - 326] | 0.83 [0.8 - 0.9] | 0.26 [0.2 - 0.3] | 21.1 [20.1 - 22] | 14.6 [13.4 - 15.6] | 40 [39.1 - 40.8] | 0.12 [0.1 - 0.2] |
| | PS | 20 [18 - 21] | 50 [46 - 55] | 391 [372 - 409] | 0.81 [0.8 - 0.9] | 0.27 [0.3 - 0.3] | 16.9 [15.6 - 18] | 12.2 [10.6 - 14.1] | 36 [35.2 - 36.7] | 0.04 [0 - 0.1] |
| 3 | $HFO_2$ | 32 [26 - 36]* | 87 [69 - 104]* | 351 [319 - 386]* | 0.68 [0.6 - 0.8]* | 0.36 [0.3 - 0.4]* | 11.6 [9.7 - 14.9]* | 7 [5.6 - 8.7] | 32.1 [30.2 - 34]* | 0.47 [0.4 - 0.6] |
| | $O_2$ | 32 [27 - 37] | 95 [78 - 113] | 335 [309 - 366] | 0.64 [0.6 - 0.7] | 0.35 [0.3 - 0.4] | 10.7 [9 - 13.3] | 6.4 [5.2 - 8.2] | 36.2 [29.2 - 37.9] | 0.68 [0.6 - 0.8] |
| | PS | 36 [31 - 40] | 101 [82 - 114] | 351 [330 - 381] | 0.75 [0.7 - 0.8] | 0.45 [0.4 - 0.5] | 9.3 [7.4 - 12.4] | 6 [5 - 7.5] | 36 [34.5 - 37.7] | 0.8 [0.7 - 0.9] |
| 4 | $HFO_2$ | 37 [34 - 39]* | 65 [59 - 72]* | 546 [481 - 596]* | 0.63 [0.6 - 0.7]* | 0.39 [0.4 - 0.4]* | 31.9 [26.1 - 37.3]* | 15.3 [11.7 - 18.3]* | 29.5 [27.8 - 32.3]* | 0.22 [0.1 - 0.3] |
| | PS | 38 [32 - 41] | 80 [69 - 95] | 452 [375 - 486] | 0.57 [0.6 - 0.6] | 0.37 [0.3 - 0.4] | 30.7 [22.5 - 34.9] | 12.2 [9.3 - 14.5] | 35.5 [33.2 - 41.1] | 0.36 [0.3 - 0.5] |
| | $O_2$ | 38 [34 - 40] | 64 [58 - 74] | 561 [490 - 616] | 0.61 [0.6 - 0.7] | 0.38 [0.3 - 0.4] | 34.7 [27.9 - 40.2] | 15.5 [11.1 - 18.5] | 36.6 [35.3 - 39.3] | 0.41 [0.3 - 0.6] |
| 5 | $O_2$ | 31 [27 - 35] | 135 [112 - 165]* | 229 [205 - 245]* | 0.57 [0.5 - 0.6]* | 0.29 [0.3 - 0.3]* | 22.4 [0 - 26.9]* | 9.2 [6.9 - 11.2]* | 46.3 [45.2 - 47.2]* | 0.56 [0.5 - 0.8]* |
| | PS | 30 [27 - 33] | 111 [96 - 129] | 265 [244 - 283] | 0.64 [0.6 - 0.8] | 0.33 [0.3 - 0.4] | 12.5 [10.8 - 14.4] | 5.55 [4.6 - 6.7] | 51.1 [50 - 52] | 1.22 [1 - 1.5] |
| | $HFO_2$ | 37 [33 - 41] | 144 [125 - 171] | 245 [232 - 259] | 0.55 [0.5 - 0.6] | 0.33 [0.3 - 0.4] | 18.4 [15.9 - 20.8] | 7.5 [6.3 - 8.7] | 42.2 [39.5 - 45.9] | 0.32 [0.3 - 0.4] |
| | PS | 33 [31 - 36] | 113 [99 - 125] | 285 [271 - 311] | 0.61 [0.6 - 0.7] | 0.34 [0.3 - 0.4] | 15.9 [13.9 - 18.2] | 7.2 [6.2 - 8.6] | 48.6 [47.6 - 49.5] | 0.71 [0.6 - 0.8] |
| | $O_2$ | 32 [30 - 34] | 124 [113 - 137] | 255 [244 - 267] | 0.66 [0.6 - 0.8] | 0.36 [0.3 - 0.4] | 17.1 [15.6 - 19.1] | 8.6 [7.7 - 9.7] | 49.8 [48.6 - 50.8] | 1.2 [1.1 - 1.4] |
| 6 | $HFO_2$ | 33 [28 - 36.3]* | 69 [54 - 94]* | 444 [331 - 575]* | 0.75 [0.7 - 0.8]* | 0.41 [0.4 - 0.4]* | 11.7 [6.6 - 16.5]* | 7.4 [4.8 - 10.1]* | 22.8 [0 - 31.1]* | 0.03 [0 - 0.1]* |
| | $O_2$ | 30 [27 - 34] | 106 [93 - 123] | 276 [253 - 303] | 0.81 [0.7 - 0.9] | 0.4 [0.4 - 0.5] | 7.3 [5.6 - 10.6] | 5.2 [4.3 - 6.3] | 28.7 [27 - 30.6] | 0.68 [0.6 - 0.8] |
| | PS | 24 [21 - 26] | 62 [55 - 71] | 366 [345 - 397] | 1.21 [1.1 - 1.4] | 0.48 [0.4 - 0.5] | 2.6 [1.8 - 3.7] | 4.3 [3.6 - 5.3] | 30.4 [29.8 - 31.1] | 0.76 [0.6 - 1] |
| 7 | $HFO_2$ | 35 [33 - 37]* | 117 [107 - 125]* | 295 [285 - 306]* | 0.69 [0.7 - 0.7]* | 0.41 [0.4 - 0.4]* | 10 [9 - 11.2]* | 5.3 [4.7 - 5.9]* | 39 [38.3 - 39.6]* | 0.33 [0.3 - 0.4]* |
| | PS | 35 [32 - 37] | 102 [92 - 113] | 334 [311 - 355] | 0.84 [0.8 - 0.9] | 0.49 [0.5 - 0.5] | 5.5 [4.3 - 7.4] | 4.2 [3.5 - 5.3] | 62.2 [55.1 - 96.1] | 0.75 [0.6 - 0.9] |
| | $O_2$ | 35 [33 - 37] | 119 [110 - 127] | 294 [282 - 305] | 0.77 [0.7 - 0.9] | 0.46 [0.4 - 0.5] | 9.9 [9.1 - 10.7] | 5.7 [5.3 - 6.2] | 63 [62.1 - 63.7] | 0.99 [0.9 - 1.1] |
| 8 | PS | 18 [17 - 21]* | 40 [36 - 47]* | 458 [401 - 478]* | 0.84 [0.8 - 0.9]* | 0.27 [0.2 - 0.3]* | 11.1 [9.8 - 12.4]* | 8.1 [7.1 - 9.1]* | NA | NA |
| | PS | 21 [18 - 23] | 46 [41 - 52] | 445 [429 - 462] | 0.82 [0.8 - 0.9] | 0.29 [0.3 - 0.3] | 11.1 [9.9 - 12.3] | 7.6 [6.8 - 8.5] | NA | NA |
| | $O_2$ | 24 [20.8 - 29] | 61 [51 - 76] | 387 [363 - 405] | 0.8 [0.7 - 0.9] | 0.32 [0.3 - 0.4] | 14.8 [13.2 - 16.1] | 8.9 [7.7 - 10.2] | NA | NA |
| | $HFO_2$ | 28 [24 - 33] | 91 [71 - 114] | 301 [269 - 335] | 0.84 [0.7 - 1.1] | 0.42 [0.3 - 0.5] | 16.6 [14.8 - 19.1] | 8.95 [7.5 - 10.3] | NA | NA |

$HFO_2$ = high-flow $O_2$, RR = respiratory rate, VT = tidal volume, Ti = inspiratory time, Ti/Ttot = inspiratory time on total cycle time, Pes swing = esophageal pressure maximal swing during inspiration, PTPes = total esophageal product time-pressure, $EtCO_2$ = end-tidal $CO_2$, VDalv/VT = alveolar dead space on tidal volume ratio. Sequences are displayed in the order they were registered. Only successful sequences are shown. * p-value for ANOVA analysis < 0.05.

**Figure 1** – Friedmann analysis of respiratory profile and effort monitoring




PTPes = total esophageal product time-pressure, Pes swing = esophageal pressure maximal swing during inspiration, RSBI = respiratory shallow index breathing score, VT = tidal volume, Ti/Ttot = inspiratory time on total cycle time, RR = respiratory rate. P-value of ≤ 0.05 are shown.

## 6.4. Discussion

In this study, we showed a significant difference in tracheostomized patients' inspiratory effort intensity during three different used modalities of spontaneous breathing trials used in current clinical settings. More specifically, PTPes and Pes Swing were lower during SBT in PS compared to disconnection with low-flow or high-flow $O_2$ at 20 L/min. Oppositely, the effect of the SBT modality on the routinely monitored breathing pattern (tidal volume, respirators rate, ratio between inspiratory time and the time of the total breath) was unpredictable and showed high variability from one patient to the other. Our data showed that breathing pattern can therefore not be used to reliably assess work of breathing during an SBT in tracheostomized patients. This underlines the fact that inspiratory effort monitoring using esophageal pressure can be used to better understand the effect of weaning trials and more generally of the effect of mechanical ventilation on tracheotomized patients with complex weaning.

Of note, because of the high number of cycles recorded with each SBT modality, most ANOVA analyses showed statistically significant difference in both respiratory pattern, inspiratory effort monitoring and $CO_2$ monitoring. However, the clinical significance of those differences is probably limited.

In intubated patients, low PS during SBT is used to compensate for the resistance of the device. But because inspiratory effort during SBT in PS is lower, we can hypothesize that the amount of assist delivered using this modality can be considered as relatively high and therefore a true ventilator assistance for patients with a tracheostomy. For this reason, in clinical practice, using this approach to wean a tracheostomized patients from MV could contribute to prolong the total duration of MV because it could interfere with the detection of the ability of the patient to breathe alone. Interestingly, all failed sequences in this study were either in $O_2$ sequences or high-flow $O_2$, which also supports this hypothesis. Our data are in line with Jubran's paper's results (28), which showed that patients who were disconnected from the ventilator during the weaning process were weaned quicker than those with a strategy of progressive reduction in PS. Moreover, a failed SBT with a tracheostomy in place has little consequences compared to a failed extubation since the patient can be reconnected to the ventilator rapidly without additional risks and without an increase in mortality, as it is the case in patients who fail an extubation and have to be re-intubated (60). This represents an additional argument in favour of using more demanding SBT in tracheostomized patients in order to hasten the MV weaning process in these patients and improve their outcome.

## 6.5. Conclusion

Using invasive monitoring to monitor inspiratory effort during different modalities of SBT provided additional information compared to standard respiratory pattern monitoring. Inspiratory effort invasive monitoring could thus be of interest to better understand the effect of weaning strategies on patients' physiology. Inspiratory effort was lower during SBT in PS compared to disconnection strategies. This suggests that SBT in PS still represent a certain amount of ventilatory assist and that using this modality could contribute to the delayed identification of patients who are able to breathe without any assistance with a risk of prolonging the duration of mechanical ventilation.

# 7. CONCLUSION

This work confirmed that tracheostomized patients suffer from high mortality and long duration of ICU and hospital stay. Predicting outcome in tracheostomized patients remains difficult, with only age and BMI being associated with favourable outcome in pre-tracheostomy variables. After tracheostomy, only the more early and frequent use of hermetic cannula cap and the number of physical therapy sessions per week were associated with favourable outcomes.

In tracheostomized patients, the use of a spontaneous breathing trial using disconnection from the ventilator (compared to pressure support reduction) was associated with stronger inspiratory effort (increased esophageal time-pressure product) no with no difference in breathing pattern. Using disconnection strategies could potentially contribute to hasten the weaning process by allowing earlier recognition of patients able to breathe without any assistance from the ventilator.

Overall, our data contribute to providing more information on tracheostomized patients, which can be used to optimize their care. However, many areas remain open for discussion and further studies are needed to improve the outcome of those patients.

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