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读书报告

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CRITICAL CARE MEDICINE

Clinical Assessment of Auto-positive End-expiratory Pressure by Diaphragmatic Electrical Activity during Pressure Support and Neurally Adjusted Ventilatory Assist

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Background

Auto-positive end-expiratory pressure (auto-PEEP) is defined as the alveolar pressure (above the set PEEP) at the end of a normal expiration.

Auto-PEEP can be caused by:(1) insufficient time for exhalation relative to the respiratory system's time constant, which causes gas trapping (dynamic hyperinflation); (2) airflow limitation with small airways collapse below a threshold pressure during expiration.

During assisted spontaneous breathing, auto-PEEP may represent a substantial workload for the patient: after the initiation of an inspiratory effort, the gas will not flow from the airways to the alveoli until the pressure generated by inspiratory muscles overcomes auto-PEEP.

Moreover, the presence of auto-PEEP will worsen the patient–ventilator interaction by affecting the ventilator's efficiency to detect patient's inspiratory efforts

However, since the ventilator is controlled by the electrical activity of the diaphragm (EAdi) rather than by airflow and pressure signals during neurally adjusted ventilatory assist (NAVA),we hypothesized that ventilator triggering would occur earlier in response to patient's demand leading to an improved patient–ventilator synchrony as compared with pressure support ventilation (PSV) in patients affected by auto-PEEP.

Accurate estimation of auto-PEEP would be clinically useful for diagnostic purposes and for selecting appropriate ventilatory settings: if auto-PEEP is due to airflow limitation, the application of an external PEEP (PEEPe) may decrease the pressure gradient between the alveoli and the airways during expiration,thus reducing the triggering effort and improving patient–ventilator synchrony.

During assisted spontaneous breathing, auto-PEEP is not easy to measure at the bedside: the use of an end-expiratory occlusion (the reference technique during controlled ventilation)is not always suitable due to incomplete patient’s relaxation.

- A reliable method, although not frequently applied in the clinical practice, is represented by esophageal pressure (Pes) measurement: the pressure decrease between the initiation of the effort and the onset of the airflow equals “dynamic” auto-PEEP.
- We reasoned that, because Pes is used to estimate the pressure generated by the respiratory muscles to overcome auto-PEEP, the same measurement could be obtained by means of EAdi during PSV and NAVA.

Materials and Methods

- We prospectively enrolled 10 intubated patients undergoing PSV, with a clinical suspicion of auto-PEEP.

- Exclusion criteria were the presence of air leaks, hemodynamic instability requiring vasoactive drugs, Richmond Agitation Sedation Score greater than 1, and contraindication to nasogastric tube replacement.

Data Acquisition

- After enrollment, a nasogastric tube equipped with NAVA electrodes (Maquet, Solna, Sweden) and an esophageal balloon (Cooper Surgical, Trumbull, CT) were positioned.

- This first personal computer by means of dedicated software (Labview; National Instruments, Austin, TX) acquired waveforms of airway pressure, airflow and EAdi and returned them as analog outputs by a digital-toanalog converter (DAQcard; National Instruments, Houston, TX) to a second personal computer.

Study Protocol

- Patients remained in PSV, PEEPe was progressively increased, in steps of 2 cm H_2O, from 2 to 14 cmH_2O. Each level was maintained for 3 min. PEEP was then set back to the baseline clinical level for 3 min; patients were switched to NAVA with a level aiming at similar peak pressures as those observed in PSV at baseline PEEPe. The PEEP trial was then repeated with the same levels previously indicated.

Data Analysis

- At first, we computed the elastance of the chest wall as the difference between end-inspiratory and end-expiratory Pes divided by tidal volume, during a short phase of controlled ventilation.
- Muscle pressure (Pmusc) was then calculated as the difference between Pes (filtered to damp the heart artifacts) and the chest wall elastic recoil curve (equal to the instant-by-instant product of the volume above end-expiration by chest wall elastance).

- For each of the seven PEEP levels applied both during PSV and NAVA, we analyzed 20 tidal volumes avoiding waveform sections of poor signal quality.

- In each patient, we also measured the Pmusc/EAdi index as the ratio between airway pressure decrease and the corresponding EAdi value during one end-expiratory occlusion.
- For each tidal volume, we defined the following variables: Apparent auto-PEEP; auto-Eadi; auto-$PEEP_{EAdi}$; ID_{EAdi}; $EAdi_{peak}$

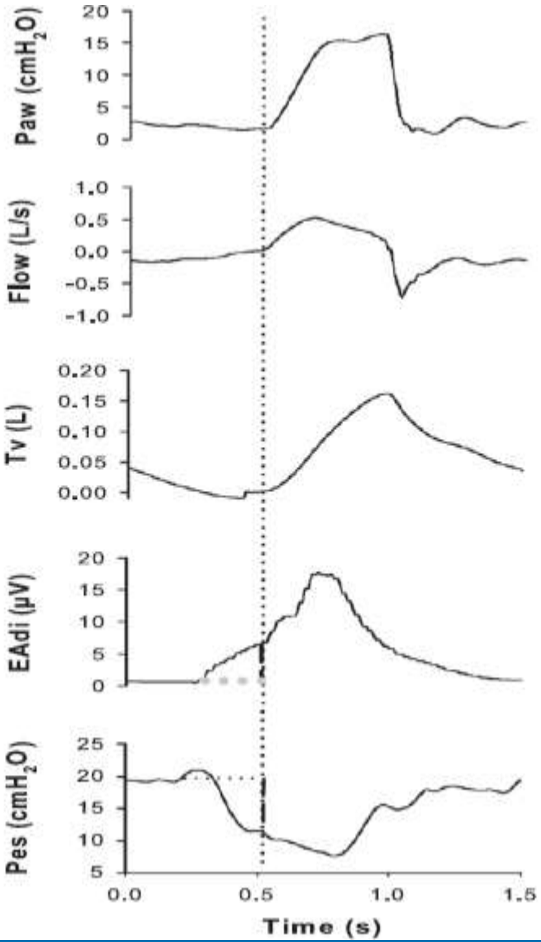

Fig. 1. Example of airway pressure (Paw), airflow (flow), volume (Tv), electrical activity of the diaphragm (EAdi), and esophageal pressure (Pes) recorded during pressure support ventilation. Auto-positive end-expiratory pressure was defined as the deflection of esophageal pressure at the time of the flow onset (*vertical dashed line* on the Pes tracing) from the Pes baseline (*horizontal dotted line* on the Pes tracing, corresponding to approximately 8 cm H_2O in this example). In analogy, intrinsic EAdi (auto-EAdi) was defined as the value of EAdi at the onset of the inspiratory airflow (*vertical dashed line* on the EAdi tracing corresponding to approximately 7 μV in this example). Inspiratory delay was defined as the temporal delay between the onset of EAdi activity and the onset of inspiratory flow (*horizontal dotted line* on the EAdi tracing corresponding to approximately 200 ms in this example).

- auto-$PEEP_{EAdi}$: EAdi-based calculation of auto-PEEP, as the product of auto-EAdi × Pmusc/EAdi index/1.5.The 1.5 correction was introduced to account for the fact that during tidal ventilation, the “dynamic Pmusc/EAdi index” is about 1.5-fold smaller than the “occlusion Pmusc/EAdi index,” measured during one end-expiratory hold.

Statistical Analysis

- A two-way ANOVA: ventilatory mode and PEEPe.
- The 2 of 133 (1.5%) missing values were imputed to perform the ANOVA by the SPSS expectation-maximization algorithm (SPSS 19.0; IBM, Chicago, IL), using the PEEP variable as predictor.
- Bland–Altman analysis was used to compare the agreement between apparent auto-PEEP and auto-PEEPEAdi, taking into account that each subject contributes with multiple values.
- Correlation between variables was assessed by linear regression.

Results

Table 1. Clinical Data of the Patient Population

Age	74 (75–78)
SAPS II	47 ± 14
Male, n (%)	4 (40%)
Previous pulmonary conditions, n (%)	
COPD	5 (50%)
Active smoke	2 (20%)
Silicosis	1 (20%)
None	2 (20%)
ICU admission diagnosis, n (%)	
COPD exacerbation	4 (40%)
Sepsis	3 (30%)
Postoperative	2 (20%)
Trauma	1 (10%)
ICU survivors, n (%)	8 (80%)
Pa_{O_2}/F_{IO_2} ratio (mmHg)	222 ± 62
Pa_{CO_2} (mmHg)	52.5 ± 14.8
Clinical PEEPe (cm H_2O)	9 ± 3
Clinical pressure support (cm H_2O)	4 (6–12)
Days of intubation	4 (6–8)
Respiratory system compliance (ml/cm H_2O)	43 ± 15
Respiratory system resistance (cm H_2O l^{-1} s^{-1})	17 ± 4
Respiratory system time constant (s)	0.71 ± 0.30

Data are represented as median (range interquartile) or mean ± SD.

COPD = chronic obstructive pulmonary disease; ICU = intensive care unit; PEEPe = extrinsic positive end-expiratory pressure; SAPS = Simplified Acute Physiology Score.

Effects of Ventilatory Mode and PEEPe on Apparent Auto-PEEP

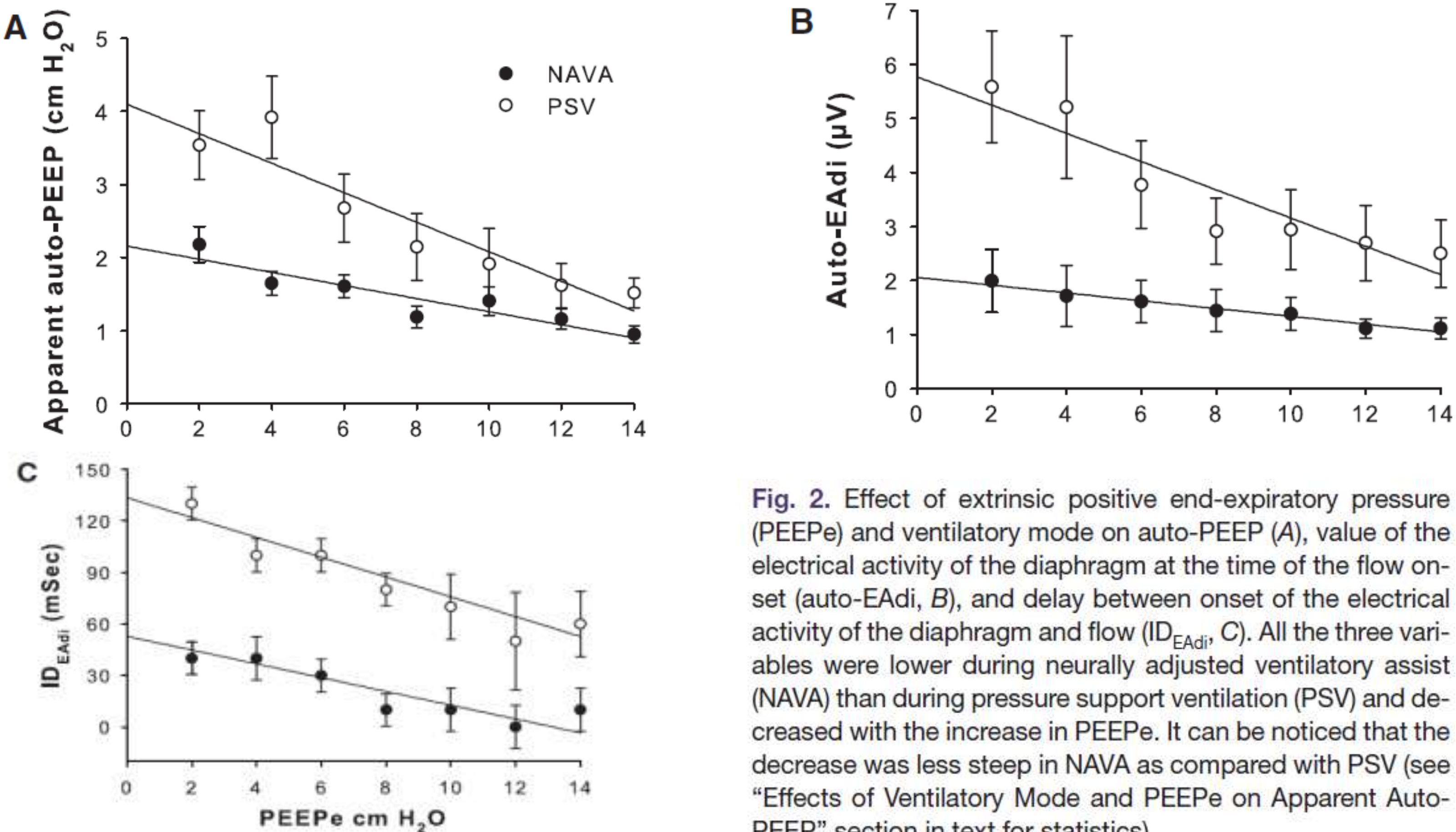

Fig. 2. Effect of extrinsic positive end-expiratory pressure (PEEPe) and ventilatory mode on auto-PEEP (*A*), value of the electrical activity of the diaphragm at the time of the flow onset (auto-EAdi, *B*), and delay between onset of the electrical activity of the diaphragm and flow (ID_{EAdi}, *C*). All the three variables were lower during neurally adjusted ventilatory assist (NAVA) than during pressure support ventilation (PSV) and decreased with the increase in PEEPe. It can be noticed that the decrease was less steep in NAVA as compared with PSV (see "Effects of Ventilatory Mode and PEEPe on Apparent Auto-PEEP" section in text for statistics).

Table 2. Main Ventilatory Variables during the Study

		PEEPe (cm H_2O)							ANOVA *P* Values		
		2	4	6	8	10	12	14	PEEPe	Mode	Interaction
Vt (ml)	NAVA	0.40±0.17	0.40±0.15	0.42±0.15	0.39±0.18	0.43±0.17	0.45±0.18	0.42±0.16	<0.001	0.464	0.920
	PSV	0.36±0.17	0.35±0.18	0.39±0.17	0.41±0.17	0.42±0.16	0.41±0.15	0.40±0.15			
Peak EAdi (μV)	NAVA	16.7±9.1	14.3±8.5	14.1±7.3	12.8±6.5	13.4±6.3	11.8±5.3	12.1±5.3	<0.001	0.194	0.048
	PSV	20.9±12.1	22.4±13.1	18.7±11.9	15.2±9.6	16.6±9.5	12.7±6.1	13.8±7.3			
Peak Pmusc (cm H_2O)	NAVA	10.0±3.9	8.1±3.8	7.7±3.5	6.8±3.4	6.7±3.6	6.2±3.8	4.6±1.9	<0.001	0.279	0.002
	PSV	10.4±3.2	11.9±4.7	9.9±4.9	8.0±3.6	7.4±3.1	6.2±2.7	6.2±2.6			
Baseline EAdi (μV)	NAVA	0.48±0.21	0.45±0.15	0.48±0.21	0.43±0.10	0.47±0.13	0.47±0.19	0.44±0.15	0.028	0.156	0.04
	PSV	0.82±0.54	0.89±0.83	0.74±0.59	0.5±0.19	0.56±0.32	0.46±0.25	0.47±0.24			
P0.1 (cm H_2O)	NAVA	3.5±1.7	2.7±0.9	2.8±1.2	2.4±0.5	2.3±0.6	2.0±0.9	2.0±1.1	<0.001	0.619	0.442
	PSV	3.6±1.7	3.1±1.8	2.7±1.2	1.8±0.8	2.1±1.0	2.1±1.2	1.9±1.5			
Driving Pr. (cm H_2O)	NAVA	12.0±5.3	10.7±5.8	10.0±5.1	9.3±4.7	9.8±5.3	9.1±5.9	9.2±4.9	0.103	0.014	0.03
	PSV	7.1±4.2	7.2±4.6	7.3±4.5	7.3±4.4	7.2±4.4	7.2±4.6	7.4±4.5			

Data are expressed as mean ± SD.

Driving pr = diving pressure (difference between PEEPe and peak inspiratory airway pressure); EAdi = electrical activity of the diaphragm; NAVA = neurally adjusted ventilatory assist; PEEPe = estrinsic positive end-expiratory pressure; Pmusc = muscle pressure; PSV = pressure support ventilation; Vt = tidal volume.

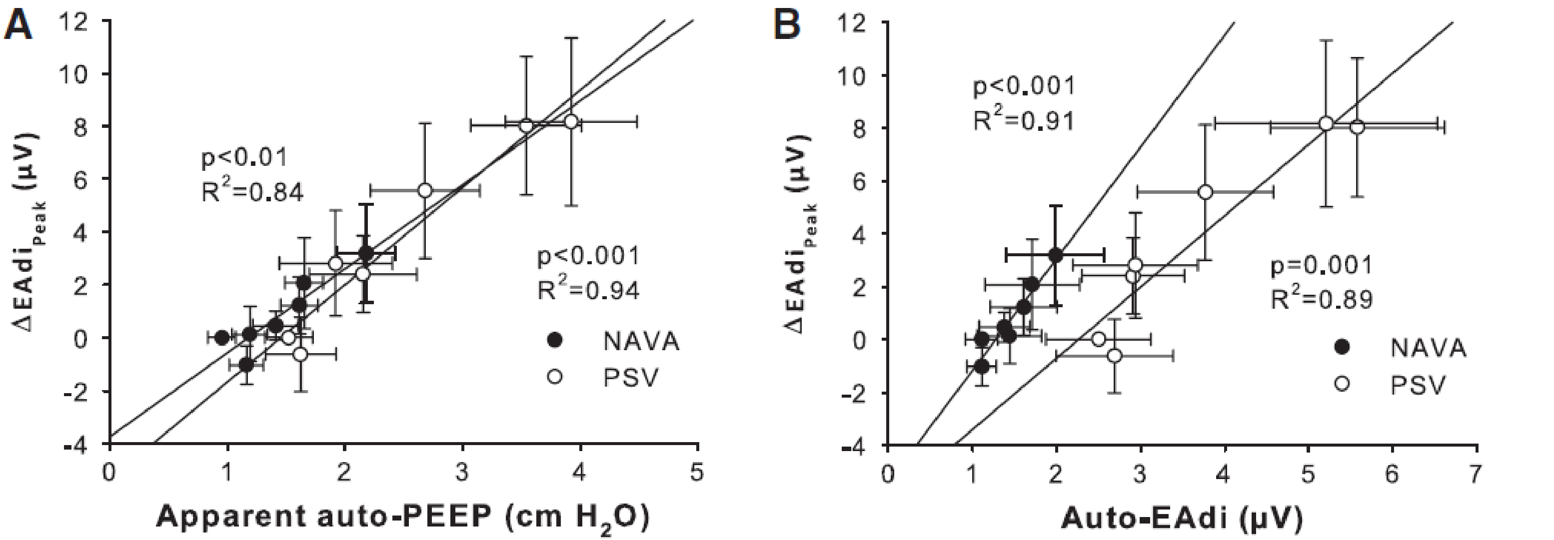

Fig. 3. The graphs show the correlation between the change in peak electrical activity of the diaphragm (EAdi) for each positive end-expiratory pressure (PEEP) level in comparison with 14 cm H_2O ($\Delta EAdi_{peak}$) and the respective changes in auto-PEEP (*A*) and in auto-EAdi (*B*). The highly significant correlation suggests that the observed decrease of peak EAdi was largely explained by the decrease of auto-PEEP (and thus of auto-EAdi), offered by the counterbalance of PEEPe. NAVA = neurally adjusted ventilatory assist; PSV = pressure support ventilation.

Table 3. Inspiratory and Expiratory Times

		PEEPe (cm H_2O)							ANOVA *P* Values		
		2	4	6	8	10	12	14	PEEPe	Mode	Interaction
RR (1/min)	NAVA	27±12	26±11	25±11	25±11	25±11	23±10	23±10	<0.001	0.609	0.263
	PSV	26±12	27±12	25±10	23±10	23±10	22±9	22±8			
Ti (s)	NAVA	0.82±0.32	0.83±0.30	0.86±0.32	0.84±0.30	0.87±0.30	0.87±0.28	0.88±0.26	0.006	0.656	0.065
	PSV	0.76±0.28	0.79±0.30	0.81±0.27	0.84±0.22	0.92±0.29	0.87±0.20	0.86±0.19			
Te (s)	NAVA	1.89±1.13	2.02±1.37	2.17±1.56	2.11±1.31	2.16±1.58	2.23±1.30	2.29±1.34	0.299	0.249	0.474
	PSV	2.27±1.98	2.09±1.66	1.97±1.01	2.26±1.37	2.10±1.13	2.25±1.18	2.29±1.22			

Data are expressed as mean ± SD.

NAVA = neurally adjusted ventilatory assist; PEEPe = estrinsic positive end-expiratory pressure; PSV = pressure support ventilation; RR = respiratory rate; Te = expiratory times; Ti = inspiratory times.

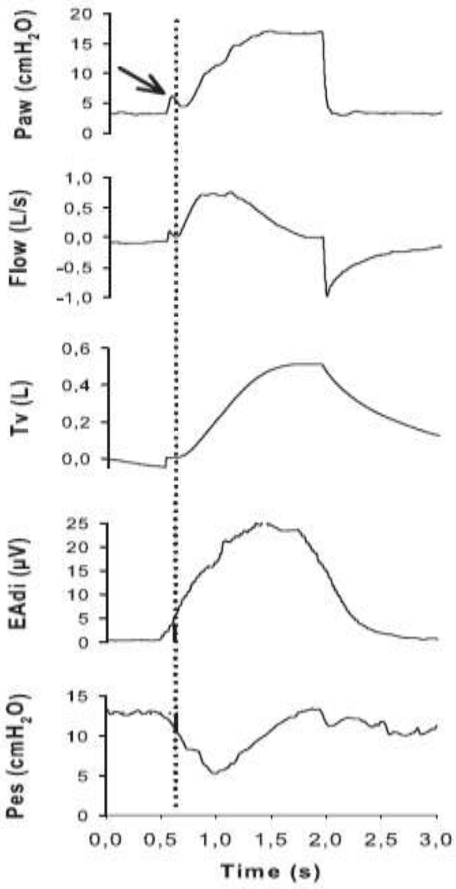

Fig. 4. Typical shape of the airway pressure (Paw) trace during neurally adjusted ventilatory assist (NAVA) in the presence relevant of auto-positive end-expiratory pressure (PEEP): when the triggering threshold is reached on the electrical diaphragm activity (EAdi), the ventilator closes the expiratory valve, causing, in the presence of auto-PEEP, an abrupt raise in Paw (*black arrow*). If the raise in Paw numerically exceeds the product of EAdi by NAVA level (*i.e.*, the level of assistance set on the ventilator during NAVA), the ventilator will deliver only a minimal flow (or none), resulting in a transient decrease of Paw; later, the increase of EAdi (and consequently of the EAdi by NAVA-level product) will cause a "normal" NAVA airway pressure inspiratory profile. Pes = esophageal pressure; Tv = Tidal volume.

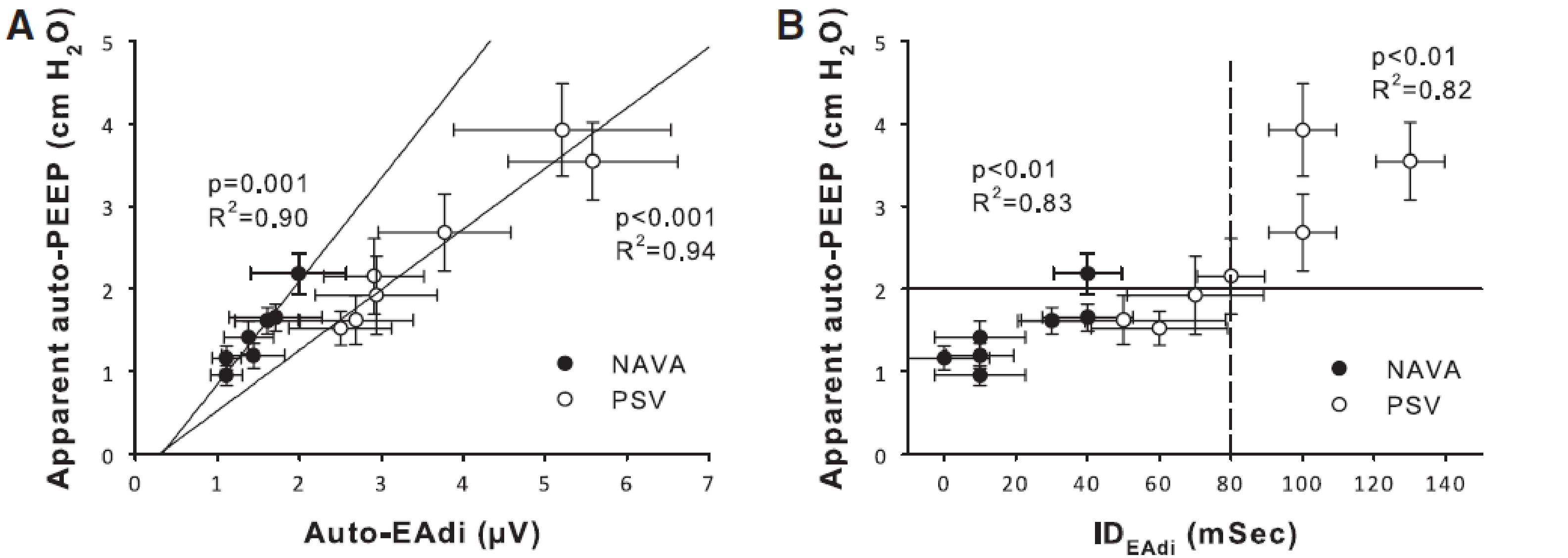

Fig. 5. The graphs show the tight correlation existing between auto-positive end-expiratory pressure (auto-PEEP) and value of the electrical activity of the diaphragm at the time of the flow onset (auto-EAdi) (*A*) and between auto-PEEP and inspiratory delay measured by electrical activity of the diaphragm at the time of the flow onset (ID_{EAdi}, *B*). Each *point* represents the average of the values measured at one level of PEEPe in neurally adjusted ventilatory assist (NAVA, *filled symbols*) and in pressure support ventilation (PSV, *empty symbols*). In respect to *B*, it can be noticed that both in PSV and NAVA an ID_{EAdi} lower than 80 ms is usually associated with an auto-PEEP below 2 cm H_2O.

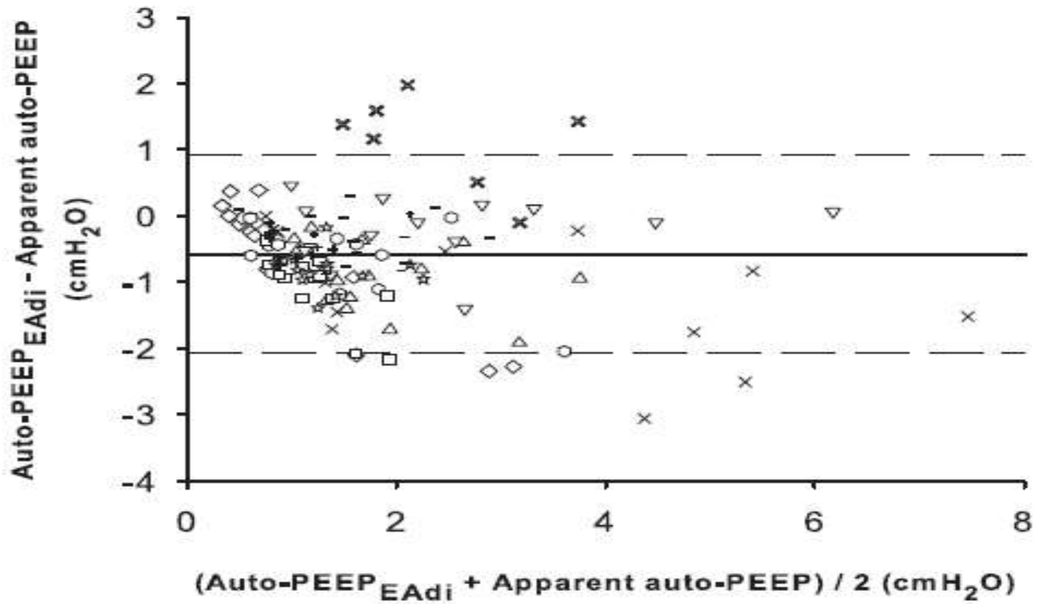

Fig. 6. Bland and Altman plot for the comparison between auto-positive end-expiratory pressure (auto-PEEP) measured by the esophageal pressure and by the diaphragmatic electromyogram (auto-PEEP$_{EAdi}$), by converting the electrical activity of the diaphragm at the time of the flow onset (auto-EAdi) to cm H_2O (95% CI between +0.99 and –2.1 cm H_2O). Each patient is indicated in the plot with a different symbol.

Discussion

- The main findings of this article can be summarized as follows:

  ①in a cohort of patients with a clinical suspicion of gas trapping, the EAdi signal provides a promising tool for monitoring the presence of auto-PEEP and the effects of the application of an PEEPe, which appears comparable to Pes.

  ②During NAVA, the effort necessary to overcome auto-PEEP was lower than during PSV, and it was less affected by the decrease of PEEPe .

- As stated, at variance from PSV, in NAVA the presence of the neural trigger prevents the need to fully counterbalance the auto-PEEP before activating the ventilator. For this reason, we used the term “apparent auto-PEEP,” indicating that in NAVA this value indicates the effort spent before activation of the ventilator , but not necessarily the end-expiratory alveolar pressure above PEEPe.

- we reasoned that, in analogy with the Pes-based measurement of dynamic auto-PEEP, the Eadi level at the onset of inspiratory flow may be proportional to dynamic auto-PEEP (for this reason we termed it “auto-EAdi”). We thus tested this hypothesis, showing proportionality between dynamic auto-PEEP and both auto-EAdi and ID_{EAdi}; this relationship was present in all patients individually and, more strongly, at the level of the entire population.

- Moreover, the variations of auto-EAdi and ID_{EAdi} at different PEEPe levels mirrored that of auto-PEEP, suggesting that auto-EAdi and ID_{EAdi} could be simply and readily used at the bedside to titrate PEEPe and to assess the effect of different therapeutic strategies.

- Our study has some limitations. Due to the rather complex experimental setup, we measured esophageal but not abdominal pressure. This limitation did not allow us to differentiate the presence of auto-PEEP from potenti
- Another limitation of the study is the relatively small sample size which is not uncommon in such studies focused on physiological variables. Moreover, we did not randomize the order of PEEPe application, but we used a stepwise increase of PEEPe like other authors did.

- In our patients, the inspiratory pressure swings in NAVA were higher in comparison with PSV. Despite our attempt of matching the level of assistance of the two ventilation modalities at the beginning of the study, the decrease in PEEPe led to an increased EAdi (increased patient’s effort), leading, in turn, to an increased airway pressure swing in NAVA.
- We might have changed the NAVA gain to obtain the same airway pressure swing at each PEEPe level but: (1) we would have introduced a confounder and (2) it was likely that the patients’ EAdi would have further increased, leading to aconsequent further airway pressure change.

- To our knowledge, this is one the first reports directly comparing NAVA and PSV in a cohort of patients with a clinically relevant auto-PEEP.
- Whether and by which mechanism NAVA also decreases gas trapping as compared with PSV should be addressed in a different study. NAVA however did not abolish entirely auto-PEEP (and auto-EAdi), and some effect of PEEPe was still evident.

- In conclusion, in a population of patients with auto-PEEP undergoing assisted ventilation, NAVA, compared with PSV, led to a decrease (but not to an abolishment) of the pressure necessary to overcome auto-PEEP, independent of the level of PEEPe. The electrical activity of the diaphragm (auto-EAdi) before the onset of the inspiratory flow provides a simple and reliable tool for continuously monitoring the presence of dynamic intrinsic PEEP at bedside.


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