The Effects of Lung Recruitment on the Phase III Slope of Volumetric Capnography in Morbidly Obese Patients

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BACKGROUND: In this study, we analyzed the effect of the alveolar recruitment strategy (ARS) and positive end-expiratory pressure (PEEP) titration on Phase III slope (S_{III}) of volumetric capnography (VC) in morbidly obese patients.

METHODS: Eleven anesthetized morbidly obese patients were studied. Lungs were ventilated with tidal volumes of 10 mL · kg^{-1}, respiratory rates of 12–14 bpm, inspiration:expiration ratio of 1:2, and F_{IO_2} of 0.4. ARS was performed by increasing PEEP in steps of five from 0 end-expiratory pressure to 15 cm H_2O. During lung recruitment, plateau pressure was limited to 50 cm H_2O, whereas tidal volume was increased to the ventilator's maximum value of 1400 mL, and PEEP was increased to 20 cm H_2O for 2 min. Thereafter, PEEP was reduced in steps of 5 cm H_2O, from 15 to 0. VC, arterial blood gases, and lung mechanics data were determined for each PEEP step.

RESULTS: S_{III} decreased from 0.014 ± 0.006 to 0.005 ± 0.005 mm Hg/mL when 0 end-expiratory pressure was compared against 15 cm H_2O of PEEP after ARS (15_{ARS}, $P < 0.05$). This decrement in S_{III} was accompanied by increases in Pao_2 (27%, $P < 0.002$) and compliance (32%, $P < 0.001$), whereas $Paco_2$ decreased by 8% ($P < 0.038$) when comparing values before and after ARS. A good prediction of the lung recruitment effect by S_{III} was derived from the receiver operating characteristic curve analysis (area under the curve of 0.81, sensitivity of 0.75, and specificity of 0.74; $P < 0.001$).

CONCLUSION: The S_{III} in VC was useful to detect the optimal level of PEEP after lung recruitment in anesthetized morbidly obese patients.

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During general anesthesia, morbidly obese patients develop considerable amounts of atelectasis in dependent lung areas, much more than normal weight patients.[1–5] Such "compression atelectasis" has a known negative effect on gas exchange and lung mechanics.[5–7] Lung recruitment maneuvers (RMs), one of which is the alveolar recruitment strategy (ARS), are ventilatory strategies which were developed to reverse anesthesia-induced lung collapse.[7,8] The positive effects of lung recruitment on pulmonary physiology have been demonstrated in anesthetized patients of varying body masses.[7,9,10]

Noninvasive means of monitoring the effects of ARS and positive end-expiratory pressure (PEEP) on lung function are needed at the bedside. In theory, real-time and breath-by-breath respiratory variables related to the collapse-recruitment physiology of the lungs could help in performing RMs more safely and in determining the optimal level of PEEP for each patient.

Our group described the effect of lung recruitment on volumetric capnography (VC) curves (the curve formed by the expired CO_2 concentration plotted against expired tidal volume [VT]) not only in anesthetized patients[11,12] but also in an experimental model of acute lung injury.[13] Dead space and several VC-derived variables changed favorably after lung recruitment and at adequate levels of PEEP, as could be documented by improved arterial oxygenation, improved respiratory mechanics, and reduced areas of collapse on computed tomography images.

Of all VC-derived variables, the slope of Phase III (S_{III}) is of particular physiological interest because it is an indicator of both CO_2 transport within the airways (ventilation) and the CO_2 delivered to the pulmonary capillaries (perfusion).[14–18] Thus, this variable has also been associated with the ventilation/perfusion (V/Q) relationship in the lungs.[19–21] There is clear evidence suggesting that any increment in S_{III} is a reflection of impaired V/Q matching, whereas decrements indicate its improvement.[22–26] Considering the above concepts,

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it seems that S_{III} is an on-line breath-by-breath variable that could provide valuable information about the effects of RMs and PEEP on lung function in anesthetized patients.

The goal of this observational study was twofold: 1) to test the role of S_{III} as a noninvasive real-time VC-derived variable for monitoring the effects of ARS and PEEP during a titration process and 2) to identify other variables derived from VC that could describe the lung collapse-recruitment phenomenon in a noninvasive way. This protocol was performed in morbidly obese patients, a good clinical model of anesthesia-induced atelectasis,[4–5] which magnifies the typical changes in pulmonary physiology because of lung collapse routinely seen in normal weight patients.

METHODS

The study was approved by the local ethics committee of the University Hospital Hamburg-Eppendorf, Germany. We examined 11 patients with body mass indexes (BMI, weight/height^2) $>40\ kg \cdot m^{-2}$ undergoing bariatric laparoscopic surgery. After obtaining written informed consent, we enrolled only patients without known cardiovascular and pulmonary diseases.

In the induction room, patients lay in the supine position. We inserted a 20 G radial artery catheter under local anesthesia. After induction of anesthesia, a central venous catheter (Certofix-Trio-Set 5730, B. Braun, Melsungen, Germany) and a pulmonary artery catheter (Swan-Ganz, Baxter, Irvine, CA) were introduced into the same internal jugular vein. Cardiac output was measured in triplicate using the thermodilution method. Pulmonary vascular pressures and all other measurements were performed at the end of expiration. The catheters for rather extensive hemodynamic monitoring were inserted immediately after induction of anesthesia but served primarily the needs of a subsequent intraoperative study in the same patients, investigating the effects of capnoperitoneum and PEEP on heart and lung function. In the current study, we analyzed the data of only a subset of 11 of 19 morbidly obese patients enrolled in the original study (in preparation for publication) who had complete sets of CO_2 and reference data.

The current study protocol was completed before moving the patient into the operating room where the surgery took place.

One liter of colloidal solution (RheoHAES, B. Braun, Melsungen, Germany) was administered for intravascular volume expansion before induction of anesthesia. IV saline solution infusion was kept at 5 $mL \cdot kg^{-1}$ (lean body weight) during the study. This preload optimization was necessary to minimize potential hemodynamic impairment because of high airway pressures if patients presented with a relative or inadvertent hypovolemia.[27]

Oxygen (100%) was administered for 3 min. Thereafter, anesthesia was induced with etomidate 0.15–0.3 $mg \cdot kg^{-1}$, sufentanyl 0.1–0.5 $\mu g \cdot kg^{-1}$, and succinylcholine 1 $mg \cdot kg^{-1}$. Balanced anesthesia was maintained with sevoflurane plus IV boluses of 0.1–0.5 $\mu g \cdot kg^{-1}$ sufentanyl and 0.075–0.15 $mg \cdot kg^{-1}$ rocuronium as needed. After tracheal intubation, the lungs were ventilated using a Cicero EM (Dräger, Lübeck, Germany) in a volume-controlled mode with a VT of 10 $mL \cdot kg^{-1}$ lean body weight, a respiratory rate of 10–14 bpm, an inspiratory-to-expiratory ratio of 1:2, F_{IO_2} of 0.4, and initially without PEEP (ZEEP). Minute ventilation was adjusted by changing the respiratory rate to maintain P_{aCO_2} within the normal range.

VC and Lung Mechanics Variables

For VC and respiratory mechanics measurements, we used the respiratory profile monitor COSMOplus (Respironics, Wallingford, CT). Its Capnostat® sensor was inserted between the endotracheal tube and Y-piece of the ventilator. Data were continuously recorded using the software Aplus (Novametrix, Wallinford, CT).

The VC is traditionally divided into three phases.[21] Phase I represents expired gases free of CO_2. Phase II is formed by the rapid increase in expired CO_2 coming from lung acini, whereas Phase III consists of gas resident in the alveolar space. The maximum slope of Phase II (S_{II}) was calculated by using linear regression from the data points between the start of Phase II and 40% of the expired volume. S_{III} was calculated by linear regression, considering all data points between 40% and 80% of VC. Both slopes are expressed as mm Hg/mL.

VD_{aw} is the airway dead space as determined by Fowler method.[28] Physiologic dead space (VD_{phys}) was calculated using Enghoff modification of Bohr formula[29] as:

$$VD_{phys} = (Paco_2 - Peco_2)/Paco_2 \times VT$$

where $PeCO_2$ is the mean expired partial pressure of CO_2.

Next, the ratio of physiological VD/VT was calculated as:

$$VD/VT = VD_{phys}/VT$$

VD_{alv} was computed by subtracting VD_{aw} from VD_{phys}. The ratio of alveolar dead space to alveolar VT (VD_{alv}/VT_{alv}) was then obtained by dividing VD_{alv} by the alveolar part of the tidal volume ($VT_{alv} = VT - VD_{aw}$). The arterial to end-tidal partial pressure of CO_2 ($Pa\text{-}ETco_2$) was also calculated.

Dynamic compliance (C_{DYN}) was calculated as VT divided by δ pressure (plateau pressure minus total PEEP). Expiratory airway resistance (R_{AW}) was computed as δ pressure divided by expiratory flow. Peak expiratory flow (P_{EF}) was defined as the maximum value of expiratory flow of a breath. The expiratory time constant (E_{TC}) was calculated as the product of C_{DYN} and R_{AW}.

Two new variables derived from the VC and lung mechanics were developed and tested. These variables

are related to the CO_2 elimination kinetic during expiration:

1. The time-constant for eliminating CO_2 (Tau-CO_2), represented as the amount of CO_2 eliminated during 1 expiratory time-constant.[30] It is calculated as:

$$\text{Tau-}CO_2 = C_{DYN} \times R_{AW} \times VTCO_{2,br}$$

where $VTCO_{2,br}$ is the amount of CO_2 eliminated in 1 breath as derived from an integration of the area under the CO_2 versus volume curve.

2. Because of the fact that ARS, in conjunction with adequate levels of PEEP, increased C_{DYN}, while at the same time decreasing R_{AW} and having some transient effects on $VTCO_{2,br}$ (at least if observation intervals are shorter than the time for complete equilibration, as in this study), we modified the initial Tau-CO_2 formula by placing R_{AW} in the denominator of the above equation. This new variable derived from the "modified" Tau-CO_2 formula was referred to as CO_{2flow}:

$$CO_{2flow} = C_{DYN} \times VTCO_{2,br}/R_{AW}$$

Protocol

PEEP titration and alveolar recruitment were initiated before the start of surgery. ARS was slightly modified from our previous publications[7,9,11] to meet the higher pressure requirements of this study population. Eichenberger et al.[4] showed that morbidly obese patients developed more atelectatic areas in the perioperative period when compared with patients of normal weight. Additionally, Rothen et al.[8] observed that 1 of 16 patients still had atelectasis after lung recruitment with 40 cm H_2O of Paw. These authors found a close correlation between the Paw needed to reexpand the atelectatic lungs and the BMI. Thus, we reasoned that the pressures needed to open all collapsed lung units in morbidly obese patients with otherwise healthy lungs would be higher than those in normal weight patients because of the decreased transpulmonary pressures caused by additional abdominal and thoracic amounts of fatty tissue.[3,4,9] The lung's opening pressures were assumed to be around 50 cm H_2O of plateau pressure. Therefore, airway pressures were limited to 50 cm H_2O, whereas both PEEP and VTs were increased to the machine's maximum values of 20 cm H_2O and 1400 mL, respectively. However, because of the pressure limitation the latter value would never be reached. The high-flow rate together with the pressure limitation resulted in a decelerating flow pattern even with the ventilator's volume-controlled mode of ventilation. As shown in Figure 1, PEEP was initially increased from 0 to 15 cm H_2O in steps of 5 cm H_2O.

After 2 min at maximal airway pressures, previous ventilator settings were applied, starting at a PEEP of 15 cm H_2O (15_{ARS}), which was then decreased in steps of 5 cm H_2O to 10 (10_{ARS}), 5 (5_{ARS}), and 0 (0_{ARS}) cm H_2O. Each level of PEEP before and after ARS was maintained for exactly 3 min.

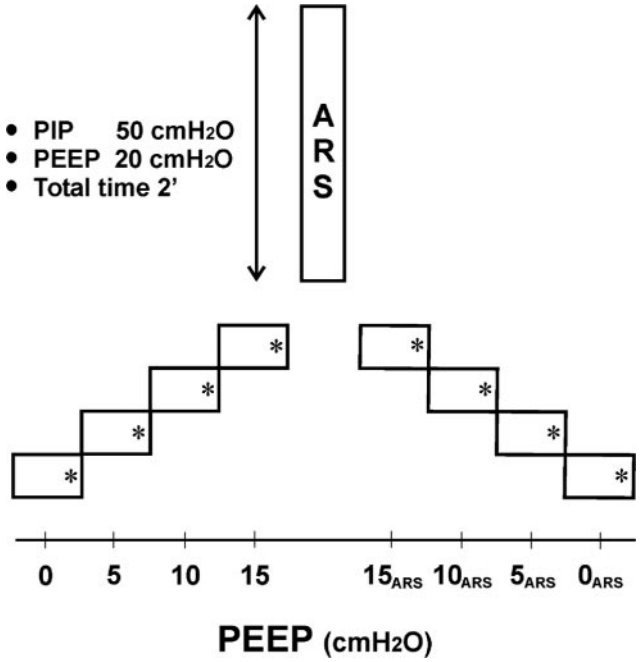

Figure 1. Symmetrical study protocol showing phases of increasing and decreasing levels of positive end-expiratory pressure (PEEP) separated by an alveolar recruitment strategy (ARS). Numbers on *x* axis show the level of PEEP applied during each 3-min period, as depicted by a rectangle. $Index_{ARS}$ = level of PEEP after an alveolar recruitment strategy. * = time points at which data were collected.

Data for analyzing VC and respiratory mechanics were taken starting at the third minute, and a mean value for each variable was calculated from approximately 12 breaths. Hemodynamic values and arterial blood for blood gas analysis were taken at the end of the third minute, just before changing PEEP. Samples were processed without delay by the blood gas analyzer ABL System 615 (Radiometer, Copenhagen, Denmark). From previous protocols, it was known that during the actual RM no steady-state condition would be reached. Therefore, we elected not to take blood samples for gas analysis at this step.

Analysis of the Recruitment Effect

Pao_2, shunt, C_{DYN}, and the study of CO_2 kinetics ($Paco_2$ or dead space) are known markers of the effects of lung recruitment.[13,31,32] Therefore, we used them to determine the physiological efficacy of PEEP applied before and after the ARS. Shunt was calculated according to the following formula and assumptions:

Because the CvO_2 needed for the formula $CO = VO_2/CaO_2 - CvO_2$ could not be obtained during our short study periods, the assumption that $VO_2 = VCO_2 \times RQ$ (0.85) was used instead. Thus, $CvO_2 = VO_2/CO - CaO_2$, now allowing the classic shunt formula to be applied as: $Shunt = CcO_2 - CaO_2/CcO_2 - CvO_2$.

Statistical Analysis

Statistical analysis was performed using the program SPSS version 15.0 (SPSS, Chicago, IL). Variables

were analyzed by one-way analysis of variance and Tukey honestly significant difference criterion. Results are presented as mean and standard deviation. Sensitivity and specificity of a 20% decrease in S_{III} to detect a lung recruitment effect were evaluated by constructing the receiver operating characteristics curve (ROC)[33] (Area Under the Curve, AUC = 0.7, $P < 0.05$). An AUC of 0.5 would mean no predictive value at all (pure chance), whereas an AUC of 1 signifies the best possible prediction. A $P < 0.05$ was considered significant. We considered changes in $Pao_2 \geq 20\%$, in $C_{DYN} \geq 40\%$, in $VD_{alv}/VT_{alv} \leq 20\%$, and in $Paco_2 \leq 5\%$ as cutoffs for defining a recruitment effect.

RESULTS

Nine men and two women morbidly obese patients undergoing anesthesia for laparoscopic gastric banding were studied. The mean patient age was 38 ± 6 yr. Mean height was 1.68 ± 0.1 m and mean weight was 144 ± 29 kg, corresponding to a mean BMI (weight/height^2) of 51 ± 10 kg/m^2.

The effect of lung recruitment on S_{III} is presented in Figure 2. S_{III} showed significantly higher values before than after lung recruitment at 15_{ARS}. S_{III} increased again when PEEP decreased to values below 15 cm H_2O. Regression analysis showed that S_{III} together with S_{II} and $VTCO_{2,br}$ predict the real $Paco_2$ value according to the following equation: $Paco_2 = 719.2 \times S_{III} + 23.74 \times S_{II} + 1.039 \times VTCO_{2,br} + 4.107$ ($R^2 = 0.84$, $P < 0.05$). No good correlations were found between S_{III} and Pao_2, VD_{alv}/VT_{alv}, or C_{DYN} at a high variability among these 11 patients (Fig. 2). However, the receiver operating characteristic analysis showed good sensitivity and specificity of S_{III} to detect lung recruitment effects (Table 1).

Arterial oxygenation improved with lung recruitment (Fig. 2). Pao_2 values after lung recruitment were higher than those at the same level of PEEP before ARS. The highest Pao_2 value was observed at 15_{ARS} and was statistically different from baseline (ZEEP).

Dead space variables during the protocol are shown in Table 2. In general, the inefficiency of ventilation decreased with lung recruitment and ventilation at 15 cm H_2O of PEEP. VD_{alv}, VD_{alv}/VT_{alv}, and $Pa\text{-}ETco_2$ showed significant changes after ARS compared with ZEEP ventilation before recruitment. Both Pao_2 and dead space variables declined when PEEP was decreased stepwise from 15_{ARS} to 0_{ARS}, suggesting a derecruitment of previously recruited lung areas.

Data on ventilation and lung mechanics are shown in Table 3. Lung mechanics improved after ARS. C_{DYN} increased with PEEP and lung recruitment, reaching the highest values at 15_{ARS}. R_{AW} decreased with increasing PEEP, reaching the lowest values at 15 cm H_2O both before and after recruitment. Similar to gas exchange, C_{DYN} and R_{AW} showed a progressive deterioration when PEEP went from 15_{ARS} to 0_{ARS}. E_{TC} was prolonged and reached significant differences after ARS when compared with ventilation without recruitment. All values of P_{EF} after lung recruitment were lower than those before ARS.

Despite the fact that $VTCO_{2,br}$ did not change significantly throughout the entire protocol, Tau-CO_2 showed consistent increments after lung recruitment, describing a combined positive effect of ARS on lung mechanics and CO_2 elimination (Fig. 3). CO_{2flow}, however, described the impact of lung recruitment in a more pronounced way, showing a pattern similar to Pao_2 and C_{DYN} in Figure 2.

Hemodynamic data are provided in Table 4. Mean systemic and pulmonary arterial pressures, cardiac filling pressures, and cardiac output remained stable and within normal ranges throughout the entire protocol while shunt presented an almost exact mirror image of Pao_2. No complications occurred.

DISCUSSION

This study in morbidly obese anesthetized patients showed that an ARS in conjunction with adequate levels of PEEP decreased the S_{III} of the VC curve, reflecting improved global lung function. This suspected improvement was confirmed by simultaneous and positive changes in arterial oxygenation and CO_2, shunt, dead space, and respiratory mechanics, which were most pronounced after the lung recruitment.[7,9,13,31,32]

Two main clinical implications can be deduced from this study. First, the association between VC-derived variables and the collapse-recruitment physiology suggests that monitoring these variables on a breath-by-breath basis could guide RMs and identify the appropriate level of PEEP in mechanically ventilated patients. Second, lung recruitment together with a PEEP of 15 cm H_2O showed the best effect on respiratory physiology in these morbidly obese patients undergoing general anesthesia. Thus, it can be reasoned that it was the active lung recruitment that induced these improvements in lung function while PEEP maintained them. This same level of PEEP without lung recruitment did not show the same physiological effect in morbidly obese patients, as also observed by Santesson[34] and Erlandsson et al.[35] Their results showed some similarities with our data, and 15 cm H_2O of PEEP without prior lung recruitment had an inconsistent and limited impact on cardiopulmonary physiology.

Effects of Lung Recruitment on S_{III}

The origin of S_{III} of the expired CO_2-volume curve has been investigated over the last decades.[12–17] From the ventilatory point of view, S_{III} is caused by two kinds of inhomogeneities in the transport of gas within the airways: "convection-dependent inhomogeneity," which is a large-scale inhomogeneity within and between different ventilated lung zones mediated by a convective transport of CO_2, and "diffusion-convection-dependent

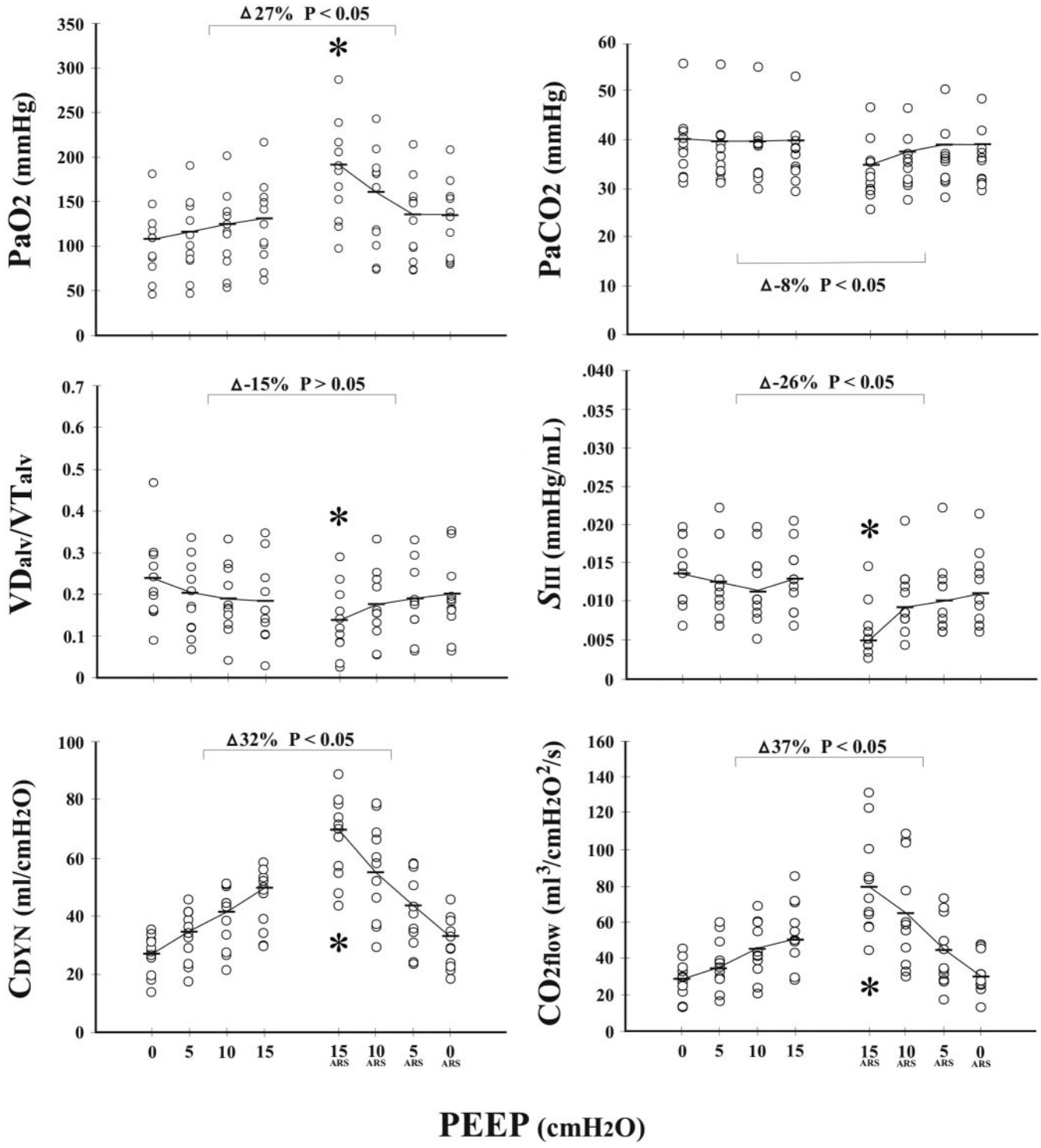

Figure 2. Individual responses to the lung recruitment maneuver for Pao_2, $Paco_2$, dead space $(VD)_{alv}$/tidal volume $(VT)_{alv}$, the slope of Phase III (S_{III}), dynamic compliance (C_{DYN}) and CO_{2flow}. Δ = differences in the mean values summarizing all conditions before and after the alveolar recruitment strategy (ARS) are presented as percentage values above each graphic. A P value <0.05 was considered significant. * = significant difference between 0 positive end-expiratory pressure (PEEP) and 15_{ARS}.

inhomogeneity," which is caused by the interaction of both convective and diffusive CO_2 transport within asymmetric small airways.[36] As an example, asthmatic and emphysematous patients show high S_{III} because of the known increases in R_{AW}, which also affect the CO_2 transport within the lungs.[22,23]

From the perfusion point of view, S_{III} is caused by the continuous elimination of CO_2 molecules through the alveolar-capillary membrane, as this gas is delivered to the lungs by the pulmonary blood flow. It was postulated that the effect of lung perfusion on S_{III} is responsible for approximately 10% of the sloping.[18]

Table 1. Receiver Operating Characteristic (ROC) Analysis

Variable	Cutoff (%)	AUC	Sensitivity	Specificity	*P*
Pao_2	>20	0.81	0.75	0.74	<0.001
C_{DYN}	>40	0.84	0.78	0.76	<0.001
VD_{alv}/VT_{alv}	<20	0.67	0.65	0.62	<0.001
$Paco_2$	<5	0.81	0.67	0.66	<0.001

Prediction of the recruitment effect by a decrease in the slope of Phase III (S_{III}) was tested by calculating the area under the curve (AUC) of the ROC curve comparing zero positive end-expiratory pressure (PEEP) (ZEEP) before lung recruitment against the value at 15 cm H_2O after it. We used a % change in S_{III} ≤20% and a cutoff in the partial pressure of oxygen (Pao_2) ≥20%, in dynamic compliance (C_{DYN}) >40%, in the ratio of alveolar dead space to alveolar tidal volume (VD_{alv}/VT_{alv}) ≤20% and in the partial pressure of carbon dioxide ($Paco_2$) ≤5%. A *P* value <0.05 was considered statistically significant.

Table 2. Data on Dead Space and Other Volumetric Capnography Variables During the Protocol

	PEEP (cm H_2O)				ARS			
	0	5	10	15	15_{ARS}	10_{ARS}	5_{ARS}	0_{ARS}
VD_{aw} (mL)	113 ± 13*	116 ± 13	124 ± 12	135 ± 15	117 ± 16	107 ± 15*	105 ± 15*	107 ± 13*
VD_{alv} (mL)	131 ± 46†	122 ± 43	110 ± 38	101 ± 44	84 ± 46	99 ± 45	106 ± 42	110 ± 48
VD_{phys} (mL)	244 ± 48	239 ± 43	234 ± 42	236 ± 48	201 ± 48	206 ± 50	211 ± 46	216 ± 51
VD/VT	0.39 ± 0.08	0.39 ± 0.07	0.38 ± 0.06	0.38 ± 0.07	0.32 ± 0.06	0.33 ± 0.07	0.34 ± 0.07	0.35 ± 0.08
Pa-$ETco_2$ (mm Hg)	6.3 ± 0.3†	5.7 ± 0.3	5.6 ± 0.5	5.6 ± 0.6	2.9 ± 0.4	4.4 ± 0.4	5.5 ± 0.3	6.5 ± 0.3
$VTCO_{2,br}$ (mL)	16.6 ± 2.3	16.6 ± 2.5	16.2 ± 2.5	16.6 ± 3.4	16.8 ± 3.3	17.3 ± 2.8	17.3 ± 3.1	17.2 ± 2.9
S_{II} (mm Hg/mL)	0.39 ± 0.08	0.41 ± 0.09	0.39 ± 0.13	0.36 ± 0.07	0.34 ± 0.07	0.35 ± 0.07	0.36 ± 0.07	0.38 ± 0.08

Data are presented as mean ± SD.

$Index_{ARS}$ = level of positive end-expiratory pressure (PEEP) applied after an alveolar recruitment strategy (ARS); VD_{aw} = airway dead space; VD_{alv} = alveolar dead space; VD_{phys} = physiological dead space; VD/VT = ratio of physiological dead space to tidal volume; Pa-$ETco_2$ = arterial to end-tidal partial pressure differences of CO_2; $VTCO_{2,br}$ = carbon dioxide elimination per breath; and S_{II} = slope of Phase II.

* Vs 15, $P < 0.05$.

† Vs 15_{ARS}, $P < 0.05$.

Table 3. Data on Ventilation and Lung Mechanics

	PEEP (cm H_2O)				ARS				
	0	5	10	15	20_{ARS}	15_{ARS}	10_{ARS}	5_{ARS}	0_{ARS}
PIP (cm H_2O)	27 ± 4*	28 ± 4*	30 ± 5	34 ± 4	50 ± 1	30 ± 3	27 ± 5*	26 ± 6*	25 ± 5*
PLP(cm H_2O)	21 ± 6	23 ± 5	24 ± 6	27 ± 7	50 ± 1	24 ± 4	20 ± 6	20 ± 4	20 ± 5
Paw (cm H_2O)	11 ± 2*†‡§	13 ± 2†‡	17 ± 3†	21 ± 3‡	29 ± 3	20 ± 2	16 ± 2	13 ± 3	11 ± 3
VT (mL)	613 ± 72	614 ± 69	609 ± 80	618 ± 62	1007 ± 132	614 ± 68	617 ± 62	611 ± 65	616 ± 62
RR (bpm)	12 ± 1.3	12 ± 1.2	12 ± 1.1	11 ± 1.5	11 ± 1.4	11 ± 1.2	11 ± 1.2	11 ± 1.0	11 ± 1.1
C_{DYN} (mL/cm H_2O)	30 ± 6*†‡	36 ± 9†‡	42 ± 10†‡	48 ± 10†	39 ± 15	68 ± 13	57 ± 16	44 ± 12	33 ± 8
R_{AW} (mL · cm $H_2O^{-1} \cdot s^{-1}$)	18 ± 3.9	17 ± 3.2	16 ± 2.0	15 ± 1.8	17 ± 4.1	15 ± 3.7	16 ± 3.6	19 ± 4.3	19 ± 3.7
P_{EF} (L/s)	36 ± 6	37 ± 6‖	39 ± 5‡‖	40 ± 5†‡	45 ± 6	32 ± 6	31 ± 5	31 ± 5	32 ± 5*
E_{TC} (s)	0.98 ± 0.2†‡	0.96 ± 0.1†‡	0.92 ± 0.2†‡	0.91 ± 0.1†‡	0.81 ± 0.1	1.27 ± 0.3	1.25 ± 0.3	1.20 ± 0.2	1.16 ± 0.2

Data are presented as mean ± SD.

$Index_{ARS}$ = level of positive end-expiratory pressure (PEEP) after an alveolar recruitment strategy; PIP = peak airway pressure; PLP = plateau pressure; Paw = mean airway pressure; VT = tidal volume; RR = respiratory rate; C_{DYN} = respiratory dynamic compliance; R_{AW} = expiratory airway resistance; P_{EF} = expiratory peak flow; E_{TC} = expiratory time constant.

* Vs 15, $P < 0.05$.

† Vs 15_{ARS}, $P < 0.05$.

‡ Vs 10_{ARS}, $P < 0.05$.

§ Vs 10, $P < 0.05$.

‖ Vs 5_{ARS}, $P < 0.05$.

Our group has confirmed the perfusion-dependent mechanism in the genesis of S_{III} in anesthetized patients.[19] Therefore, S_{III} depends highly on the spatial and temporal distribution of ventilation and perfusion and can therefore be considered a general index of V/Q matching.[18–20]

Considering the above concepts, changes in S_{III} can be explained best by the effect that lung recruitment has on the transport of CO_2 from the capillary blood into the airway opening. First, increasing the area for gas exchange by actively recruiting previously collapsed lung acini will naturally decrease the resistance to CO_2 diffusion through the alveolar-capillary membrane. Second, increasing the cross-sectional area of the airways will result in decreased resistance to intrapulmonary CO_2 transport by both diffusion and convection. The latter mechanism seems to be the most relevant for decreasing S_{III}. This hypothesis has

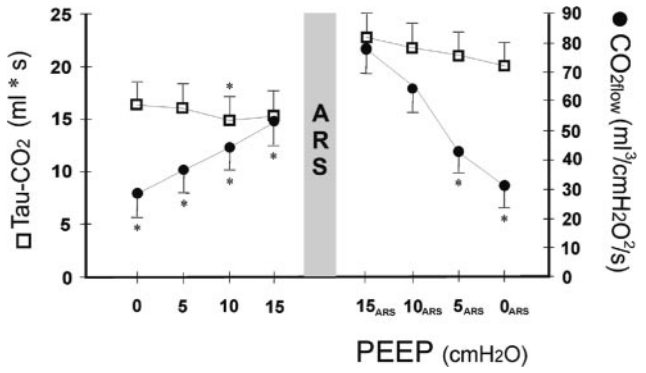

Figure 3. Time constants for CO_2 elimination throughout the study protocol. Tau-CO_2 = $C_{DYN} \times R_{AW} \times VTCO_{2,br}$, where C_{DYN} is the dynamic compliance, R_{AW} is the expiratory airway resistance, and $VTCO_{2,br}$ is the amount of CO_2 eliminated in one breath. $CO_{2flow} = C_{DYN} \times VTCO_{2,br}/R_{AW}$, using the same variables as above but in a modified arrangement, with R_{AW} in the denominator. $Index_{ARS}$ = level of positive end-expiratory pressure (PEEP) after an alveolar recruitment strategy. Data are presented as mean ± SD. * Vs 15_{ARS}, $P < 0.05$.

already been shown in normal weight patients with anesthesia-induced atelectasis[11,12] and is now confirmed in these morbidly obese patients. In contrast to these results, Blanch et al.[37] found no differences in VC indices when PEEP levels of 0, 5, 10, and 15 cm H_2O were applied; however, this was without prior recruitment in patients with normal lungs or in patients with acute lung injury or acute respiratory distress syndrome. Their results are almost identical to our data obtained before the lung RM, in which changes were small and nonsignificant. The physiologic differences between the effect of PEEP with and without lung recruitment are well known[7,8,13,32] and can easily explain such contradictory results.

Mechanism Behind Change in S_{III} Induced by Lung Recruitment

As we have already pointed out, mechanisms affecting the CO_2 transport within the lungs during expiration are the main determinants of S_{III}. Expiratory flow is a passive process that depends exclusively on the mechanical properties of the respiratory system. Thus, any change in respiratory mechanics induced by lung recruitment will play a major role in the genesis of S_{III} because the expiratory flow patterns change accordingly. As opposed to CO_2 kinetics, the effect of lung collapse and recruitment on respiratory mechanics is well known.[7,9–11] Our results fit well with these studies showing that the elastic properties of the respiratory system increase and airway flow resistance decreases when lung volumes are restored by RMs and PEEP.

These changes in lung mechanics can be explained by the concept of expiratory time constant (E_{TC}). The E_{TC} describes how fast the passive respiratory system responds to an external mechanical perturbation during expiration. Classically, a short E_{TC} goes along with a fast response, whereas a long E_{TC} indicates a delayed attainment of a new equilibrium within the respiratory system. At ZEEP, the lower C_{DYN} caused by atelectasis allows the equilibrium to be reached very quickly while the VT is distributed within a smaller lung. This leads to decreased global compliance and increased P_{EF}. The opposite mechanism is observed after lung recruitment: higher C_{DYN} allows a slower and more homogeneous expiratory flow. E_{TC} increases despite a decrement in R_{AW} mainly because of a more-than-proportional increase in C_{DYN}. VT is now distributed within more functional lung tissue, the characteristic of an "open-lung" condition. Increased compliance and decreased P_{EF} are the consequences.

The relationship between the effects of ARS and PEEP on lung mechanics and CO_2 kinetics is represented by the Tau-CO_2 concept (Fig. 3). Despite stable hemodynamics (Table 4) and strict protocol timing, this composite variable showed that the amount of CO_2 eliminated within 1 E_{TC} was highest at 15_{ARS}, a condition related to the most favorable lung condition, as reflected by oxygenation and dead space. The CO_{2flow} variable showed an even better profile than the Tau-CO_2 concept for monitoring the recruitment effect, because the lower R_{AW} seen after recruitment, which is now in the denominator, will augment the

Table 4. Hemodynamic Data

	PEEP (cm H_2O)				ARS				
	0	5	10	15	20_{ARS}	15_{ARS}	10_{ARS}	5_{ARS}	0_{ARS}
HR (beats/min)	69 ± 4	67 ± 5	66 ± 6	64 ± 6	78 ± 11	68 ± 7	65 ± 8	67 ± 8	68 ± 8
MAP (mm Hg)	81 ± 14	75 ± 10	78 ± 11	79 ± 10	80 ± 19	80 ± 13	83 ± 14	85 ± 15	84 ± 16
MPAP (mm Hg)	23 ± 7	24 ± 6	26 ± 6	26 ± 5	28 ± 4	25 ± 5	24 ± 6	25 ± 7	25 ± 5
PCWP (mm Hg)	14 ± 3	14 ± 2	16 ± 3	16 ± 4	19 ± 4	17 ± 3	16 ± 3	16 ± 3	15 ± 2
CVP (mm Hg)	14 ± 4	14 ± 4	13 ± 3	15 ± 4	18 ± 3	15 ± 3	14 ± 4	14 ± 3	14 ± 4
CO (L/min)	6.7 ± 1.5	6.5 ± 1.5	6.4 ± 1.6	6.3 ± 1.6	5.4 ± 1.1	6.1 ± 1.6	6.1 ± 1.5	6.4 ± 1.6	6.5 ± 1.7
Shunt (%)	0.14 ± 0.07*†‡	0.14 ± 0.06*†‡	0.13 ± 0.06*†	0.11 ± 0.05*	—	0.06 ± 0.03	0.08 ± 0.04	0.10 ± 0.04	0.10 ± 0.03

Data are presented as mean ± SD.

$Index_{ARS}$ = level of positive end-expiratory pressure (PEEP) after an alveolar recruitment strategy; MAP = mean systemic arterial blood pressure; MPAP = mean pulmonary arterial pressure; PCWP = pulmonary capillary wedge pressure; CVP = central venous pressure; CO = cardiac output; HR = heart rate.

* Vs 15_{ARS}, $P < 0.05$.

† Vs 10_{ARS}, $P < 0.05$.

‡ Vs 5_{ARS}, $P < 0.05$.

signal of lung improvement (Fig. 3). The physiological rationale of CO_{2flow} goes beyond this simple mathematical association and is related to the above explanations. R_{AW} to expiratory flow has an indirect correlation with CO_2 transport within the lungs, thereby explaining why a decrement in R_{AW} also decreases S_{III}.[38]

The main limitation of our study, beyond the small number of patients, is the fact that for methodological and ethical reasons we could not apply the different levels of PEEP in random order. The physiologic response to PEEP is totally different if it is used alone or in conjunction with a prior recruitment. Lung recollapse after lung recruitment is a pressure-dependent mechanism that is affected by the level of PEEP applied. Therefore, a perfectly designed study protocol would have applied all pressure levels in random order, with disconnections between any one of the PEEP steps and additional recruitment interventions before applying each one of the postrecruitment $PEEP_{ARS}$ levels. Such a pure but rather radical protocol would not only have led to surfactant liberation[39] by extensive lung RMs but also to yet another prolongation of the study time. Thus, this kind of study can only be performed under experimental conditions.

Similarly, because of organizational limitations, the time at each PEEP level had to be limited to only 3 min, and therefore, the impact of longer time periods on the variables of interest was not assessed. Additionally, $ETco_2$ and $VTCO_{2,br}$ values stabilized within the first minute at any PEEP level, supporting the fact that the 3-min time frame chosen was enough to obtain reliable data.

Cardiovascular stability during the entire protocol excluded major hemodynamic interference with $S_{III.}$ Despite general hemodynamic stability, we could not measure the distribution of pulmonary blood flow within the lungs. In theory, an uneven distribution of blood flow through different lung regions with different efficiencies for gas exchange could have increased S_{III} regardless of constant total amounts of such flow. However, the magnitude of the effect of an uneven distribution of pulmonary blood flow was estimated to be around 10% of total S_{III} and thus should not have influenced our results in an undue manner.[18,19]

In conclusion, the S_{III} of the VC curve decreased after lung recruitment and adequate levels of PEEP because of a decreased resistance to CO_2 elimination within alveoli and airways. This slope provides aggregate information about gas exchange at the alveolar-capillary membrane, gas transport within airways, and respiratory mechanics. Because it can be measured noninvasively at the bedside on a breath-by-breath basis, this variable may be useful for guiding recruitment and for identifying appropriate levels of PEEP in anesthetized patients with impaired lung function, such as those in this study.

Note added in proof: See also Böhm et al.[40] in this issue which reports different findings in the same patients.

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