# Impact of the Anesthetic Conserving Device on Respiratory Parameters and Work of Breathing in Critically Ill Patients under Light Sedation with Sevoflurane

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## ABSTRACT

**Background:** Sevoflurane sedation in the intensive care unit is possible with a special heat and moisture exchanger called the Anesthetic Conserving Device (ACD) (AnaConDa®; Sedana Medical AB, Uppsala, Sweden). The ACD, however, may corrupt ventilatory mechanics when used during the weaning process of intensive care unit patients. The authors compared the ventilatory effects of light-sedation with sevoflurane administered with the ACD and those of classic management, consisting of a heated humidifier and intravenous sedation, in intensive care unit patients receiving pressure-support ventilation.

**Methods:** Fifteen intensive care unit patients without chronic pulmonary disease were included. A target Richmond Agitation Sedation Scale level of −1/−2 was obtained with intravenous remifentanil (baseline 1-condition). Two successive interventions were tested: replacement of the heated humidifier by the ACD without sedation change (ACD-condition) and sevoflurane with the ACD with an identical target level (ACD-sevoflurane-condition). Patients finally returned to baseline (baseline 2-condition). Work of breathing, ventilatory patterns, blood gases, and tolerance were recorded. A steady state of 30 min was achieved for each experimental condition.

**Results:** ACD alone worsened ventilatory parameters, with significant increases in work of breathing (from 1.7 ± 1.1 to 2.3 ± 1.2 J/l), minute ventilation, $P_{0,1}$, intrinsic positive end-expiratory pressure (from 1.3 ± 2.6 to 4.7 ± 4.2 cm $H_2O$), inspiratory pressure swings, and decreased patient comfort. Sevoflurane normalized work of breathing (from 2.3 ± 1.2 to 1.8 ± 1 J/l), intrinsic positive end-expiratory pressure (from 4.7 ± 4.2 to 1.8 ± 2 cm $H_2O$), inspiratory pressure swings, other ventilatory parameters, and patient tolerance.

**Conclusions:** ACD increases work of breathing and worsens ventilatory parameters. Sevoflurane use *via* the ACD (for a light-sedation target) normalizes respiratory parameters. In this patient's population, light-sedation with sevoflurane and the ACD may be possible during the weaning process. **(Anesthesiology 2014; 121:808-16)**

SEDATION is of particular concern in the management of intensive care unit (ICU) patients under mechanical ventilation.[1,2] Sedation overuse has been shown to prolong mechanical ventilation and length of ICU stay.[3] Protocols including daily sedation withdrawal and ventilator weaning tests reduced 1-yr mortality rates.[4] Some patients, however, require deep sedation for short periods of time, but these levels may be difficult to achieve with standard hypnotics.[5] These limitations may be overcome by continuous use of short-acting sedative agents.[6–8] Sevoflurane is an inhalational, short-acting, volatile anesthetic[9,10] that can be administered in the ICU *via* a specific heat and moisture exchanger (HME) called the Anesthetic Conserving Device (ACD) (AnaConDa®; Sedana Medical AB, Uppsala, Sweden).[11–13] This device, which is placed between the Y piece

### What We Already Know about This Topic

- Inhalational agents are critical components of our practice of anesthesiology, but seldom used outside of the operating room despite their potential for other therapeutic applications
- Sevoflurane sedation in the intensive care unit is possible with a special heat and moisture exchanger called the Anesthetic Conserving Device (ACD) (AnaConDa®; Sedana Medical AB, Uppsala, Sweden)

### What This Article Tells Us That Is New

- In intensive care unit patients, ACD increases the work of breathing and worsens ventilatory parameters
- Sevoflurane use *via* the ACD with a light-sedation target normalizes respiratory parameters and may provide an alternative method for sedation, at least, for weaning patients from mechanical ventilation

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of the ventilatory circuit and the endotracheal tube, has been shown to be safe and effective for prolonged sedation with volatile anesthetics in the ICU[14,15] and was associated with reduced wake-up and extubation times when used with sevoflurane.[13] Nevertheless, the ACD could corrupt ventilatory mechanics because of the increased dead space and airflow resistance generated by the system. Furthermore, the use of an ACD increases apparent dead space to a greater extent than can be explained by its internal volume. This is caused by adsorption of carbon dioxide in the ACD during expiration and release of carbon dioxide during inspiration.[16,17] Thus, use of sevoflurane in the ICU would not be possible if it cannot be used during the weaning process and for awake sedation. Similar to other volatile anesthetics, sevoflurane has properties such as bronchodilation that may decrease work of breathing (WOB).[18] Therefore, we hypothesized that sevoflurane could attenuate the adverse effects of ACD on WOB in pressure support ventilation (PSV). To test this hypothesis, we compared the ventilatory effects of sevoflurane administered with the ACD with those of classic management with a heated humidifier (HH) and intravenous sedation in consecutive ICU patients receiving PSV.

## Materials and Methods

This prospective, nonrandomized, controlled trial was conducted in the 16-bed medical-surgical ICU at Clermont-Ferrand University Hospital (France). The protocol was approved by the Institutional Review Board (Comité de Protection des Personnes Sud-Est I, Saint-Etienne, France, No. 2009–20), and written informed consent was obtained from the patients or their nearest relatives (Trial registration: EudraCT number: 2009-013687-39; ClinicalTrials.gov Identifier: NCT 01017744).

### Study Population

Adult patients were included if they were recovering from an acute state that justified mechanical ventilation, in PSV under light sedation with intravenous remifentanil (Richmond Agitation Sedation Scale objective −1 or −2). Exclusion criteria were a history of chronic pulmonary disease, persistent respiratory failure, hypoxemia requiring an inspired oxygen fraction more than 0.5, sequential organ failure assessment score more than 8, pathologic condition of the esophagus, pregnancy, intracranial disease, or familial or personal history of malignant hyperthermia.

### Study Protocol

The study protocol is presented in figure 1. An esophageal balloon catheter (Smartcath; Bicore Monitoring Systems, Irvine, CA) was inserted through the nose to monitor esophageal pressure ($P_{es}$), with its correct position verified by the occlusion method.[19] Patients were placed in a semirecumbent position, and the protocol was initiated after tracheal suctioning. All patients were ventilated with an Avea ventilator (Viasys Healthcare-Critical Care Group, Palm Springs, CA), which allowed a continuous monitoring of the patient total WOB as described in the Measurements section.[20] A pneumotachograph connected to a pressure transducer (Bicore) was inserted between the endotracheal tube and the Y piece of the ventilatory circuit. The flow signal was integrated to yield tidal volume (Vte). A line was placed at the Y piece of the ventilatory circuit connected to an infrared gas analyzer (Vamos monitor; Dräger Medical, Lübeck, Germany) to monitor inspired and end-tidal sevoflurane fraction in the total gas mixture ($Fi_{sevo}$/$Fet_{sevo}$). Ventilatory parameters in PSV were set by the clinician in charge of the patient, according to our institute practice guidelines; that is, the level of PSV was titrated to expired Vte of 6 to 8 ml/kg of ideal body weight external positive end-expiratory pressure (PEEP) from 4 to 10 cm $H_2O$, and the inspiratory trigger was set at a maximum sensitivity (0.3 l/min); expiratory cycling was set at 25% of peak inspiratory flow rate; and inspired oxygen fraction was adjusted to maintain $Spo_2$ greater than 0.9. A HH (MR 850®; Fisher & Paykel Healthcare, Panmure, New Zealand) was placed on the inspiratory limb. Heart rate, arterial blood pressure, and pulse oxymetry were continuously monitored.

After an initial 30-min period in this condition (baseline 1 condition), an ACD was placed between the endotracheal tube and the Y piece of the respiratory circuit. The HH was withdrawn and sedation with intravenous remifentanil was maintained for 30 min (ACD condition). Sevoflurane infusion through the ACD was then started while remifentanil was decreased to an arbitrary rate of 0.025 $\mu g\ kg^{-1}\ min^{-1}$. The sevoflurane infusion rate was progressively increased to achieve a stable target sedation level (Richmond Agitation Sedation Scale −1 or −2), after which the patient was ventilated for 30 min under sevoflurane sedation (ACD-SEVO condition). The patient then returned to the original condition for 30 min. After complete removal of sevoflurane from the gas mixture, as assessed by a $Fet_{sevo} = 0$ for at least 15 min, the patient was returned to the original baseline condition (baseline 2 condition). Ventilator settings were unchanged during the four conditions, especially pressure support level. The dead space from the end of the endotracheal tube to the Y piece of the ventilator under baseline 1 and 2 conditions was 40 ml, equivalent to the volume of the flexible tube with an angular joint, whereas the dead space with the ACD under ACD and ACD-SEVO conditions was 140 ml (data given by the manufacturers).

### Measurements

Data were recorded during the last 5 min of each of the four conditions. For each respiratory cycle, ventilatory parameters were integrated by the ventilator software (Bicore®) to calculate the total WOB, using an automatic Campbell Diagram resulting from a classical analysis of $P_{es}$–Vt tracing.[21,22] Briefly, WOB was determined as the area enclosed between the inspiratory $P_{es}$–Vt curve and the static esophageal chest wall pressure–volume curve, using a theoretical chest wall

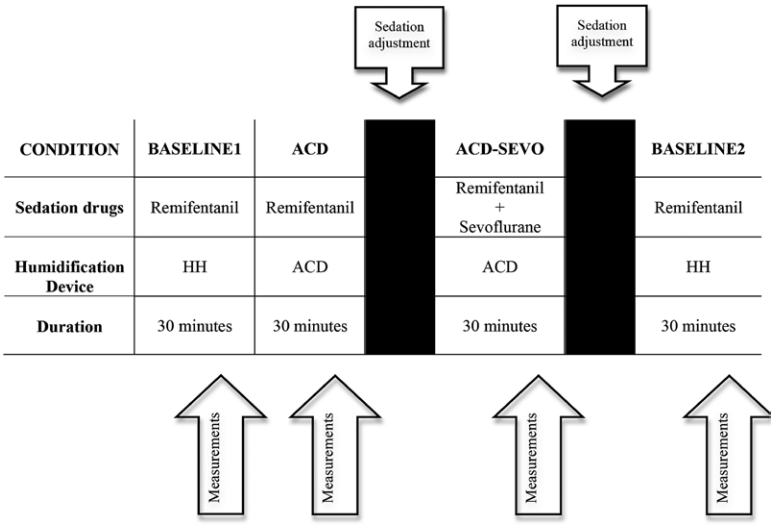


**Fig. 1.** Design of the study. ACD = Anesthetic Conserving Device (AnaConDa®; Sedana Medical AB, Uppsala, Sweden); HH = heated humidifier; SEVO = sevoflurane.

compliance of 200 ml/cm $H_2O$ for all patients.[20,23,24] Airway occlusion pressure at 0.1 s (P0.1), an index of respiratory drive corresponding to the pressure generated at the airway opening in the 100 ms of an occluded inspiration,[25] was estimated from the Paw tracing during the effort to trigger the ventilator. Esophageal pressure variation ($dP_{es}$) and peak inspiratory ($V'_{insp}$) and expiratory ($V'_{exp}$) flows were measured. Classical ventilatory parameters were also determined, including tidal volume (Vte), minute ventilation (Ve), respiratory rate, inspiratory time (Ti), expiratory time (Te), and airway pressure at the Y piece (Paw). All signals were digitalized at a sampling rate of 110 Hz (Polybench Data® software; Applied Biosignals, Weener, Germany) and stored in a laptop computer for subsequent analysis. For each of the conditions, Paw, $P_{es}$, and flow signal recordings were visually inspected to determine major patient-ventilator asynchronies (*e.g.*, ineffective triggering, double triggering, autotriggering, premature cycling, and delayed cycling), as described.[26,27] A severe asynchrony was defined as an asynchrony rate more than 10%. Manual offline analysis of 10 breaths during each of the conditions, while stable, was used to determine intrinsic positive end-expiratory pressure (PEEPi), defined as the difference in $P_{es}$ between the onset of inspiratory effort and the point at which instantaneous expiratory flow reached 0. An arterial blood sample was taken during the last 5 min of each condition and analyzed. Analgesia and sedation levels were evaluated using the behavioral pain scale[28] and Richmond Agitation Sedation Scale,[29,30] respectively.

### Statistical Analysis

Data are reported as means ± SDs. Continuous outcomes with repeated measures, such as WOB, were compared using repeated-measures two-way ANOVA followed by the Tukey–Kramer test for multiple comparisons (or the equivalent Friedman test). Multivariate analysis using mixed models was performed to assess changes in different parameters over time. In these models with random subject effects (random intercept and slope), parameters were estimated by restricted maximum likelihood. Interactions were tested and all models were checked for residual normality. Because of atypical kinetics concerning longitudinal data, sensitivity analysis was considered (data not shown). Remifentanil doses were compared using a nonparametric Wilcoxon test. All statistical analyses were performed using Stata V12 (StataCorp., College Station, TX), with significance (type I error) set at 0.05.

## Results

Fifteen consecutive patients were included; their demographic and clinical characteristics are summarized in table 1. Mean duration of mechanical ventilation at inclusion was 6 ± 3 days and mean PSV level was 10 ± 2 cm $H_2O$. Two morbidly obese patients (patients 2 and 6) were included. Ventilatory parameters for each condition are presented in table 2. No parameter differed significantly between baseline 1 and baseline 2 conditions. Minute ventilation with the ACD was 15% higher than with baseline 1 and baseline 2 due to an increase in Vte. Vte was also increased from 15% with ACD-SEVO, but Vm was not, due to a slight decrease in respiratory rate with sevoflurane. Relative to the baseline conditions, PEEPi and P0.1 were dramatically increased with the ACD (+ 260% and + 55%, respectively, $P < 0.05$) but not when sevoflurane was added (ACD-SEVO condition). WOB was increased by 35% ($P < 0.05$) with the device (ACD condition), but was reduced to baseline conditions with sevoflurane (ACD-SEVO condition) (fig. 2). Similar changes were observed in the magnitude of inspiratory effort, as characterized by $P_{es}$ swings. The ACD, with and without sevoflurane, decreased arterial pH by increasing $Paco_2$, +23% alone and +17% with sevoflurane (table 3). There were no effects on oxygenation parameters.

**Table 1.** Patients' Characteristics at Inclusion

| Patient No. | Sex | Age (yr) | SAPSII | BMI ($kg/m^2$) | Diagnosis | SOFA | PEEPe ($cm H_2O$) | Remifentanil Infusion Rate ($\mu g \cdot kg^{-1} \cdot min^{-1}$) | P/F | PS ($cm H_2O$) |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | M | 71 | 79 | 28 | Septic shock | 3 | 10 | 0.11 | 273 | 8 |
| 2 | F | 66 | 68 | 46 | Septic shock | 3 | 5 | 0.08 | 215 | 12 |
| 3 | M | 54 | 42 | 27 | Pneumonia | 3 | 10 | 0.10 | 246 | 16 |
| 4 | M | 68 | 36 | 25 | Septic shock | 3 | 10 | 0.15 | 298 | 8 |
| 5 | M | 45 | 33 | 19 | Septic shock | 3 | 6 | 0.13 | 276 | 8 |
| 6 | M | 70 | 39 | 42 | Pneumonia | 3 | 8 | 0.17 | 293 | 12 |
| 7 | M | 36 | 62 | 28 | Electrocution | 2 | 8 | 0.13 | 271 | 8 |
| 8 | M | 42 | 35 | 22 | Dental cellulitis | 2 | 5 | 0.08 | 380 | 7 |
| 9 | F | 45 | 59 | 21 | Pneumonia | 3 | 6 | 0.08 | 320 | 10 |
| 10 | F | 73 | 55 | 28 | Pneumonia | 2 | 5 | 0.04 | 389 | 12 |
| 11 | F | 68 | 74 | 19 | Septic shock | 3 | 5 | 0.03 | 278 | 8 |
| 12 | M | 55 | 73 | 25 | Septic shock | 3 | 5 | 0.13 | 301 | 10 |
| 13 | F | 74 | 66 | 34 | Peritonitis | 1 | 5 | 0.08 | 406 | 8 |
| 14 | M | 64 | 43 | 29 | Polytrauma | 3 | 5 | 0.17 | 273 | 8 |
| 15 | F | 47 | 30 | 19 | Peritonitis | 2 | 6 | 0.25 | 340 | 12 |
| Mean ± SD | | 58±13 | 53±17 | 27±8 | | 2.6±0.6 | 6.6±2 | 0.11±0.06 | 304±54 | 9.8±2.5 |

BMI = body mass index; PEEPe = external positive end-expiratory pressure; P/F ratio = partial oxygen pressure in arterial blood divided by inspired oxygen fraction; PS = pressure support level; SAPSII = Simplified Acute Physiologic Score on admission; SOFA = Sepsis-related Organ Failure Assessment score on day of inclusion.

**Table 2.** Patients' Respiratory Parameters during Each Study Period

| | Baseline 1 | ACD | ACD-SEVO | Baseline 2 |
|---|---|---|---|---|
| WOB (J/l)* | 1.7±1.1 | 2.3±1.2† | 1.8±1.0 | 1.6±0.9 |
| RR (breaths/min)* | 24.4±7.7 | 25.4±6.9 | 23.0±5.8‡ | 24.3±6.4 |
| $Vt_e$ (ml)* | 477±153 | 541±153§ | 535±163§ | 445±134 |
| $Vt_e$/kg (ml/kg)* | 6.6±2.2 | 7.5±2.3§ | 7.6±2.5§ | 6.4±1.8 |
| Vm (l)* | 11.9±4.1 | 13.1±3.5§ | 12.2±2.9 | 11.6±3.8 |
| Ti (s)* | 0.9±0.3 | 0.9±0.4 | 1.0±0.5‡ | 0.8±0.2 |
| Te (s) | 1.9±1.4 | 1.9±1.2 | 1.9±1.2 | 1.8±1.3 |
| P0.1 ($cm H_2O$)* | –6.2±3.9 | –9.7±4.1† | –6.7±3.3 | –5.8±4.3 |
| dPes ($cm H_2O$)* | 29.8±16.4 | 35.8±14† | 31.3±16.3 | 29.5±13.1 |
| $V'_{insp}$ (l/min)* | 54.7±17.9 | 58.1±14.4†é | 50.1±14.5 | 50.1±14.7 |
| $V'_{exp}$ (l/min) | 29.8±11.4 | 29.2±7.0 | 28.7±8.7 | 27.9±6.9 |
| PEEPi ($cm H_2O$)* | 1.3±2.6 | 4.7±4.2† | 1.8±2.0 | 1.5±2.8 |

Values are presented as mean ± SD.

* Repeated-measures ANOVA $P < 0.05$. † $P < 0.05$ *vs.* baseline 1. ACD-SEVO and baseline 2. ‡ $P < 0.05$ *vs.* Baseline 1. ACD and baseline 2. § $P < 0.05$ *vs.* baseline 1 and baseline 2.

ACD = Anesthetic Conserving Device (AnaConDa®; Sedana Medical AB, Uppsala, Sweden); $dP_{es}$ = esophageal pressure variation; P0.1 = occlusion pressure; PEEPi = intrinsic positive end-expiratory pressure; RR = respiratory rate; SEVO = sevoflurane; Te = expiratory time; Ti = inspiratory time; $V'_{exp}$ = peak expiratory flow; $V'_{insp}$ = peak inspiratory flow; Vm = minute ventilation; Vte = tidal volume; Vte/kg = tidal volume divided by ideal body weight; WOB = work of breathing.

When we assessed hemodynamics, we found that mean arterial pressure was higher with the ACD than under all other conditions. Patient comfort was altered by the ACD alone. With a stable remifentanil infusion dose, behavioral pain scale score significantly increased compared with baseline conditions from 3 to more than 5. Target Richmond Agitation Sedation Scale scores were maintained under all conditions. As expected, remifentanil infusion rate decreased during the ACD-SEVO condition, from 0.16 $\mu g\ kg^{-1}\ min^{-1}$ to $0.025 \pm 0.03\ \mu g\ kg^{-1}\ min^{-1}$. Mean $Fet_{sevo}$ to reach the desired sedation level during ACD-SEVO was 0.5±0.1%. None of the patients showed any severe asynchrony under any of the conditions tested.

## Discussion

Our study demonstrated that ACD increases WOB. At low dose, sevoflurane relieves this increased work. Because of this matter of fact, in general ICU patients, light sedation with sevoflurane through the ACD is possible in PSV. Thus, sevoflurane sedation may allow the transition from deep sedation with full ventilatory support to spontaneous breathing.

Total WOB can be divided into four steps: overcoming inspiratory resistance, overcoming the elastic recoil pressure of the lungs and chest wall, overcoming PEEPi to generate a gas flow to the distal airways, and a final, normally insignificant step linked to the contraction of expiratory muscles, since expiration is a physiologically passive process.

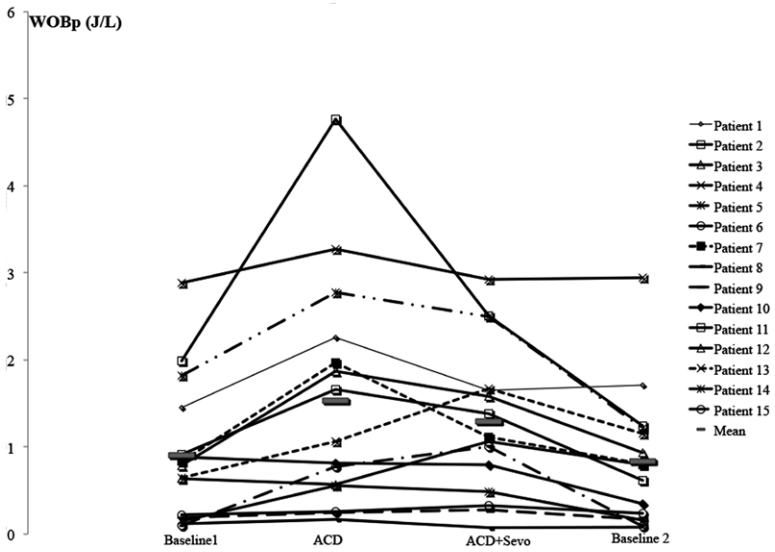


**Fig. 2.** Individual representations of work of breathing (WOB) at different steps of the study. WOB was increased with the device (Anesthetic Conserving Device [ACD] [AnaConDa®; Sedana Medical AB, Uppsala, Sweden]), but was reduced to baseline conditions with sevoflurane (ACD-SEVO). There were no difference between baseline 1 and baseline 2. Because of atypical kinetics concerning longitudinal data, sensitivity analysis was considered. Results are not different, with or without patient no. 2 and with or without patient nos. 2 and 4 (data not shown). J/L = Joule/liter; SEVO = sevoflurane; WOBp = work of breathing patient.

**Table 3.** Arterial Blood Gases, Hemodynamics, and Comportemental Scores

| | Baseline 1 | ACD | ACD-SEVO | Baseline 2 |
|---|---|---|---|---|
| pH* | 7.41 ± 0.07 | 7.34 ± 0.10† | 7.35 ± 0.10† | 7.40 ± 0.07 |
| $Paco_2$ (mmHg)* | 39 ± 10 | 48 ± 14† | 46 ± 12‡ | 42 ± 12 |
| $Pao_2$ (mmHg) | 86 ± 18 | 94 ± 26 | 93 ± 22 | 91 ± 23 |
| $Sao_2$ (%) | 95 ± 3 | 95 ± 4 | 95 ± 4 | 96 ± 3 |
| MAP (mmHg)* | 96 ± 13 | 104 ± 12§ | 96 ± 17 | 92 ± 9 |
| HR (bpm)* | 89 ± 16 | 96 ± 18 | 98 ± 18‡ | 92 ± 17 |
| RASS | −1.2 ± 0.6 | −1.1 ± 0.6 | −1.3 ± 0.4 | −1.3 ± 0.5 |
| BPS* | 3.0 ± 0.3 | 5.4 ± 0.8§ | 3.1 ± 0.3 | 3.1 ± 0.3 |
| [Remifentanil]* ($\mu g \cdot kg^{-1} \cdot min^{-1}$) | 0.11 ± 0.06 | 0.16 ± 0.03 | 0.025‖ | 0.12 ± 0.03 |

Data are presented as mean ± SD.

* Repeated-measures ANOVA $P < 0.05$. † $P < 0.05$ *vs*. baseline 1 and baseline 2. ‡ $P < 0.05$ *vs*. baseline 1. § $P < 0.05$ *vs*. baseline 1. ACD-SEVO and baseline 2. ‖$P < 0.05$ *vs*. baseline 1. ACD and baseline 2.

ACD = Anesthetic Conserving Device (AnaConDa®; Sedana Medical AB, Uppsala, Sweden); BPS = behavioral pain scale; HR = heart rate; MAP = mean arterial pressure; $Paco_2$ = arterial partial pressure of carbon dioxide; $Pao_2$ = arterial partial pressure of oxygen; RASS = Richmond agitation sedation scale; Remifentanil = remifentanil infusion dose; $Sao_2$ = oxygen saturation of arterial blood; SEVO = sevoflurane.

This expiratory component is present in cases of PEEPi and elevated expiratory resistance, especially in patients with chronic obstructive pulmonary disease, when active expiration occurs. These different components may be evaluating using a Campbell diagram, which is associated with the measure of gastric pressure, to consider possible active expiration.[31] An increase in WOB, due to increased minute ventilation to maintain alveolar ventilation, was previously demonstrated with classic HME compared with HH in patients without a pathologic pulmonary condition and in patients difficult to wean.[32,33] The additional instrumental dead space generated by placing the filter on the ventilatory circuit next to the Y piece increases anatomical dead space, requiring enhancement of minute ventilation to maintain alveolar ventilation. The dead space of classical HMEs ranges from 30 to 100 ml, whereas ACD dead space volume was measured at 100 ml. Thus, WOB increased with HME by expansion of minute ventilation (*i.e.*, increased dead space), PEEPi, and, to a lesser extent, accentuation of resistance. This phenomenon could be accentuated by an additional dead space effect demonstrated with the ACD and linked to carbon dioxide rebreathing called "apparent dead space." Indeed, in two recently published articles, Sturesson *et al.*[16,17] have shown that the introduction of an ACD without any inhaled agent was associated with a carbon dioxide–free expirate equivalent to increased airway dead space exceeding the internal volume of the device by 180 ml regardless of the carbon dioxide flux or respiratory rate. Division of WOB into its four components using the Campbell diagram was not possible in our study because

the software only calculated total WOB and gastric pressure was not monitored. Nevertheless, our study showed an increase in both PEEPi and minute ventilation associated with the ACD. Inspiratory and expiratory components of WOB seemed to be altered when compared with previous findings. Even if PEEPi levels were low under baseline conditions, since no chronic obstructive pulmonary disease patient was included in the study, they increased dramatically following use of the ACD, from a mean 1.3 ± 2.6 cm $H_2O$ to 4.7 ± 4.2 cm $H_2O$ while the patients were ventilated with external PEEP (mean 6.6 ± 2 cm $H_2O$), supporting a finding of dynamic hyperinflation.[34] However, no ineffective efforts, which occur frequently with elevated PEEPi,[35] were observed, validating our WOB results. Ineffective or wasted efforts cannot be measured using the Campbell diagram because they fail to trigger the ventilator.[36] The increase in PEEPi could be associated with an increase in minute ventilation induced by the increased dead space or "apparent dead space" of the device and/or the increased expiratory resistance caused by the ACD. However, peak expiratory flow did not differ between conditions, making the latter alternative unlikely. Although flow resistance could be generated by the HME, the resistances of classical HME and HH were identical.[37] The manufacturer of the ACD reported that its resistance was 2.5 cm $H_2O$ $L^{-1}$ $s^{-1}$, identical to that of the HME. Even if our methodological approach precludes the real evaluation of these points, it is hard to assume that sevoflurane would be able to decrease WOB without influencing respiratory resistances.

Sevoflurane sedation through the ACD normalized WOB to a level comparable to dead space-free HH (fig. 3). P0.1 is a reflection of the central ventilatory drive and correlates with WOB.[38] Similarly, P0.1 normalized with sevoflurane. Bronchodilation is induced by some volatile anesthetics, especially sevoflurane, both in animal models[18,39,40] and in humans,[41–43] although the exact pulmonary mechanism remains unclear. Sevoflurane bronchodilation may be altered during chronic inflammatory processes, such as chronic obstructive pulmonary disease [44] and asthma.[45] Some inhalational anesthetics, including sevoflurane, are used in patients with refractory status asthmaticus,[46] and these anesthetics have been associated with hypoxemia induced by ventilation-perfusion mismatch.[47] We found that oxygenation parameters were not altered by sevoflurane. WOB normalization with sevoflurane was associated with restoration of baseline PEEPi and Vm, resulting from a reduction in respiratory rate caused by an increase in Vte. Nevertheless, it was not possible to determine the impact of each component of WOB on this global effect. The inhaled bronchodilator albuterol had a beneficial effect on WOB predominantly by acting on PEEPi during weaning from mechanical ventilation.[48] Sevoflurane decreased the central ventilatory response to hypoxia and hypercarbia, even at a hypoanesthetic concentration (0.1 minimum alveolar concentration [MAC]).[49,50] This may result in a normalization of minute ventilation, despite an increase in $Paco_2$ and a decrease in pH. However, these values were subnormal and not really clinically relevant (pH 7.35 ± 0.10; $Paco_2$ 46 ± 12 mmHg).

Decreases in WOB and P0.1 may reflect a sevoflurane-induced reduction in ventilatory drive. However, oxygenation and sedation level remained stable, and remifentanil also induced respiratory depression.[51] Nevertheless, at the concentrations used, remifentanil may reduce ventilatory drive less than sevoflurane.[52] Discomfort associated with the ACD was also observed with classical HME in difficult to wean, not sedated, patients.[33]

Our study had several limitations. On the one hand, this study is a practical demonstration and does not separate out the contributions of the ACD *versus* the offset from remifentanil *versus* the offset from sevoflurane. On the other hand, this is a theoretical limit, which does not preclude the clinical message. The level of pressure support was the same under the conditions tested. Increased pressurization with the ACD may have normalized WOB by compensating for the excess load of the artificial system. Compensation of the endotracheal tube, with a pressure support of 5.7 ± 2 cm $H_2O$, was demonstrated in chronic obstructive pulmonary disease patients,[24] and compensation of the HME with a pressure support of 5 to 8 cm $H_2O$.[32] Even if the statistical analysis had been more accurate, there was no randomization in the order of crossover in this study. Since crossover would have necessitated multiple manipulations of the ventilatory circuit, it was rejected by our ethics committee. Thus, the order was Baseline-ACD-ACD+sevo-Baseline for all patients. Moreover, separation of WOB into its components was not possible in our study, necessitating the use of theoretical chest wall compliance. Measurements of exact chest wall compliance would have necessitated deep sedation for total muscle relaxation and ventilatory adaptation of the patient. Use of theoretical chest wall compliance introduces some degree of error, but this degree is the same when comparing different components of WOB in individual patients and did not therefore invalidate comparisons.[24] Sevoflurane-induced bronchodilation may have been improved by using a higher sevoflurane concentration (1 MAC).[41] However, the concentrations were titrated to a clinical sedation objective corresponding to clinical practice, whereas higher concentrations may have dramatically impaired ventilatory drive. Also, ventilation/perfusion ratios could have been impaired with longer sevoflurane administration even if determinants of these ratios are much more complex in ICU patients than in patients in the operating room.

In conclusion, our study showed that light sedation with sevoflurane using the ACD was possible during the weaning of severe ICU patients. In experimental conditions, the ACD device increases the WOB but at low dose, sevoflurane relieves this increase work.

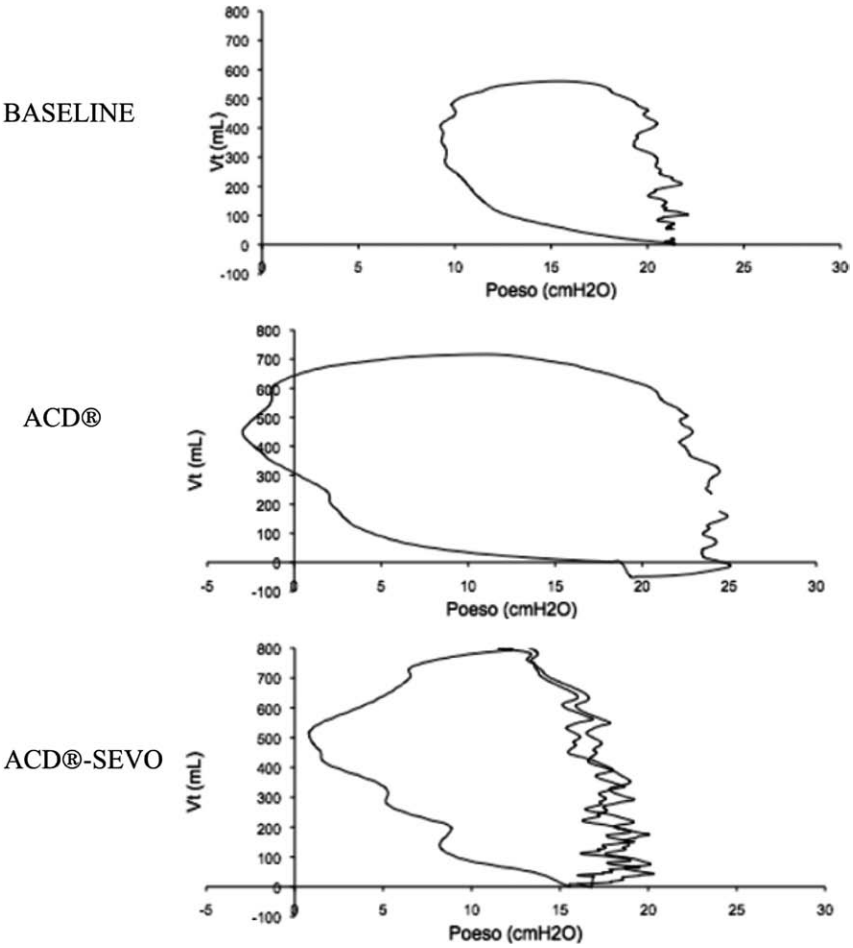


**Fig. 3.** Campbell diagram of a representative patient. Here is represented the relation between esophageal pressure (Poeso) and tidal volume (VT) in three experimental conditions. The increased Poeso swings shown in the Anesthetic Conserving Device (ACD) (AnaConDa®; Sedana Medical AB, Uppsala, Sweden) condition are decreased by the addition of sevoflurane. SEVO = sevoflurane.

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## Competing Interests

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