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Martin Dres
Matthieu Schmidt
Alexis Ferre
Julien Mayaux
Thomas Similowski
Alexandre Demoule

Diaphragm electromyographic activity as a predictor of weaning failure

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M. Dres and M. Schmidt contributed equally to this work.

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M. Dres · M. Schmidt · A. Ferre · J. Mayaux · T. Similowski · A. Demoule (✉)
Service de Pneumologie et Réanimation médicale, Groupe Hospitalier Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, 47-83 Boulevard de l'Hôpital, 75651 Paris Cedex 13, France
e-mail: alexandre.demoule@psl.aphp.fr
Tel.: +33-1-42167761
Fax: +33-1-70247282

M. Schmidt · T. Similowski · A. Demoule
Université Paris 6-Pierre et Marie Curie, ER10, Paris, France

A. Demoule
UMRS 974, Institut National de la Santé et de la Recherche médicale, Paris, France

Abstract *Purpose:* To compare breathing pattern descriptors and diaphragm electromyographic activity (EAdi)-derived indices obtained from a neurally adjusted ventilatory assist catheter during a spontaneous breathing trial (SBT) in patients successfully and unsuccessfully separated from the ventilator and to assess their performance as a potential marker to discriminate these two categories of patients. *Methods:* Fifty-seven ready-to-wean patients were included in a prospective observational study. During a 30-min SBT (pressure support 7 cmH_2O, zero end expiratory pressure), tidal volume (V_T) and respiratory rate (RR) were obtained from the flow signal at baseline and at 3, 10, 20 and 30 min during the SBT. EAdi-derived indices were simultaneously computed: maximum of the EAdi ($EAdi_{max}$), area under the inspiratory curve of EAdi ($EAdi_{AUC}$), the difference between $EAdi_{max}$ and $EAdi_{min}$ (ΔEAdi), $EAdi_{max}/V_T$, $EAdi_{AUC}/V_T$ and $\Delta EAdi/V_T$. Patients, successfully (success group; $n = 35$) and unsuccessfully (failure group; $n = 22$) separated from the ventilator were compared. *Results:* At baseline, the breathing pattern was similar in the two groups, whereas $EAdi_{max}$ and $EAdi_{AUC}$ were significantly lower in the success group ($p < 0.05$). In the failure group, RR and RR/V_T increased significantly during the trial, V_T decreased, whereas $EAdi_{max}$ and $EAdi_{AUC}$ did not change. At 3 min, the areas under the receiver operating characteristic-curve of RR/V_T and the EAdi-derived indices to predict weaning outcome were 0.83 for the rapid shallow breathing index (RSBI), 0.84 for $EAdi_{max}/V_T$, 0.80 for $EAdi_{AUC}/V_T$ (0.80) and 0.82 for $\Delta EAdi/V_T$. The coefficient of variation for V_T decreased in the failure group while that for $EAdi_{max}$ remained unchanged. *Conclusions:* EAdi-derived indices provide reliable and early predictors of weaning outcome. However, the performance of these indices is not better than the RR/V_T.

Keywords Mechanical ventilation · Patient–ventilator weaning · Neurally adjusted ventilator assist

Introduction

The rapid discontinuation of mechanical ventilation (MV) is a major objective of intensive care unit medicine. Current guidelines recommend that weaning from the ventilator be achieved using a two-step strategy [1]. First, there should be an assessment of the readiness of the patient for weaning; this is to be followed by the second step, which should be a spontaneous breathing trial (SBT) as a diagnostic test to determine the likelihood of successful extubation [2]. Various weaning predictors derived from breathing pattern analyses have been developed to enable the likelihood of a successful weaning to be assessed as early and accurately as possible [3–6]. Since the success of weaning depends on the capacity of respiratory muscle to overcome the load that impedes the respiratory system, most of these indices are surrogates of the load capacity balance. The most commonly studied of these indices is the ratio of respiratory frequency (respiratory rate) to tidal volume (RR/V_T), otherwise known as the rapid shallow breathing index (RSBI) [3], and one of the most accurate is the variability of breathing pattern descriptors [6]. Central respiratory drive, which is increased during weaning failure, constitutes an alternative approach for predicting weaning. Occlusion pressure (P0.1) and P0.1-derived parameters are among its surrogates [7–12], but the performance of these parameters remains controversial [13]. In addition, although P0.1 is a marker of respiratory drive, it is influenced by muscle strength. This is in contrast to the diaphragm electromyographic activity (EAdi)-derived indices, which have recently become easier to determine with the availability of the neurally adjusted ventilatory assist (NAVA) catheter [14]. Deemed to be used in conjunction with the NAVA mode, which subordinates the ventilator cycle and level of assistance to EAdi, the NAVA catheter consists of a nasogastric feeding tube equipped with a multiple-array esophageal electrode that provides real time access to EAdi.

In the study reported here, we hypothesized that EAdi would provide reliable predictors of weaning success. Our aim was therefore to compare patients successfully separated from the ventilator and the endotracheal tube with those who were not, in terms of various EAdi-derived indices recorded during the SBT. We also compared the performance of these indices to the performance of the RR/V_T. Finally, because it has been demonstrated that indices of breathing variability can discriminate weaning success from weaning failure [6], we also sought to evaluate the indices of EAdi variability to predict weaning success.

Materials and methods

The study was conducted over a 12-month period (1 November 2010 to 1 November 2011) in a ten-bed Intensive Care Unit (ICU) within an 1,800-bed university hospital. The protocol was approved by the institutional review board of the French Learned Society for Intensive Care Medicine (no. 11–321). Informed consent was obtained from the patients.

Patients

Patients intubated and ventilated for at least 24 h were eligible for inclusion in the study if (1) they had been previously mechanically ventilated with NAVA mode and the NAVA catheter had been left in place [the preconditions for NAVA are listed in the Electronic Supplementary Material (ESM)] and (2) they met the predefined readiness-to-wean criteria on the daily screening (see ESM). Patients with neuromuscular diseases and those for whom life support would be withheld or withdrawn were not included in the study.

Spontaneous breathing trial protocol

As soon as the patients fulfilled the readiness-to-wean criteria, a 30-min SBT was performed with the patient connected to the ventilator (pressure support level 7 cmH_2O, zero end expiratory pressure). The SBT was considered to be a failure if at least one the following criteria was present: (1) blood oxygen saturation (SpO_2) of <90 % with a fraction of inspired oxygen (FiO_2) of ≥50 %; (2) acute respiratory distress (RR ≥ 40/min, agitation, cyanosis); (3) systolic arterial blood pressure of ≥180 mmHg; (4) cardiac arrhythmias; (5) respiratory acidosis [pH < 7.32 with an arterial carbon dioxide tension ($PaCO_2$) of ≥50 mmHg]. If none of these failure criteria was present, the SBT was considered as successfully completed and the patient was extubated. This decision was taken by the physician in charge of the patient. The patient was reconnected if signs of intolerance (see above) were present. The separation from the ventilator and the endotracheal tube was considered a success when spontaneous breathing could be sustained without any form of ventilatory support at 48 h after extubation. Conversely, cases of failure included patients who failed the SBT and patients requiring reintubation or any form of ventilator support (including non-invasive ventilation for post-extubation acute respiratory failure) during the first 48 h after extubation. Patients were only studied once, at the first SBT.

Data acquisition

Diaphragm electromyographic activity (obtained from the NAVA catheter; see ESM for detailed EAdi signal processing), airway pressure and flow were acquired at 100 Hz from the ventilator via a RS232 interface connected to a computer using commercially available software (Servo-I® RCR ver. 3.6.2; Maquet Critical Care, Solna, Sweden). Physiologic variables were measured at baseline and at 3, 10, 20 and 30 min during the SBT. Arterial blood gases were sampled at the end of the SBT.

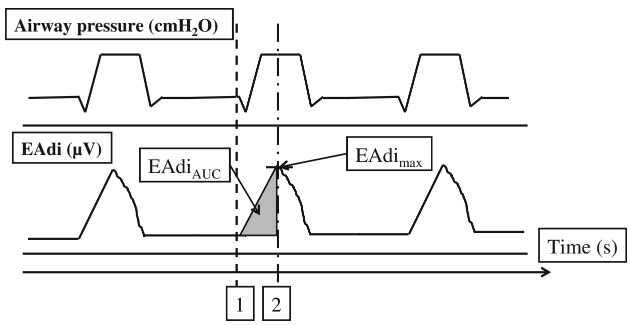


Fig. 1 Schematic representation of the airways pressures and diaphragm electromyographic activity (*EAdi*) signals. *Upper panel* Airway pressure recording, *lower panel* EAdi recording. *Dotted line no. 1* indicates the start of the rise of the EAdi signal, *dashed line no. 2* shows the peak of the EAdi ($EAdi_{max}$). *Grey area* represents the area under the curve of EAdi ($EAdi_{AUC}$)

Data analysis

Respiratory rate (RR), tidal volume (V_T), maximum EAdi ($EAdi_{max}$) and the area under the curve of the EAdi during inspiratory time ($EAdi_{AUC}$, integrated from baseline to peak; Fig. 1) were calculated at the very beginning of the SBT (baseline) and at 3, 10, 20 and 30 min during the SBT. The rapid shallow breathing index (RR/V_T), the $EAdi_{max}/V_T$, the $EAdi_{AUC}/V_T$ and the difference between $EAdi_{max}$ and the lowest EAdi value reported to the V_T ratio ($\Delta EAdi/V_T$) were also computed.

The coefficient of variation (CV), defined as the standard deviation (SD) reported for the mean of both V_T and $EAdi_{max}$, was calculated at 3 and 30 min for a duration of 3 min at each time-point using a software routine developed for Matlab (Mathworks, Natick, MA).

Statistical analysis

The statistical analysis was performed with Prism ver. 4.01 software (GraphPad Software, San Diego, CA). The results are expressed as the median [25–75 % interquartile range (IQR)]. The normality of the distribution was evaluated with the Kolmogorov–Smirnov test. For a given time-point, patients successfully (success group) and unsuccessfully (failure group) separated from the ventilator were compared using Student's *t* test or the Mann–Whitney *U* test as appropriate. Within a given group (success or failure), the five time-points (baseline, 3, 10, 20 and 30 min) were compared using analysis of variance (ANOVA) for repeated measures or the Friedman Test. Categorical variables were compared with the χ^2 test or Fisher's exact test. Differences were considered to be significant when $p < 0.05$. The predictive performance of RR/V_T and EAdi-derived indices at the 3 min time-point was finally assessed with receiver operating characteristic (ROC) curves [15]. For RR/V_T, the cut-off of 100 breaths $min^{-1}\ l^{-1}$ was retained [3], while for EAdi-derived indices, the cut-off was obtained for each index by determining the better sensitivity and specificity.

Results

Patients's characteristics

A convenience sample of 57 consecutive patients were enrolled in this study (see flow chart in ESM Fig. E1), of whom 35 and 22 patients were successfully and unsuccessfully separated from the ventilator, respectively. In the failure group, the endotracheal tube was not removed at the end of the SBT in 19 patients, and the endotracheal tube was removed but ventilatory support was required within 48 h for three patients. The two groups were similar in terms of demographic and clinical characteristics, but there were more patients with chronic respiratory failure in the failure group (Table 1). Patients in the failure group were longer on mechanical ventilation, but ICU mortality was similar in both groups (Table 1).

Breathing pattern at baseline and during the SBT

At the initiation of the trial, V_T and RR were similar in patients in both groups, but the RR/V_T was higher in patients in the failure group (Table 2). Figure 2 depicts the V_T, RR and RR/V_T at baseline and at 3, 10, 20 and 30 min during the SBT (see also ESM Table E1). During the SBT, RR increased significantly in the failure group and decreased significantly in the success one. Simultaneously, V_T decreased in the failure group, whereas it remained stable in the success group. The RR/V_T ratio did not change over time in the success group, while it increased significantly in the failure group. Overall, 3 min after the beginning of the SBT, V_T, RR and RR/V_T were significantly different between patients who were successfully weaned and those who were not.

EAdi-derived indices at baseline and during the SBT

Table 2 presents the EAdi-derived variables at baseline and Fig. 3 depicts the $EAdi_{max}$, $EAdi_{AUC}$, $EAdi_{max}/V_T$, $EAdi_{AUC}/V_T$ and $\Delta EAdi/V_T$ at baseline and during the SBT at 3, 10, 20 and 30 min (see also ESM Table E1). At the initiation of the trial, all of the EAdi-derived variables were different between patients who were successfully weaned and those who were not (Table 2). These differences remained significant during the entire SBT. However, during the SBT, EAdi-derived variables remained stable throughout the SBT in both the success and failure group with the exception of $EAdi_{max}/V_T$ and $\Delta EAdi/V_T$, which increased significantly in the failure group (Fig. 3).

Table 1 Patients' characteristics

Characteristics	Success group ($n = 35$)	Failure group ($n = 22$)	p
Age (years)	59 (52–72)	67 (58–77)	0.08
Male, n (%)	22 (63)	11 (50)	NS
Body mass index (kg m^{-2})	25 (21–27)	28 (21–36)	NS
SAPS II	67 (54–78)	66 (48–79)	NS
Past history, n (%)			
Respiratory disease	7 (20)	10 (45)	0.04
Cardiovascular disease	10 (28)	5 (23)	NS
Reasons for initiating mechanical ventilation, n (%)[a]			
Acute on chronic respiratory failure	2 (5)	6 (30)	0.06
Community-acquired pneumonia	6 (17)	6 (27)	NS
Cardiogenic pulmonary oedema	6 (17)	5 (23)	NS
Extrapulmonary septic shock	7 (19)	1 (5)	NS
Coma	8 (22)	3 (15)	NS
Post-operative acute respiratory failure	3 (8)	0 (0)	NS
Others	3 (8)	1 (5)	NS
Duration of mechanical ventilation prior to the SBT (days)	2 (1–4)	4 (2–6)	NS
Total duration of mechanical ventilation (days)	2.5 (1.0–4)	6 (4–11)	0.02
ICU mortality, n (%)	5 (14)	3 (14)	NS

Unless specified otherwise, data are expressed as the median, with the interquartile range (IQR) given in parenthesis

Success Patients successfully separated from ventilator, *Failure* patients who were unsuccessfully separated from the ventilator, *SAPS* simplified acute physiologic score, *ICU* intensive care unit, *SBT* spontaneous breathing trial, *NS* not significant

[a] Several reasons could justify the mechanical ventilation for the same patient

Table 2 Breathing pattern and diaphragm electromyographic activity-derived indices at baseline

Breathing pattern and EAdi-derived indices at baseline	Success group ($n = 35$)	Failure group ($n = 22$)	p
RR (breaths min^{-1})	29 (23–35)	31 (26–38)	NS
V_T (ml kg^{-1} IBW)	6.1 (5.4–7.5)	5.9 (4.5–6.6)	0.07
RR/V_T (breaths $min^{-1}.l^{-1}$)	60 (42–90)	100 (74–123)	<0.01
$EAdi_{max}$ (μV)	10 (5–18)	17 (9–28)	0.02
$EAdi_{AUC}$ ($μV^2$)	4 (2–7)	7 (3–11)	0.04
$EAdi_{AUC}/V_T$ ($μV^2$ l^{-1})	10 (5–16)	19 (10–33)	<0.01
$EAdi_{max}/V_T$ (μV l^{-1})	22 (13–49)	50 (28–106)	<0.01
ΔEAdi/VV_T (μV l^{-1})	20 (10–40)	44 (23–99)	<0.01

Data are expressed as the median, with the IQR given in parenthesis

EAdi Diaphragm electromyographic activity, *RR* respiratory rate, V_T tidal volume, $EAdi_{max}$ peak of the EAdi, $EAdi_{AUC}$ area under the curve of the EAdi during inspiratory time, *ΔEAdi* difference between $EAdi_{max}$ and the lowest EAdi value

Performance of RR/V_T and EAdi-derived indices at 3 min into the SBT

Figure 4 presents the ROC curves and performance of the RR/V_T (threshold of 100 breaths min^{-1} l^{-1}), $EAdi_{max}/V_T$, $EAdi_{AUC}/V_T$ and ΔEAdi/V_T at 3 min into the SBT. The best values of sensibility, specificity and AUC were obtained with a threshold of 28 μV l^{-1} for $EAdi_{max}/V_T$, 11 $μV^2$ l^{-1} for $EAdi_{AUC}/V_T$ and 26 μV $L^{-1}$for ΔEAdi/V_T. The sensitivity and the specificity of these two indices were similar to the performance of RR/V_T.

Variability of the V_T and the $EAdi_{max}$

The CV of the V_T at the onset of SBT was similar in both the success and failure patients [18 (IQR 13–28) vs. 17 (IQR 11–34) %, respectively]. This decreased significantly in both groups during the SBT to reach, by the end of the SBT, 12 (IQR 8–25) % in the success group patients and 12 (IQR 9–21) % in the failure group patients. The CV of $EAdi_{max}$ was also similar in both groups at onset of SBT [success group: 30 (IQR 24–43) %; failure group: 27 (IQR 18–36) %]. However, while the CV of $EAdi_{max}$ decreased during the SBT in success group patients [18 (IQR 9–32) %], it remained unchanged in failure patients [27 (IQR 18–36) %].

Tolerance of the SBT

By the end of the SBT, patients of the failure group had a higher systolic blood pressure, a lower pH and a higher $PaCO_2$ (see ESM Table E2).

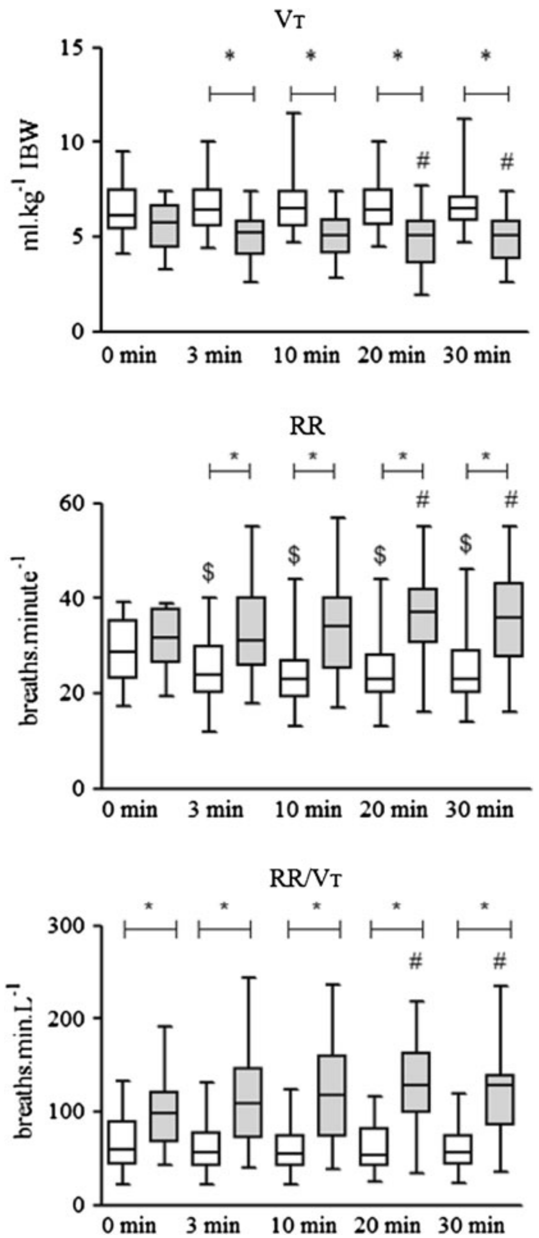


Fig. 2 Breathing pattern during the spontaneous breathing trial (SBT). Tidal volume (V_T) (*upper panel*), respiratory rate (*RR*) (*middle panel*) and RR/V_T ratio (*lower panel*) at baseline and during the SBT (3, 10, 20 and 30 min) in patients successfully separated from the ventilator (*white boxes*; success group) and those who were not (*grey boxes*; failure group). *Line inside the boxes* median, *limits of the boxes* 75th and 25th percentile of the data (interquartile range), *whiskers* minimum to maximum. *$p < 0.05$ vs. failure group, #$p < 0.05$ vs. baseline within the failure group, \$$p < 0.05$ within the success group

Discussion

To our knowledge, this study is the first to report a direct and physiologic approach with NAVA of neuro-mechanical coupling during the weaning of mechanical ventilation. Our major findings can be summarized as follows: (1) several of the EAdi-derived indices measured during the SBT were significantly different between patients successfully separated from the ventilator and those for whom separation failed; (2) these differences occurred early during the SBT and were even present at baseline; (3) 3 min after the beginning of the SBT, the performance of EAdi-derived indices of neuromechanical coupling was similar to—but not better than—the performance of the RR/V_T ratio; (4) variability of the EAdi signal is not a reliable predictor of weaning failure.

Breathing pattern and EAdi-derived indices during SBT

During the SBT, we observed what has previously been widely described: an increase in the RR with a concomitant decrease in the the V_T in the failure group and no change in the success group [16, 17]. These changes resulted in the development of a rapid shallow breathing pattern in patients who failed the SBT, as suggested by the increased RR/V_T ratio. The RR/V_T ratio was not used as a SBT failure criterion because it might certainly have caused a bias in its comparison with the EAdi-derived indices.

Interestingly, $EAdi_{max}$ and $EAdi_{AUC}$ were higher in the failure than in the success group from the very beginning of the SBT, suggesting that patients who fail the SBT may have a higher respiratory drive at baseline [16]. However, the EAdi did not change significantly during the course of the SBT in either group. This latter observation suggests that the central respiratory drive to the diaphragm did not increase in failure group patients despite these patients developing a rapid shallow breathing. Taken together, these data suggest that during weaning failure, extradiaphragmatic inspiratory muscles, such as sternomastoid and ribcage muscles, are proportionally more recruited than the diaphragm. This suggestion is consistent with the well-observed preferential recruitment of extradiaphragmatic inspiratory muscle during loaded breathing [18]. Hence, EAdi might not be the best surrogate of inspiratory muscles failure during weaning. Of course, the steady EAdi concomitant with the development of a rapid shallow breathing strongly suggests an altered neuro-mechanical coupling.

Beyond ventilatory drive, neuro-mechanical coupling as a marker of weaning failure

We computed various indices of neuro-mechanical coupling, namely $EAdi_{max}/V_T$, $EAdi_{AUC}/V_T$ and $\Delta EAdi/V_T$. These indices reflect the ability of the diaphragm to convert respiratory drive into ventilation. We showed that patients in the weaning failure group had a severe impairment of the neuromechanical coupling of the

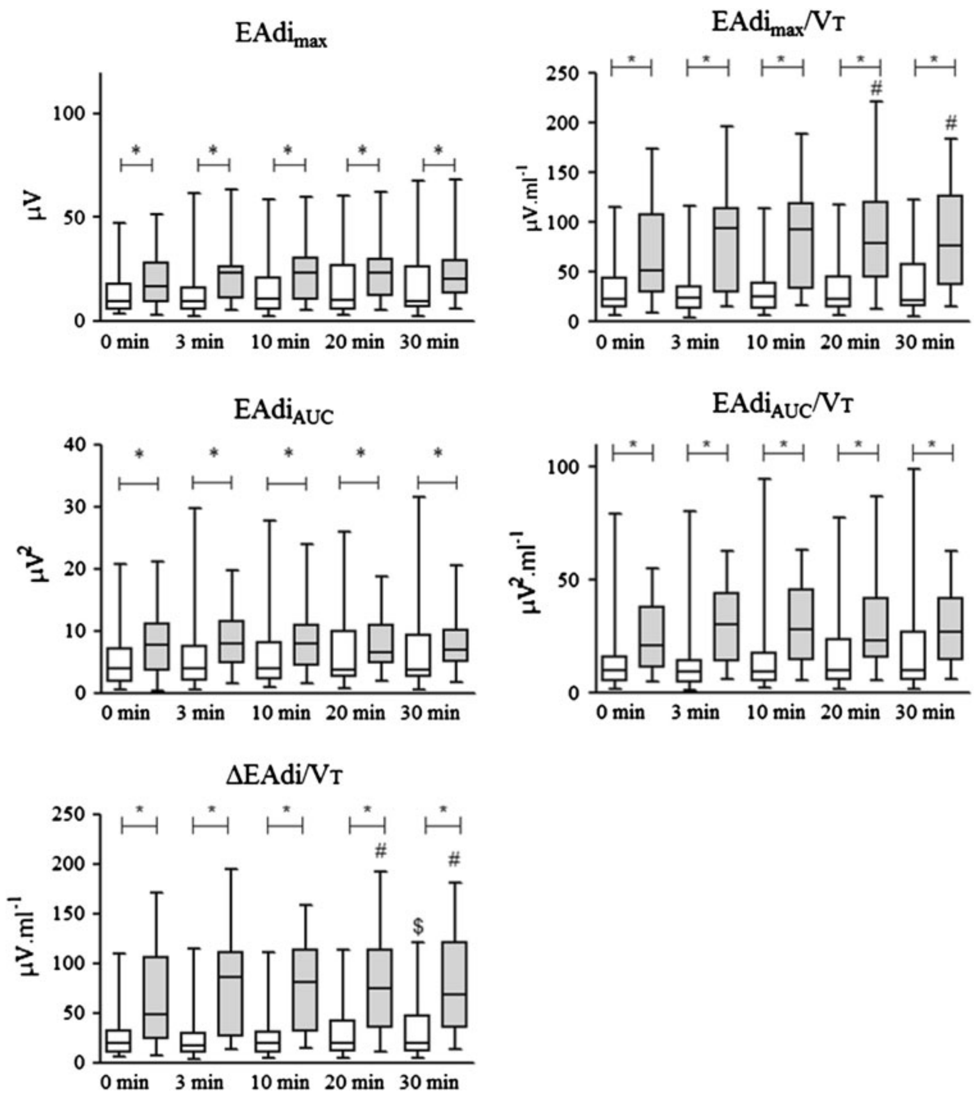


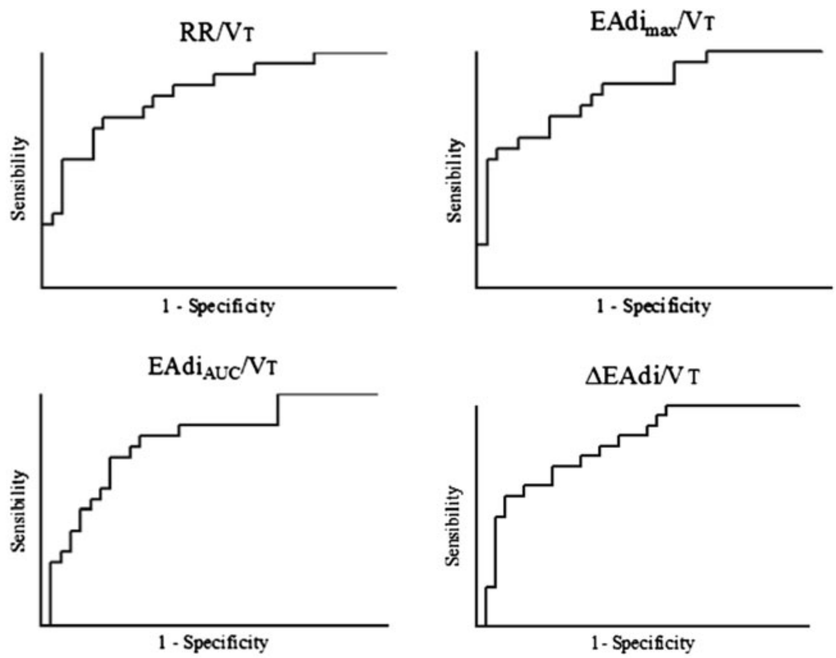
Fig. 3 Diaphragm electromyogaphic activity-derived indices during the SBT. $EAdi_{max}$ (*upper left panel*), $EAdi_{AUC}$ (*middle left panel*), amplitude between the maximal and lowest EAdi ($\Delta EAdi)/V_T$) ratio (*lower left panel*), $EAdi_{max}/V_T$ ratio (*right upper panel*) and the $EAdi_{AUC}/V_T$ ratio (*middle right panel*) at baseline and during the SBT (3, 10, 20 and 30 min) in patients successfully separated from the ventilator (*white box*) and those who were not (*grey box*). *Line inside the boxes* Median, *limits of the boxes* 75th and 25th percentile of the data (IQR), *whiskers* minimum to maximum. $^*p < 0.05$ versus failure group, $^{\#}p < 0.05$ versus baseline within the failure group, $^{\$}p < 0.05$ within the success group

diaphragm, which was not only present from the beginning of the SBT, but also increased progressively during the entire SBT. All of these indices were able to efficiently discriminate success from failure patients as early as 3 min after the beginning of the SBT. However, the performance of these indices was not superior to the performance of RR/V_T. The fact that the SBT was performed with a pressure support of 7 cmH_2O may have lowered the performance of EAdi-derived indices to discriminate patients who were successful in the SBT from those who failed as 7 cmH_2O of pressure support lowers the performance of the RR/V_T. Indeed, even if the good performance of RR/V_T is well demonstrated while the patient is disconnected from the ventilator and breaths room air without pressure support [2], this is not the case under pressure support [19, 20].

Our results differ slightly from those of Wolf et al. [21] who recently observed in children that the $V_T/\Delta EAdi$ ratio after 1 h of SBT decreased dramatically in patients who were successfully weaned while it remained unchanged in those who were not. The different duration of the SBT (1 h vs. 30 min) and the different age of the population (children have indeed a lower rib cage compliance than adults) may explain this discrepancy.

Variability of EAdi

Variability in the various descriptors of the breathing pattern has been shown to be reliably predict weaning success [6]. We therefore sought to evaluate the performance of EAdi variability to predict weaning failure. First, we did not observe an earlier described difference in the CV of the V_T between patients who were successfully separated from the ventilator and those who were not [6]. This is not highly surprising since we performed SBT



	Threshold	Sensibility	Specificity	AUC
RR/V_T	100	60	86	0.83
$EAdi_{max}/V_T$	28	77	71	0.84
$EAdi_{AUC}/V_T$	11	82	63	0.80
$\Delta EAdi/V_T$	26	73	69	0.82

Fig. 4 Receiving operating curves (ROC) for breathing pattern and EAdi-derived indices during the SBT. ROC curves for the RR/V_T ratio (*upper left panel*), $EAdi_{max})/V_T$ ratio (*upper right panel*), $EAdi_{AUC}/V_T$ ratio (*lower left panel*) and $\Delta EAdi/V_T$ ratio (*lower right panel*) to predict the success or failure of the separation of patients from the ventilator at 3 into the SBT. Threshold, sensibility, specificity and area under the ROC curve (AUC) are provided in the *table*

with pressure support and not while the patient was disconnected from the ventilator [22]. Pressure support indeed unloads the respiratory system and therefore alters the load capacity balance of the respiratory system, of which the breathing pattern variability is a surrogate [23]. Secondly, the variability of the EAdi was similar among patients who succeeded and those who failed the SBT. This result is consistent with the findings of a previous study conducted by our group, which showed that the underlying variations in central respiratory neural output activity seem not to be particularly sensitive to the mechanical load [24].

Study limitations

Our study has several limitations. First, it was a single-centre study with a relatively small sample size. Second, to keep the study observational, we only included patients who had been previously ventilated in NAVA, which constitutes a selection bias. Indeed, in our unit, NAVA is given to patients with a poorer tolerance for pressure support ventilation and a longer duration of mechanical ventilation; these patients are eventually more likely to be difficult to wean. In addition, we restricted the study to patients ventilated for more than 24 h, which could explain why chronic obstructive pulmonary disease (COPD) patients were overrepresented in our patient cohort. Third, the SBT was performed with a minimal pressure support of 7 cmH_2O and not with the patient disconnected from the ventilator and breathing room air without pressure support. Compared to a SBT without pressure support ("T-piece"), pressure support ventilation with or without positive end-expiratory pressure (PEEP) is known to markedly modify the breathing pattern and inspiratory muscle effort [20, 25]. Hence, the performance of EAdi-derived indices might have been higher during a SBT performed with a T-piece or PEEP without pressure support. However, in our unit and for safety reasons, the standard of care is to perform the SBT with the patients connected to the ventilator. Because we wished to perform a "real life" study, we did not change the SBT procedure standardly used at our hospital [1]. Fourth, there were more COPD patients in the failure group than in the success group. In these patients, dynamic hyperinflation may have altered neuromechanical coupling and diaphragmatic performance [26–28]. Moreover, patients with chronic respiratory diseases are known to strongly recruit their extradiaphragmatic inspiratory muscles when facing increased inspiratory load [29]. Fifth, the NAVA catheter has been designed to trigger and adjust ventilatory assist and not for weaning. Thus, it cannot provide information, such as the ratio of high to low frequencies of the electromyograph (H/L), which predicts diaphragm fatigue or excessive loading [30, 31]. Moreover, although we have some information, we do not know the whole signal processing of the technique and have unfortunately no access to raw data. In addition, there might be an inter-subject variability in EAdi recording, depending on many factors and, to date, there is no study that has compared EAdi in large populations of patients. Finally, the study was not strictly blinded. Indeed, the physician in charge of the patients could see the EAdi recordings during the SBT, which may have influenced his/her decision regarding extubation. For this reason, we used strict criteria of SBT success and failure, which are actually those used in our ICU in daily clinical practice. Of note, we did not consider RR/V_T as a criterion for extubation despite its good performance as an index of SBT success or failure as this would have biased the comparison of the performance of this index to the performance of EAdi-derived indices.

Conclusions

EAdi-derived indices collected via the NAVA catheter during the SBT provide reliable predictors of successful separation from the ventilator. These indices can discriminate early in the SBT the ongoing success or failure of separation from the ventilator. However, the performance of these indices is not better than the performance of the rapid shallow breathing index. Therefore, the benefit of EAdi-derived indices during the SBT remains unclear.

Conflicts of interest The Association pour le Développement et l'Organisation de la Recherche en Pneumologie et sur le sommeil, a non-profit structure that supports the research activities of the "Service de Pneumologie et Réanimation Médicale, Groupe Hospitalier Pitié-Salpêtrière", has received an unrestricted research grant from Maquet France SA, Orléans, France, to support pathophysiological research studies on NAVA.

References

1. Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, Pearl R, Silverman H, Stanchina M, Vieillard-Baron A, Welte T (2007) Weaning from mechanical ventilation. Eur Respir J 29:1033–1056
2. Tobin MJ, Jubran A (2006) Weaning from mechanical ventilation. In: Tobin MJ (ed) Principles and practice of mechanical ventilation. McGraw-Hill, New York, pp 1185–1220
3. Yang KL, Tobin MJ (1991) A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 324:1445–1450
4. MacIntyre N (2007) Discontinuing mechanical ventilatory support. Chest 132:1049–1056
5. Meade M, Guyatt G, Cook D, Griffith L, Sinuff T, Kergl C, Mancebo J, Esteban A, Epstein S (2001) Predicting success in weaning from mechanical ventilation. Chest 120:400S–424S
6. Wysocki M, Cracco C, Teixeira A, Mercat A, Diehl JL, Lefort Y, Derenne JP, Similowski T (2006) Reduced breathing variability as a predictor of unsuccessful patient separation from mechanical ventilation. Crit Care Med 34:2076–2083
7. Sassoon CS, Te TT, Mahutte CK, Light RW (1987) Airway occlusion pressure. An important indicator for successful weaning in patients with chronic obstructive pulmonary disease. Am Rev Respir Dis 135:107–113
8. Sassoon CS, Mahutte CK, Te TT, Simmons DH, Light RW (1988) Work of breathing and airway occlusion pressure during assist-mode mechanical ventilation. Chest 93:571–576
9. Fernandez R, Cabrera J, Calaf N, Benito S (1990) P 0.1/PIMax: an index for assessing respiratory capacity in acute respiratory failure. Intensive Care Med 16:175–179
10. Gandia F, Blanco J (1992) Evaluation of indexes predicting the outcome of ventilator weaning and value of adding supplemental inspiratory load. Intensive Care Med 18:327–333
11. Montgomery AB, Holle RH, Neagley SR, Pierson DJ, Schoene RB (1987) Prediction of successful ventilator weaning using airway occlusion pressure and hypercapnic challenge. Chest 91:496–499
12. Sassoon CS, Mahutte CK (1993) Airway occlusion pressure and breathing pattern as predictors of weaning outcome. Am Rev Respir Dis 148:860–866
13. Fernandez MD, Piacentini E, Blanch L, Fernandez R (2004) Changes in lung volume with three systems of endotracheal suctioning with and without pre-oxygenation in patients with mild-to-moderate lung failure. Intensive Care Med 30:2210–2215
14. Sinderby C, Navalesi P, Beck J, Skrobik Y, Comtois N, Friberg S, Gottfried SB, Lindstrom L (1999) Neural control of mechanical ventilation in respiratory failure. Nat Med 5:1433–1436
15. Hanley JA, McNeil BJ (1983) A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 148:839–843
16. Jubran A, Tobin MJ (1997) Pathophysiology basis of acute respiratory distress in patients who fail a trial of weaning from mechanical ventilation. Am J Respir Crit Care Med 155:906–915
17. Laghi F, Cattapan SE, Jubran A, Parthasarathy S, Warshawsky P, Choi YS, Tobin MJ (2003) Is weaning failure caused by low-frequency fatigue of the diaphragm? Am J Respir Crit Care Med 167:120–127

18. Parthasarathy S, Jubran A, Laghi F, Tobin MJ (2007) Sternomastoid, rib cage, and expiratory muscle activity during weaning failure. J Appl Physiol 103:140–147
19. Lee KH, Hui KP, Chan TB, Tan WC, Lim TK (1994) Rapid shallow breathing (frequency-tidal volume ratio) did not predict extubation outcome. Chest 105:540–543
20. El-Khatib MF, Zeineldine SM, Jamaleddine GW (2008) Effect of pressure support ventilation and positive end expiratory pressure on the rapid shallow breathing index in intensive care unit patients. Intensive Care Med 34:505–510
21. Wolf GK, Walsh BK, Green ML, Arnold JH (2011) Electrical activity of the diaphragm during extubation readiness testing in critically ill children. Pediatr Crit Care Med 12:e220–e224
22. Bien MY, Lin YS, Shih CH, Yang YL, Lin HW, Bai KJ, Wang JH, Kou YR (2011) Comparisons of predictive performance of breathing pattern variability measured during T-piece, automatic tube compensation, and pressure support ventilation for weaning intensive care unit patients from mechanical ventilation. Crit Care Med 39:2253–2262
23. Khoo MC (2000) Determinants of ventilatory instability and variability. Respir Physiol 122:167–182
24. Schmidt M, Demoule A, Cracco C, Gharbi A, Fiamma MN, Straus C, Duguet A, Gottfried SB, Similowski T (2010) Neurally adjusted ventilatory assist increases respiratory variability and complexity in acute respiratory failure. Anesthesiology 112:670–681
25. Cabello B, Thille AW, Roche-Campo F, Brochard L, Gomez FJ, Mancebo J (2010) Physiological comparison of three spontaneous breathing trials in difficult-to-wean patients. Intensive Care Med 36:1171–1179
26. O'Donnell DE, Banzett RB, Carrieri-Kohlman V, Casaburi R, Davenport PW, Gandevia SC, Gelb AF, Mahler DA, Webb KA (2007) Pathophysiology of dyspnea in chronic obstructive pulmonary disease: a roundtable. Proc Am Thorac Soc 4:145–168
27. O'Donnell DE, Hamilton AL, Webb KA (2006) Sensory-mechanical relationships during high-intensity, constant-work-rate exercise in COPD. J Appl Physiol 101:1025–1035
28. Murphy PB, Kumar A, Reilly C, Jolley C, Walterspacher S, Fedele F, Hopkinson NS, Man WD, Polkey MI, Moxham J, Hart N (2011) Neural respiratory drive as a physiological biomarker to monitor change during acute exacerbations of COPD. Thorax 66:602–608
29. De Troyer A, Peche R, Yernault JC, Estenne M (1994) Neck muscle activity in patients with severe chronic obstructive pulmonary disease. Am J Respir Crit Care Med 150:41–47
30. Brochard L, Harf A, Lorino H, Lemaire F (1989) Inspiratory pressure support prevents diaphragmatic fatigue during weaning from mechanical ventilation. Am Rev Respir Dis 139:513–521
31. Cohen CA, Zagelbaum G, Gross D, Roussos C, Macklem PT (1982) Clinical manifestations of inspiratory muscle fatigue. Am J Med 73:308–316