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Time course of electrical activity of the diaphragm (EAdi) in the peri extubation period and its role as predictor of extubation failure in difficult to wean patients

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Abstract

Introduction Weaning patients from mechanical ventilation is crucial in the management of acute respiratory failure (ARF). Spontaneous breathing trials (SBT) are used to assess readiness for extubation, but extubation failure remains a challenge. Diaphragmatic function, measured by electrical activity of the diaphragm (EAdi), may provide insights into weaning outcomes.

Materials and methods This prospective, observational study included difficult-to-wean patients undergoing invasive mechanical ventilation. EAdi was recorded before, during, and after extubation. Patients were categorized into extubation success and failure groups based on reintubation within 48 h. Statistical analysis assessed EAdi patterns and predictive value.

Results Thirty-one patients were analyzed, with six experiencing extubation failure. Overall, EAdi increased significantly between the phases before the SBT, the SBT and post-extubation period, up to 24 h ($p < 0.001$). EAdi values were higher in the extubation failure group during SBT ($p = 0.01$). An EAdi > 30 µV during SBT predicted extubation failure with 92% sensitivity and 67% specificity. Multivariable analysis confirmed EAdi as an independent predictor of extubation failure.

Conclusions In difficult-to-wean patients, EAdi increases significantly between the phases before the SBT, the SBT and post-extubation period and is significantly higher in patients experiencing extubation failure. An EAdi > 30 µV during SBT may enhance extubation failure prediction compared to conventional parameters. Advanced monitoring of diaphragmatic function could improve weaning outcomes in critical care settings.

Keywords Weaning, Extubation, Electrical activity of the diaphragm, Mechanical ventilation, Spontaneous breathing trial

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Introduction

Weaning patients from mechanical ventilation is one of the key aspects in the treatment of patients with acute respiratory failure (ARF) who are undergoing invasive mechanical ventilation (IMV). A spontaneous breathing trial (SBT) is performed to assess and to predict if the patient is ready to be disconnected from the ventilator and whether it is safe to proceed to removal of IMV [1–3]. The failure rate of this test is approximately 10–20%, and when reintubation is necessary, it is associated with poor outcomes [4–6]. There are numerous conditions associated with extubation failure and subsequent need for reintubation, including upper airway obstruction, incomplete resolution of the primary insult, advanced age, positive fluid balance, chronic cardiorespiratory disease, prolonged mechanical ventilation, hypercapnia during separation attempts, ineffective cough, copious respiratory secretions, heart failure, and respiratory muscle weakness. These different conditions likely involve distinct pathophysiological mechanisms, making extubation failure and the need for reintubation a syndrome that is challenging to study and define [4, 7–13].

Respiratory advanced monitoring is therefore required to enhance our understanding of the pathophysiology related to the peri-extubation period, in particular in difficult to wean patients possibly allowing better personalization of the SBT. In that environment, electrical activity of the diaphragm (EAdi) provides advanced monitoring, particularly of the primary respiratory muscle, the diaphragm [14]. EAdi measures diaphragmatic depolarization and provides an insight into the respiratory center's demand on the diaphragm. Its correlation with diaphragmatic function has been established, showing a linear relationship between EAdi and respiratory muscle pressure (Pmus) within individuals, although this relationship may vary between subjects [15]. Due to its strong correlation with Pmus, EAdi and its derived indices have been used to assess diaphragmatic function [16]. In adult critically ill ventilated patients, these have been proposed as useful tools to assess diaphragmatic function, predict readiness for weaning, estimate patients' respiratory muscle effort, and evaluate the response to positive end-expiratory pressure (PEEP) titration [18, 22–25].

However, the time course of EAdi during the peri-extubation period has not been studied. Therefore, the aim of our study was to investigate the temporal patterns of EAdi during the pre and post-extubation period in difficult-to-wean patients in order to clarify its possible role as a monitoring tool in clinical practice.

Materials and methods

Study design

This study employed a prospective, single-center, cohort, and observational design. All patients admitted to the polyvalent Critical Care Department of Hospital de la Santa Creu i Sant Pau (Barcelona, Spain) with IMV over an 18-month period were screened. Patient identities were pseudonymized to ensure confidentiality. The registry was developed and implemented in accordance with the amended Declaration of Helsinki, and the study received approval from the Institutional Review Board of Hospital de Sant Pau (protocol code: IIBSP-EAD-2012-111, and Research Ethics Committee code: 55/2012). Informed consent was obtained from all patients of their next of kin. The preparation of this paper followed the STROBE recommendations.

Participants and study groups

Patients older than 18 years and invasively ventilated who were difficult to wean were included in the study. Patients were defined as difficult-to-wean when they failed an initial spontaneous breathing trial (SBT), and required up to three SBT or as long as 7 days from the first SBT to achieve extubation [17, 18]. Exclusion criteria were pregnancy, patients with pacemakers due to possible interference with the Neurally Adjusted Ventilatory Assist (NAVA) catheter, patients ventilated through a tracheostomy, and patients with do-not-resuscitate orders. We defined two groups: the "extubation failure" group, in which patients required reintubation within 48 h, and the "extubation success" group, in which reintubation within 48 h did not occur.

The primary objective of the study was to analyze the time course evolution of EAdi during the weaning phase in difficult-to-wean patients. The secondary objectives were to analyze EAdi values differences between the extubation failure and success groups and to identify a threshold at which EAdi during the SBT can be useful in order to predict which patient will fail extubation.

Study protocol

After the first SBT failure (patient meeting criteria for difficult weaning), a nasogastric probe able to record the EAdi (NAVA catheter, MAQUET, Solna, Sweden) was positioned. The catheter placement was checked for accuracy in all patients, as described [19]. NAVA catheter position and function were checked three times a day (every nursing shift) throughout the study period. Investigators were notified each time the patients were scheduled for a new SBT by the attending clinician. Continuous recording of ventilator variables (via a PCMCIA card inserted in the ventilator) was started at least one

hour before the SBT. In case of SBT success and clinical decision to extubate, the recording continued for up to 48 h post-extubation, reintubation, or discharge of the patient, whichever happened first. If the SBT failed, the recording was stopped, and a new SBT was awaited. The attending clinician assessed readiness for extubation, unaware of EAdi values. Arterial blood gases (ABG) were obtained before extubation in all patients and at 2 h post-extubation.

According to the ICU protocol, all SBTs were conducted with a pressure support (PS) of 7 cmH_2O and zero positive end expiratory pressure (PEEP) for a duration of 60 min. The first SBT was performed with the same success criteria as the subsequent SBTs recorded in the study. SBT success criteria were: a ratio of partial pressure of arterial oxygen to fraction of inspired oxygen (PaO_2/FiO_2) > 200 mmHg, respiratory rate ≤ 35 breaths per minute; efficient cough, hemodynamic stability with epinephrine or norepinephrine infusion rate not greater than 0.5 mg/h, Glasgow Coma Scale (GCS) > 8, and little or no sedation [20–22]. Sedation management was conducted as per our ICU clinical protocol. All patients deemed ready for extubation received no continuous sedation and RASS scale was used to ensure adequate mentation. Patients might still be under antipsychotics, anxiolytics, or analgesics if clinically necessary. In the post-extubation period, NIV was not systematically applied to all patients. Prophylactic NIV was prescribed by the attending clinician when deemed necessary and the decision to reintubate was taken by the attending physician based on his clinical judgment.

Data collection

All ventilator and EAdi-derived variables were obtained every minute starting from 60 min before the final and successful SBT, during the final and successful SBT, and after extubation. Ventilator related variables included inspiratory and expiratory tidal volumes, peak airway pressure (Ppeak) and PEEP. EAdi-related variables included EAdi peak and EAdi minimum. To facilitate data analysis, the EAdi recording was divided into seven different phases: 1 h before SBT, during SBT, and 1 h, 2 h, 24 h and 48 h after extubation. The mean value for each variable was calculated for each phase. Artifacts in the EAdi signal due to tracheal suctioning, coughing, and nursing care led to the exclusion of EAdi data from the last 5 min before extubation and the first 10 min after extubation. The Vt/EAdi index before extubation was calculated as a surrogate of respiratory efficiency [23]. Hemodynamic data, peripheral oxygen saturation, respiratory rate, heart rate, and mean arterial blood pressure were recorded before starting the SBT and at the end of the SBT. For reintubated patients, the main reason leading the attending clinician to the decision to reintubate was collected a posteriori from a predefined list of extubation failure mechanisms proposed in the literature [4].

Statistical analysis

The Shapiro–Wilk test was used to assess the normality of the distribution. Continuous normally distributed variables are reported as means and standard deviations, while continuous non-normally distributed variables are reported as medians and interquartile ranges (25th–75th percentiles). Continuous variables were compared using Student t-tests or Mann–Whitney rank sum tests, depending on the normality of the distribution. Categorical variables were compared using the Chi-squared (X^2) test or Fisher's exact test, as appropriate. Within each group (extubation failure vs. success), different time points were compared using repeated measures ANOVA or the Friedman test. A logistic regression analysis was performed to detect potential confounding factors and a ROC curve analysis was performed to characterize the univariate and multivariate models. Statistical significance was defined as a p value < 0.05. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 20, Chicago, IL, USA.

Results

Patients' description

Thirty-five patients admitted to the ICU with IMV and difficult weaning were included in the study. Data from 4 patients (all belonging to the extubation success group) were lost due to a malfunction in the data acquisition system. Therefore, 31 patients were analyzed. Six out of thirty-one (19%) were reintubated in the first 48 h (extubation failure group). Reasons for reintubation were: in one case, hypoxemia due to the inability to clear secretions; in another case, reintubation was due to respiratory distress and hypoxemia caused by acute cardiogenic pulmonary edema; in the remaining four cases, reintubation was performed due to progressive worsening of respiratory function and hypoxemia attributed to the non-resolution of the primary insult. The study flow chart is shown in the online supplement (OS Figure 1). Baseline characteristics of all patients and extubation success and failure groups are shown in detail in Table 1.

The duration of mechanical ventilation until extubation was significantly higher in the extubation failure group (14 days [7–15] vs. 7 days [4–11], $p = 0.04$). The ventilatory ratio was also higher in the extubation failure group compared to the extubation success group (1.95 [1.65–2.27] vs. 1.32 [1.10–1.53], $p = 0.001$). No other significant differences were found between the extubation success and failure groups at baseline,

Table 1 Baseline patients' characteristics

	All patients (n = 31)	Extubation success (n = 25)	Extubation failure (n = 6)
Demographics			
Age (years)	72 (63–77)	70 (63–77)	74 (64–76)
Gender (male), n (%)	19 (61)	14 (56)	5 (83)
Comorbidities, n (%)			
COPD	10 (32)	6 (24)	4 (66)
Heart failure	21 (68)	17 (68)	4 (66)
Admission cause, n (%)			
Pneumonia/ARDS	14 (45)	10 (40)	4 (66)
COPD exacerbation	3 (10)	2 (8)	1 (17)
Heart failure	5 (16)	5 (20)	0 (0)
Abdominal sepsis	4 (13)	4 (16)	0 (0)
Neurological	3 (10)	2 (8)	1 (17)
Trauma	2 (6)	2 (8)	0 (0)
Severity at admission			
SAPS III (points)	61 (57–76)	61 (57–76)	64 (58–72)
Length of mechanical ventilation before the extubation, (days)	7 (5–11)	7 (4–10)	14 (7–15)*

Data expressed as frequencies and percentages [n (%)] or medians and interquartile ranges (IQR or 25th–75th percentile)

COPD, chronic obstructive pulmonary disease; ARDS, acute respiratory distress syndrome

*$p \leq 0.05$ against extubation success

although there was a trend for more patients with a history of chronic obstructive pulmonary disease (COPD) in the extubation failure group (66% vs. 24%; $p = 0.067$).

EAdi time course in difficult-to-wean patient

The EAdi values before the SBT were slightly lower than during the SBT (14 μv [4–21] vs. 15 μv [7–26], $p = 0.007$) with a percentage increase of 18% [2–34]. Diaphragm efficiency, measured as Vt/EAdi during pressure support ventilation (pre-SBT phase), was significantly lower than during the SBT (28 mL/μV [15–102] vs. 31 mL/μV [13–61], $p = 0.005$). RR/Vt ratio did not differ between the pre-SBT and SBT phases (55 [43–87] vs. 53 [40–83], $p = 0.192$). From the SBT to 1 h post extubation, an increase in EAdi values of 33% [7–51] was observed at the expense of 26 patients (14 μv [7–26] vs. 18 μv [13–36], $p < 0.001$). The EAdi increase persisted for the next 24 h. EAdi values for each phase are shown in Fig. 1. The time course of the EAdi for each single patient in the different time line phases is shown in OS Figure 2. NIV was applied in the 10 COPD patients immediately after extubation. EAdi increased in all patients between the SBT and post-extubation period despite NIV (OS Table 1).

Comparison between the success and failure extubation groups

A comparison of the EAdi time course for each group and each phase is shown in Fig. 2.

Before the SBT, there were no differences in the level of ventilatory support, PEEP, or hemodynamic parameters between patients in the extubation failure and extubation success groups. Additionally, no significant differences were found in respiratory rate (RR), tidal volume (Vt), or Vt/predicted body weight (PBW). However, a significantly different mean EAdi value was observed between the failure and success groups before the SBT (36 μV [12–42] vs. 13 μV [7–20]; $p = 0.04$), and parameters of diaphragmatic neuromuscular efficiency, such as Vt/EAdi, were lower in the extubation failure than in success group. All respiratory, EAdi-derived indices and hemodynamics data before the beginning of the final and successful SBT are shown in Table 2.

During the SBT, no significant differences were observed between the extubation failure and success groups in clinical and blood gas variables, except for a statistically but not clinically significant difference in arterial pH: 7.42 (7.39–7.42) in the extubation failure group vs. 7.44 (7.42–7.47) in the extubation success group, $p = 0.039$. The mean EAdi during the SBT showed a statistically significant difference between the two groups (36 [12–43] μV vs. 14 [7–20] μV, $p = 0.01$, extubation failure vs. success, respectively). EAdi variation

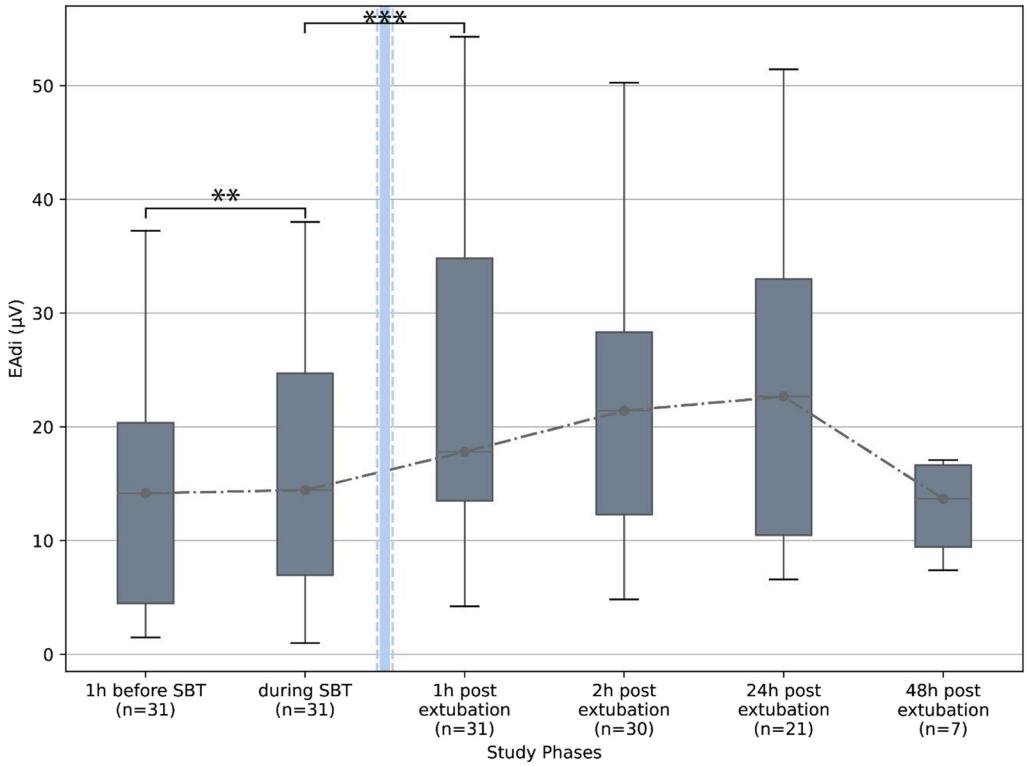

Fig. 1 EAdi boxplot of each phase for all the patients. Extubation is highlighted in blue area. All data in the "during SBT" column refer to the final and successful SBT before extubation. $^{**}p < 0.01$ between phases; $^{***} < 0.001$ between phases

comparing the pre-SBT phase and the final and successful SBT was an increase of 25% [− 2 to 36] in extubation success and an increase of 9% [0–21] in extubation failure ($p = 0.419$). In both groups EAdi remained stable across all the duration of the SBT with significantly higher values in patients later failing extubation (OS Figure 3). Patients' respiratory, hemodynamic, and arterial blood gas data during the final and successful SBT are shown in Table 3.

Analysis of EAdi as a limiting value threshold to predict extubation failure during SBT

The ROC analysis (Area Under Curve 0.76, 95% CI 0.57–0.89) revealed that the optimal cutoff points for the mean EAdi during the SBT to achieve the best efficiency (87.1%) were 35.6 μV and 37.3.6 μV. When using these EAdi thresholds during the SBT in order to predict extubation in our sample (prevalence of 19.4%), we observed a specificity of 96% and a sensitivity of 50% (positive predictive value of 75%, and a negative predictive value of 89%, AUC) and a specificity of 100% and a sensitivity of 33% (positive predictive value of 100%, and a negative predictive value of 86%), respectively. Based on other previous studies [23, 24], the limit of 30 μV was also evaluated. With this revised threshold, the results demonstrated a sensitivity of 92%, a specificity of 67%, a positive predictive value of 92%, and a negative predictive value of 67%. As shown in Fig. 3, extubation failure was more frequent in patients with EAdi > 30 μV compared to those with EAdi ≤ 30 μV (67% vs. 8%, $p = 0.006$).

The potential confounding factors were assessed through logistic regression analysis, showing a reduction in the risk ratio (RR) of extubation failure in patients with a mean EAdi during SBT greater than 30 μV when adjusting for the presence of COPD derivated from our sample. With this finding, the predictive capacity of extubation failure was compared between a univariable model (based solely on EAdi > 30 μV) and a multivariable model that included COPD. In comparison to the univariable model, the multivariable model demonstrated higher sensitivity, efficiency, and positive predictive value, with no significant difference in terms of the area under the curve (AUC) (Fig. 4). The detailed description of the stratification process and logistic regression analysis is available in the online supplement.

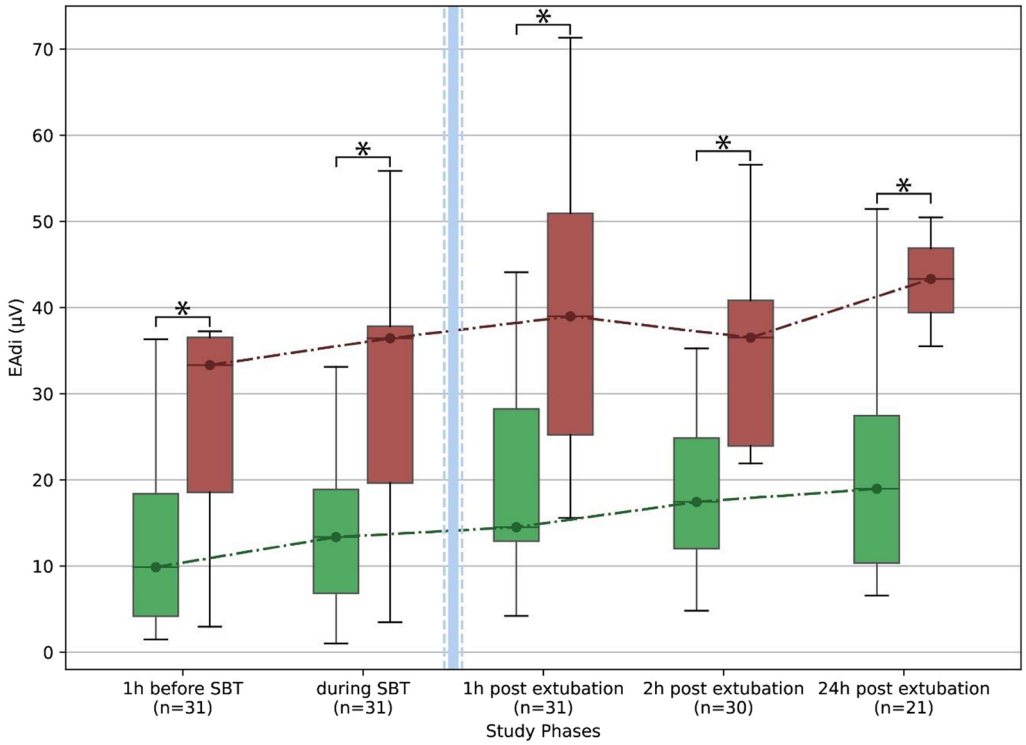

Fig. 2 EAdi boxplot for each phase for extubation success and failure groups. Extubation is highlighted in blue area; extubation success and failure groups are shown in green and red, respectively. All data in the "during SBT" column refer to the final and successful SBT before extubation. *$p < 0.05$ between groups

Discussion

The key findings of this study are as follows: (1) in difficult to wean patients EAdi increases during the SBT and in the first 24 h after extubation, being higher than during the spontaneous breathing conducted with a PS 7 cmH_2O and PEEP 0 cmH_2O; (2) during a successful SBT, patients with extubation failure presented higher levels of EAdi compared to patients with extubation success; (3) an EAdi value greater than 30 μV during the SBT could be useful in predicting extubation failure in difficult to wean patients.

In our study EAdi increased moderately when comparing the pre-SBT and the SBT phases indicating a slight increase in the respiratory load during the SBT. EAdi continued to increase after extubation and stayed at a higher level at 24 h, indicating that post-extubation respiratory load was higher than during the SBT phase (conducted with a PS 7 cmH_2O and PEEP 0 cmH_2O). That is why our trial of SBT may not accurately represent the patient's condition after extubation. A recent randomized controlled trial on the ventilator weaning concluded that spontaneous breathing trials conducted without PEEP and with a PS of 8 cmH_2O performed as well as harder SBTs with no assistance at all in terms of weaning success, with no more reintubations afterwards [25]: more patients succeed SBT and are successfully extubated in PS. However these data are valid for a general population, with simple weaning being the most frequent event. An area of uncertainty persists in difficult weaning patients (our target population), where physiological studies [26] seem to suggest that t-piece may be a safer and more physiologically adapted choice for SBT. Another study, conducted under conditions similar to those of our study by Barwing et al. [27] and using T-piece as SBT mode, observed that the EAdi increased significantly during the SBT compared to before the SBT. These observations are consistent with the findings of Cabello et al. [28] in difficult-to-wean patients. Cabello et al. physiologically described three different SBT techniques (PS with PEEP, PS without PEEP, T-piece) by measuring esophageal pressure, providing valuable data on the work of breathing (WOB) and respiratory effort of patients during these trials. They showed that the WOB and respiratory effort, calculated by monitoring with esophageal pressure, were greater with less assistance during SBT (both in terms of pressure support and PEEP), with the T-piece being the most demanding mode. Although in our study respiratory monitoring was done using EAdi instead of an esophageal pressure, our study also indicates that the

Table 2 Clinical variables one hour before start of SBT

	All patients (n = 31)	Extubation success (n = 25)	Extubation failure (n = 6)
Ventilatory parameters			
PS (cmH_2O)	8 (7–9)	8 (7–9)	8 (7–9)
PEEP (cmH_2O)	5 (5–6)	5 (5–6)	5 (5–6)
Tidal volume (ml)	398 (346–486)	380 (333–469)	410 (378–530)
Tidal volume (ml/Kg of predicted body weight)	6.7 (5.5–7.4)	6.3 (5.5–7.1)	6.5 (6.2–8.0)
Respiratory rate (RR)	24 (19–27)	22 (18–25)	27 (23–30)
Respiratory rate/Vt (RR/L)	53 (40–83)	52 (39–83)	57 (48–76)
Ventilatory ratio	1.40 (1.14–1.70)	1.32 (1.10–1.53)	1.95 (1.65–2.27)**
EAdi derived indices			
$EAdi_{max}$(μV)	14 (4–21)	10 (4–19)	33 (12–37)*
Vt PBW/EAdi (ml/Kg/uV)	0.46 (0.26–1.46)	0.56 (0.29–1.61)	0.22 (0.22–0.37)
Tidal volume/EAdi (ml/μV)	28 (15–103)	30 (18–112)	15 (13–51)
Haemodinamic parameters			
Systolic blood pressure (mmHg)	128 (102–140)	125 (101–141)	135 (108–143)
Diastolic blood pressure (mmHg)	60 (50–60)	60 (50–60)	55 (40–63)
Mean arterial pressure (mmHg)	80 (72–87)	80 (73–88)	78 (68–89)
Heart rate (bpm)	80 (75–100)	80 (73–95)	82 (74–103)
Sedation			
RASS	0 (0–0)	0 (0–0)	0 (0–0.25)

Data expressed as medians and interquartile ranges (IQR or 25th–75th percentile)

SBT, spontaneous breathing trials; PS, pressure support; PEEP, positive end-expiratory pressure; RR, respiratory rate; EAdi, electrical activity of the diaphragm in μV; PBW, predicted body weight; RASS, Richmond Agitation Sedation Scale

*$p \leq 0.05$ against extubation success; **$p \leq 0.001$ against extubation success

SBT conducted with a PS 7 cmH_2O and PEEP 0 cmH_2O does not place patients in the same ventilatory demand situation they will experience post-extubation. Both the data from Cabello's group and ours reinforce the idea that a possible respiratory overload imposed by the way in which the SBT is performed can be limiting during the extubation process in selected difficult-to-wean patients. However, data from a recent large RCT [25] focused on patients who had a high risk of extubation failure (i.e., > 65 years of age or had an underlying chronic cardiac or respiratory disease) comparing SBT performed with the use of either PSV with 8 cmH_2O and no PEEP or a T-piece did not show differences in reintubation performed within 7 days (15 vs. 14%; PSV and T-piece group respectively). Those apparent contradictory data respect our findings may be explained because the trial conducted by Thille et al. included mainly simple weaning patients (80%) guided with usual respiratory monitoring while our data focus on difficult weaning and patients monitored with EAdi. For all this, it is therefore possible that advanced respiratory monitoring (i.e. EAdi or esophageal pressure) should be conducted in selected patients in whom the SBT has previously failed, in order to better predict extubation outcome.

Patients who experienced extubation failure in our study showed significantly higher EAdi levels throughout all phases, including during the SBT, compared to those who had successful extubation. In our study, although conventional parameters for assessing SBT failure did not differ between the groups, the EAdi levels were different, possibly indicating that the diaphragm muscle was not prepared for the imposed mechanical load even during mechanical ventilation. Possible physiological explanations include lower compliance of the respiratory system (in particular due to dynamic hyperinflation) or lower neuromuscular efficiency of the diaphragm, or a combination of these two factors. In fact, the neuromuscular efficiency of the diaphragm was already impaired previously to extubation in patients who later required reintubation. The increase in diaphragmatic activity measured by EAdi and electromyography during the SBT in patients who subsequently require reintubation has been documented in other studies [23, 29]. However, it is worth noting that both studies involved patients who were not classified as difficult-to-wean, and they evaluated SBT failure per se. In contrast, the main point of

Table 3 Clinical variables during the SBT (PS 7 cmH2O and zero PEEP)

	All patients (n = 31)	Extubation success (n = 25)	Extubation failure (n = 6)
Respiratory parameters			
Tidal volume (ml)	327 (324–496)	353 (314–486)	389 (360–542)
Tidal volume (ml/kg of predicted body weight)	6.3 (5.7–7.4)	6.3 (5.5–7.1)	6.5 (6.2- 7.9)
Respiratory rate (RR)	24 (19–27)	23 (18–27)	25 (23–31)
FIO_2(%)	35 (30–40)	35 (30–40)	35 (30–40)
Respiratory rate/Vt (RR/L)	55 (43–87)	55 (36–89)	59 (47–76)
P0.1 (cmH_20)	0.5 (0.3–0.9)	0.4 (0.3–0.8)	1.4 (0.5–2.4)
EAdi derived indices			
$EAdi_{max}$ (μV)	14.4 (6.9–25.6)	13.4 (6.7–19.6)	36.0 (11.6–42.9)**
Tidal volume/EAdi (ml/μV)	32 (14–53)	42 (17–54)	13 (10–45)
Vt of PBW/EAdi (ml/Kg/μV)	0.44 (0.23–0.89)	0.64 (0.29–0.90)	0.21 (0.17–0.35)
Blood gas sample analysis			
pH	7.44 (7.41–7.46)	7.44 (7.42–7.47)	7.42 (7.39–7.42)*
$PaCO_2$(mmHg)	39 (36–45)	39 (35–44)	44 (38–53)
PaO_2(mmHg)	75 (69–87)	74 (67.7–86.0)	80 (72–91)
HCO_3 (mEq/L)	27.4 (25.0–29.0)	27.4 (25.0–28.9)	28.0 (25.0–29.0)
PaO_2/FIO_2 (ratio)	218 (185–250)	215 (184–248)	232 (195–265)
Haemodinamic parameters			
Systolic blood pressure (mmHg)	130 (110–140)	130 (115–140)	135 (105–158)
Diastolic blood pressure (mmHg)	60 (50–60)	60 (55–60)	55 (44–66)
Heart rate (bpm)	84 (80–100)	84 (80–100)	82 (78–96)

Data expressed as medians and interquartile ranges (IQR or 25th–75th percentile) RR, respiratory rate; FiO_2, inspired fraction of O_2 ; P0.1: airway occlusion pressure in cmH_2O; EAdi, electrical activity of the diaphragm in μV; PBW, predicted body weigh; $PaCO_2$, partial pressure of CO_2 in mmHg; PaO_2, partial pressure of O_2 in mmHg; HCO_3^-, concentration of HCO_3^- in blood in mmol/L *$p \leq 0.05$ against extubation success; **$p \leq 0.01$ extubation success

our study focuses on a population that is already challenging for weaning from IMV and assesses the actual failure of extubation following a successful SBT, where conventional parameters did not indicate SBT failure. These observations suggest that variables usually monitored during the SBT may be insufficient for detection of weaning failure in high risk patients; may be in particular those with COPD and that EAdi monitoring may have a role in difficult-to-wean patients. Moreover, our data indicate that in some patients electrical activation of the diaphragm can be very high even before the SBT, during PSV, when clinical signs of respiratory distress are absent

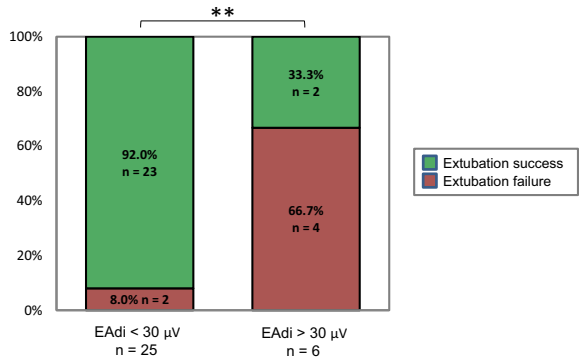

Fig. 3 Proportion of EAdi > 30 μV in extubation success and failure groups. EAdi: electrical activity of the diaphragm. **$p < 0.01$ between groups

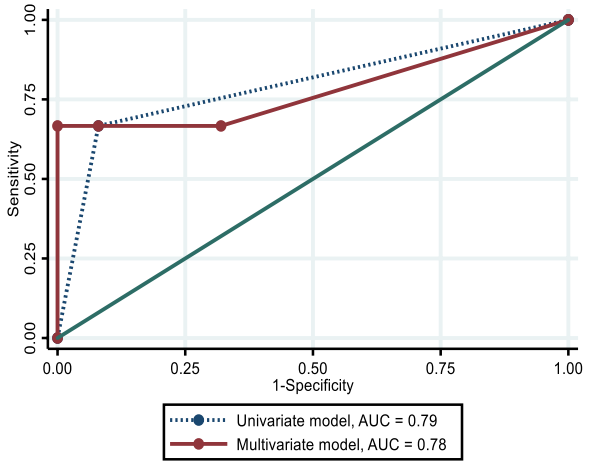

Fig. 4 ROC curve of the univariate and multivariate model to predict extubation failure. AUC: area under the curve

(or at least not easily detected) and arterial blood gases are normal. This condition is associated with subsequent extubation failure in our cohort (4 patients out of 6 with EAdi > 30 μV). We could speculate that starting EAdi monitoring before the SBT might allow identification of patients with high EAdi values as at very high risk of failure, and indicate the use of harder and longer SBT (i.e. 2 h t-tube), coupled with systematic prophylactic NIV after extubation in order to avoid extubation failure.

Our study has several limitations. First, due to its physiological nature a convenience sample of limited size was used. Second, it is a single-center physiological study, so the results must be confirmed and validated in bigger sample size and in other centers. Third, we performed all SBTs with PSV which prevented the observation of EAdi behavior during more demanding trials such as the T-piece and may explain the relatively high incidence of extubation failure. Fourth, due to technical reasons, tidal volume was not measured in the post-extubation period, thus making the calculation of the Vt/EAdi ratio unavailable and therefore impossible to determine the patients' neuromuscular efficiency after extubation. Fifth, another limitation regarding the association of EAdi with extubation failure is that it does not monitor the activity of accessory muscles, which might significantly contribute to tidal volume without any influence on the EAdi.

In conclusion, in difficult-to-wean patients, the EAdi during spontaneous breathing trial could be a good tool to predict extubation failure: an EAdi value greater than 30 μV during the SBT appears to enhance the prediction of extubation failure compared to conventional parameters.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13054-024-05092-x.

Supplementary Information 1. Supplemental details about extubation failure and COPD patients.

Supplementary Information 2. Figure 1: Study Flowchart. SBT: Spontaneous breathing trial; EAdi: electrical activity of the diaphragm.

Supplementary Information 3. Figure 2: Time Course of the EAdi in all patients, across different phases. Extubation is highlighted in blue area.

Supplementary Information 4. Figure 3: EAdi time course during the SBT. The SBT was divided in 10 time points of 6 min each. A: all patients (p = ns at Friedman test). B: comparison of the EAdi during the SBT by success (green boxes) and failure (red boxes) groups; * = p < 0.05 for extubation success vs. failure at each time point.

Supplementary Information 5. Table 1.

Supplementary Information 6. Table 2.

Supplementary Information 7. Table 3.

Supplementary Information 8. Table 4.

Supplementary Information 9. Table 5.

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Author contributions
TM, FR and JM conceived and designed the study. FJPG, and TM contributed to patient recruitment. APG and SI contributed to the algorithm to analyse raw data and to perform statistical analysis. FJPG, TM, FR, IM and JM made important intellectual contributions and actively participated in the interpretation of the data. FJPG and TM wrote the paper. FR, SI, APG, IM, JM made contributions to the writing and conceptual presentation of the results.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The Institutional Review Board of Hospital de Sant Pau (protocol code: IIBSP-EAD-2012-111, and Research Ethics Committee code: 55/2012). Informed consent was obtained from all patients of their next of kin. The preparation of this paper followed the STROBE recommendations.

Competing interests
The authors declare no competing interests.

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