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Physiological effects of reduced tidal volume at constant minute ventilation and inspiratory flow rate in acute respiratory distress syndrome

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Abstract *Objective:* To assess the effect of changes in tidal volume (V_T) with a constant inspiratory flow and minute ventilation ($\dot{V}_E$) on gas exchange and oxygen transport in acute respiratory distress syndrome (ARDS).
Design: A crossover study of three V_T in two study groups, using patients as their own controls.
Setting: A medical-surgical intensive care unit in a tertiary care center.
Patients: Eight patients with ARDS and seven postoperative cardiac surgery patients with uncomplicated recoveries were studied during volume-controlled mechanical ventilation.
Interventions: During controlled mechanical ventilation, patients were first ventilated with a V_T of 9–11 ml/kg. V_T was then increased to 12–14 ml/kg (+ 25%) for 30 min and subsequently decreased to 6–8 ml/kg (− 25%) for 30 min by adjusting the respiratory rate (RR) while the inspiratory flow rate, $\dot{V}_E$, and inspiratory duty cycle (T_L/T_{TOT}) were kept constant. At the end, patients were ventilated with the baseline settings for another 30 min.
Measurements and results: V_E, carbon dioxide production ($\dot{V}CO_2$) and oxygen consumption ($\dot{V}O_2$) were measured continuously with a gas exchange monitor, and cardiac output and arterial and mixed venous blood samples were taken at the end of each 30-min period to assess CO_2 removal and oxygen transport. Alveolar minute ventilation ($\dot{V}_A$) and the deadspace to tidal volume ratio (V_D/V_T) were calculated from the Bohr equation. Despite large changes in V_T, arterial oxygenation (P_aO_2) and oxygen transport ($\dot{D}O_2$) were unchanged throughout the study. When V_T was increased, physiological V_D increased from 448 ± 34 ml to 559 ± 46 ml (mean ± SE) in ARDS ($P < 0.001$) and from 281 ± 22 ml to 357 ± 35 ml in CABG ($P < 0.05$). With the small V_T, V_D decreased to 357 ± 22 ml in ARDS ($P < 0.01$), and to 234 ± 24 ml in CABG ($P < 0.05$). In ARDS, V_D/V_T decreased from 0.57 ± 0.03 to 0.55 ± 0.03 ($P < 0.05$) with the large V_T, and increased to 0.60 ± 0.03 ($P < 0.01$), when V_T was reduced. In CABG, V_D/V_T did not change significantly. ARDS patients had a higher P_aCO_2 than cardiac patients ($P < 0.001$), and only minor changes in P_aCO_2 were observed (for ARDS and CABG respectively, baseline 5.9 ± 0.3 kPa and

4.1 ± 0.1 kPa, large V_T 5.7 ± 0.3 kPa and 4.1 ± 0.2 kPa, small V_T 6.2 ± 0.3 kPa and 4.2 ± 0.2 kPa; $P < 0.05$).

Conclusions: Tidal volumes can be reduced to 6–8 ml/kg in ARDS patients without compromising oxygen transport, while adequate CO_2 elimination can be maintained.

Key words ARDS · Mechanical ventilation · Oxygen transport · Gas exchange · Respiratory deadspace · Tidal volume

Introduction

The challenge in mechanical ventilatory support in ARDS is finding a balance between adequate gas exchange and oxygen transport, while preventing further lung damage. With conventional volume-cycled ventilation, a relatively large tidal volume (V_T) has been used, while adjusting the respiratory rate to reach an acceptable arterial PCO_2, and FIO_2 and positive end-expiratory pressure (PEEP) have been titrated to achieve appropriate arterial oxygenation [1]. This approach has been implicated in ventilator-induced lung injury because of the high peak-airway pressures often encountered [2]. In addition, overdistending the lung may reduce the perfusion of healthy alveoli and reduce cardiac output [3]. Alternative modes of ventilation, e.g., inverse ratio ventilation, pressure release ventilation and high-frequency ventilation, have recently been proposed to avoid these harmful effects [4, 5, 6]. However, the possibilities of the conventional volume controlled ventilation have not been fully explored. In an earlier study, we found that effective gas exchange may also be achieved by traditional volume controlled ventilation with simultaneously reduced V_T and flow rates [7]. The aim of this study was to assess the effect of an isolated V_T change with unaltered minute ventilation ($\dot{V}_E$), inspiratory flow and (T_I/T_{TOT}) on gas exchange and oxygen transport in the treatment of ARDS.

Patients and methods

Eight patients with ARDS and a control group of seven patients requiring mechanical ventilation after coronary artery bypass surgery (CABG) were included in the study. All CABG patients had previously normal lungs. The patients with lung injury fulfilled the following clinical criteria for ARDS: a triggering event known to be associated with the development of ARDS, bilateral diffuse lung infiltrates in the chest X-ray, $P_aO_2 < 8.0$ kPa on a FIO_2 of at least 0.4 and PEEP higher than 5 cm H_2O, and no cardiogenic cause (confirmed by pulmonary artery catheterization) [1]. The ARDS group was studied 5 ± 1 days (mean ± SE, range: 1–8) after the diagnosis of ARDS was made and when the patients were hemodynamically stable. Hemodynamic stability was verified by normotension, normal peripheral capillary perfusion as evaluated clinically, and a pulmonary artery occlusion pressure of 8–12 mmHg. None of the patients had any signs of pulmonary edema prior to the diagnosis of ARDS. The severity of the lung injury was assessed according to the scoring system described by Murray and associates [8]. The mean P_aO_2/FIO_2 ratio was 13.2 ± 0.7 kPa (99 ± 5 mmHg). Seven patients had a lung injury score equivalent to severe lung injury (≥ 2.5), and one patient a score of 2.3 corresponding to mild-to-moderate lung injury. Three patients had a PEEP level equal to or exceeding 9 cm H_2O, and five patients had a PEEP below 9 cm H_2O (the cutoff limit for scores exceeding 2 for PEEP in the Murray scoring system). The PEEP level was selected according to the individual patient needs by the attending physician. The characteristics of the ARDS patients are presented in Table 1. The mean duration of mechanical ventilation at the time of the study was 104 ± 20 hours (range: 35–192). The CABG group (6 male/1 female, ages = 55 ± 5 years) was studied on the day of operation, 5.9 ± 0.4 h after admission to the intensive care unit. The P_aO_2/FIO_2 ratio was 35.6 ± 4.7 kPa (267 ± 35 mmHg). Informed consent was obtained from the patient or, when appropriate, from the family. This study was approved by the Ethics Committee of the hospital.

All studies were conducted using the controlled mechanical ventilation mode of a Siemens Servo 900C ventilator (Siemens, Solna, Sweden) and square wave inspiratory flow. The ventilator settings are presented in Table 2. Slight hyperventilation was allowed in the CABG group to prevent an increase in the pulmonary vascular resistance in the early postoperative period (arterial PCO_2 4.1 ± 0.1 kPa). The baseline value of hemoglobin (Hb) was 118 ± 3 g/l in ARDS and 113 ± 5 g/l in CABG. No blood transfusions were given during the study. All patients were sedated with oxycodone and diazepam, and pancuronium or vecuronium was used for muscle relaxation. No spontaneous breathing efforts were observed clinically or from the airway pressure gauge or the trigger indicator of the ventilator. Gas exchange was monitored continuously, and when the minute-to-minute results were stable, data collection was started. After the baseline (baseline 1.), V_T was first increased by 25% (1.25 V_T), and reduced thereafter to 75% of the baseline V_T (0.75 V_T). At the end, measurements were repeated with the baseline settings (baseline 2). The duration of each period was 30 min. The V_T was altered by changing the respiratory rate. Hence, in addition to the V_T, only the inspiratory time (T_I) and the duration of the breath (T_{TOT}) changed, whereas the inspiratory flow, inspiratory duty cycle (T_I/T_{TOT}) and minute ventilation ($\dot{V}_E$) were constant. The small variability of the measured $\dot{V}_E$, despite unchanged $\dot{V}_E$ setting, reflects the combined variability of the measurement and the ventilator. Cardiac output ($\dot{Q}$) was measured and blood samples were taken at the end of each period. FIO_2 and PEEP were kept at the baseline levels throughout the study. Periods lasting 30 min were chosen since the study protocol was designed to assess the acute effects of a ventilatory change on gas exchange and oxygen transport. Body CO_2 stores may not reach a steady state in this time, but the validity of the gas exchange measurement even in non-steady-state conditions has been shown previously [9]. The non-randomized order of changes in V_T was selected due to safety considerations. To minimize the risk of worsening pulmonary hypertension in ARDS, the higher V_T was tested first, because we believed this would result in a slightly lower starting P_aCO_2 at the low V_T. Intrinsic PEEP ($PEEP_i$) was assessed from the pressure manometer after

Table 1 Characteristics of the ARDS patients. The lung injury score is calculated according to Murray et al. [8]

Age (years)	Sex	Days from ARDS diagnosis	Predisposing condition	Outcome	Lung injury score
34	M	6	Multiple fractures, fat embolism	Died	3.7
64	M	7	Emergency coronary bypass surgery	Survived	2.7
31	M	4	Pneumonia	Died	4.0
64	M	3	Perforated prepyloric ulcer, peritonitis	Survived	2.7
47	M	3	Flail chest, pulmonary contusion	Died	2.3
58	M	7	Acute pancreatitis	Died	2.7
36	M	1	Postoperative peritonitis	Survived	3.0
58	F	8	Pneumonia	Survived	2.7
49 ± 5		5 ± 1			3.0 ± 0.2

Table 2 Ventilator settings (1.25 V_T V_T increased 25% from baseline; 0.75V_T V_T decreased 25% from baseline, V_T tidal volume, *RR* respiratory rate, *PEEP* positive end-expiratory pressure, FIO_2 fraction of oxygen in inspired air)

	V_T (ml/kg)	RR (breaths/min)	PEEP (cm H_2O)	FIO_2 (fraction)
ARDS				
Baseline[a]	9.3 ± 0.9	18.9 ± 1.6**	9.0 ± 1.6**	0.58 ± 0.03**
1.25V_T	12.2 ± 1.4	14.8 ± 1.5**	9.0 ± 1.6**	0.58 ± 0.03**
0.75V_T	7.0 ± 0.6	24.4 ± 1.6**	9.0 ± 1.6**	0.58 ± 0.03**
CABG				
Baseline	9.6 ± 0.2	12.1 ± 0.2	5.0 ± 0.0	0.43 ± 0.02
1.25V_T	12.9 ± 0.3	8.8 ± 0.2	5.0 ± 0.0	0.43 ± 0.02
0.75V_T	7.4 ± 0.3	15.6 ± 0.2	5.0 ± 0.0	0.43 ± 0.02

[a] Mean of the two measurements at baseline ventilator settings $^{**}P < 0.01$ (difference between patient groups)

occluding the expiratory port of the ventilator at end-expiration using the built-in end-expiratory occlusion function of the ventilator.

$\dot{V}CO_2$, $\dot{V}O_2$ and $\dot{V}_E$ were measured continuously with a gas exchange monitor (Deltatrac, Datex/Instrumentarium, Helsinki, Finland), which has been previously described in detail [10] and validated in this laboratory [11]. The relative error of the measurements under the study conditions is 5% [11–13]. The last 5 min of $\dot{V}CO_2$ and $\dot{V}O_2$ preceding each blood sampling were included in the data analysis. The coefficient of variation for $\dot{V}CO_2$ and $\dot{V}O_2$ was 2.2 ± 5% and 2.9 ± 3%, respectively. Cardiac output was measured in triplicate with 10 ml of room-temperature injectate (built-in cardiac output computer of the Kone 565 Patient Monitor, Kone Instruments, Helsinki, Finland) and the mean value used for calculations. Arterial and mixed venous blood samples were analyzed immediately after sampling. Blood gases were measured with a standard blood gas analyzer (IL 1302, Instrumentation Laboratories, Lexington, Mass.) and oxygen saturations with a co-oximeter (IL 282, Instrumentation Laboratories, Lexington, Mass.). Alveolar ventilation ($\dot{V}_A$) was calculated as

$$\dot{V}_A = 0.115^* \dot{V}CO_2/PaCO_2 \quad (1)$$

where $\dot{V}_A$ is in liters per minutes, and STPD, and P_aCO_2, in kilopascals. The ratio of physiologic dead space (V_D) to V_T was calculated as $V_D/V_T = 1 - \dot{V}_A/\dot{V}_E$. From this ratio and V_T, V_D was obtained. This approach has been separately validated: a change in V_D can be measured with a relative error of 8.2 ± 4.7%, when the change in V_D is 73–84 ml (9–16% of V_T) [9]. Using this approach, $\dot{V}_A$ can also be measured in non-steady-state conditions. While the body CO_2 pool is changing, the measured $\dot{V}CO_2$ still reflects the elimination of CO_2 from the alveoli, but is not equal to the metabolic production of CO_2. The P_aCO_2 reflects the average or "ideal" alveolar CO_2 at the time of sampling, and $\dot{V}_A$, V_D, and V_D/V_T can be calculated, providing the temporal relationship between the P_aCO_2 sample and the measured $\dot{V}CO_2$ is preserved [9]. Arterial and mixed venous oxygen contents (CaO_2, $C\bar{v}O_2$) were calculated from the hemoglobin values (hemoglobin oxygen saturations and partial pressures). Oxygen delivery ($\dot{D}O_2$) was calculated as $\dot{D}O_2 = \dot{Q}^*CaO_2$, and venous admixture as $\dot{Q}_S/\dot{Q}_T = (C\bar{c}O_2\text{-}CaO_2)/(C\bar{c}O_2\text{-}C\bar{v}O_2)$, where $C\bar{c}O_2$ is the calculated oxygen content of the pulmonary end-capillary blood [14].

Statistical analysis

The two baseline periods were first compared by a paired *t*-test to confirm the stability of the patients' condition during the measurement. The mean value of data obtained at the two baseline periods was used to represent the baseline value in the subsequent analysis. Changes in the respiratory and oxygen transport variables were assessed with two-way analysis of variance for repeated measures (procedure MANOVA, SPSS/PC +) [15] using one grouping factor (study group) and one within subject factor (V_T). When significant effects of V_T or group-V_T interactions were observed, these were located post hoc by a paired *t*-test for comparisons between baseline vs large and small V_T within each group, and an unpaired *t*-test for between-group comparisons at each V_T level [15]. The relationship between V_T and V_D was assessed with regression analysis [15]. All

Table 3 Alveolar ventilation and CO_2 elimination[a] (V_D physiological dead space, V_D/V_T physiological dead space to tidal volume ratio, $\dot{V}_E$ minute ventilation, $\dot{V}_A$ alveolar ventilation; $\dot{V}CO_2CO_2$ production, $P_aCO_2CO_2$ partial pressure in arterial blood)

	V_T (ml)	V_D (ml)	V_D/V_T (fraction)	$\dot{V}_E$ (l/min)	$\dot{V}_A$ (l/min)	$\dot{V}CO_2$ ($ml\,kg^{-1}min^{-1}$)	P_aCO_2 (kPa)
ARDS							
Baseline	794 ± 66	448 ± 34^{d}	0.57 ± 0.03^{e}	14.3 ± 0.6^{e}	6.1 ± 0.4	3.5 ± 0.1^{e}	5.9 ± 0.3^{e}
$1.25V_T$	1052 ± 107^{b}	559 ± 46^{cd}	0.55 ± 0.03^{ae}	14.5 ± 0.6^{e}	6.6 ± 0.5	3.6 ± 0.1^{e}	5.7 ± 0.3^{d}
$0.75\ V_T$	602 ± 43^{b}	357 ± 22^{bd}	0.60 ± 0.03^{be}	14.2 ± 0.5^{e}	5.7 ± 0.4	3.4 ± 0.1^{be}	6.2 ± 0.3^{be}
CABG							
Baseline	782 ± 43	281 ± 22	0.36 ± 0.02	9.5 ± 0.5	6.1 ± 0.4	2.6 ± 0.1	4.1 ± 0.1
$1.25V_T$	1056 ± 59^{c}	357 ± 35^{a}	0.34 ± 0.02	9.3 ± 0.6	6.1 ± 0.4	2.7 ± 0.1	4.1 ± 0.2
$0.75V_T$	605 ± 44^{c}	234 ± 24^{a}	0.38 ± 0.02	9.4 ± 0.6	5.8 ± 0.4	2.6 ± 0.1^{a}	4.2 ± 0.2

Analysis of variance: effect of V_T: V_D and $\dot{V}_A$, $P < 0.001$, V_D/V_T and $\dot{V}CO_2$, $P < 0.01$, and P_aCO_2, $P < 0.05$; difference between patient groups: V_D/V_T, $\dot{V}_E$, $\dot{V}CO_2$, P_aCO_2, $P < 0.001$, V_D, $p < 0.01$; post hoc t-tests: differences from baseline within groups: $^{a}P < 0.05$, $^{b}P < 0.01$, $^{c}P < 0.001$; difference between diagnostic groups: $^{d}P < 0.01$, $^{e}P < 0.001$

data are given as mean ± SE, and a P-value < 0.05 was considered significant.

Results

Table 3 shows the parameters of alveolar ventilation and CO_2 elimination. At baseline, $\dot{V}_E$ was 51% higher in ARDS than in CABG ($P < 0.001$). This was due to both a higher CO_2 production and V_D/V_T ($P < 0.001$ for $\dot{V}CO_2$ and V_D/V_T) in the ARDS patients. Baseline P_aCO_2 was also significantly higher in the ARDS patients than in the CABG group ($P < 0.001$).

Table 3 also presents the alveolar ventilation variables obtained in both the ARDS and CABG patients with the different V_Ts. These can be interpreted in terms of Eq. (1). In both ARDS and CABG, physiological V_D (V_D phys) increased when V_T was increased, and decreased with the small V_T ($P < 0.001$). Changes in V_D/V_T ($P < 0.01$) were small. Despite the large increase in V_T at 1.25 V_T, V_D/V_T decreased only marginally in ARDS ($P < 0.05$). At the small V_T, V_D/V_T increased in seven ARDS patients, and decreased in one ($P < 0.01$; Fig. 1). No significant change in V_D/V_T was observed in CABG. V_D/V_T was higher in ARDS, reflecting a higher V_D ($P < 0.01$). V_D correlated with V_T in both ARDS and CABG (Fig. 2). The changes in V_A were small and variable when V_T was changed, and only minor overall changes in P_aCO_2 were observed (analysis of variance $P < 0.05$). $\dot{V}CO_2$ was reduced at 0.75 V_T ($P < 0.01$), and marginally also at the second baseline measurement in ARDS ($3.6 \pm 0.2\ ml\,kg^{-1}\,min^{-1}$ at the first baseline vs $3.5 \pm 0.1\ ml\,kg^{-1}\,min^{-1}$ at the second baseline: $P < 0.05$), reflecting the non-steady-state conditions during the 30-min observation periods. For other measured variables, no significant difference between the two baseline periods were observed.

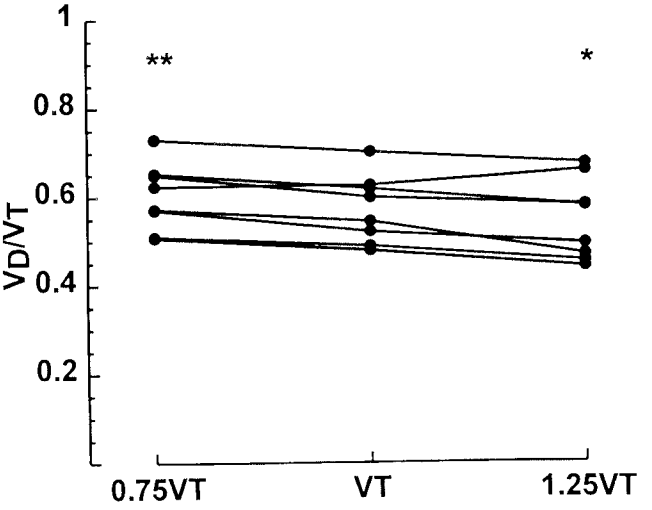

Fig. 1 Individual V_D/V_T responses in ARDS. V_T baseline ventilator settings; 0.75 V_T V_T decreased by 25% from baseline settings; 1.25 V_T V_T increased 25% from baseline settings. $^{*}P < 0.05$, $^{**}P < 0.01$, compared with baseline

Table 4 shows the oxygen transport variables during the study. Despite large changes in V_T, $\dot{Q}$ was unchanged throughout the study in both groups. Consequently, $\dot{D}O_2$ did not change significantly. However, major changes were observed in some patients. The individual changes in $\dot{D}O_2$ in ARDS are shown in Fig. 3. A trend of higher $\dot{D}O_2$ with the smaller V_Ts can be observed (Fig. 3). Despite the lower P_aO_2, $\dot{D}O_2$ was higher in the ARDS patients than in the CABG group due to the higher $\dot{Q}$ ($P < 0.01$). At baseline, CaO_2 was 144 ± 4 ml/l in ARDS and 156 ± 6 ml/l in CABG (NS), and no change was observed during the study. Similarly, there was no difference in the mixed venous

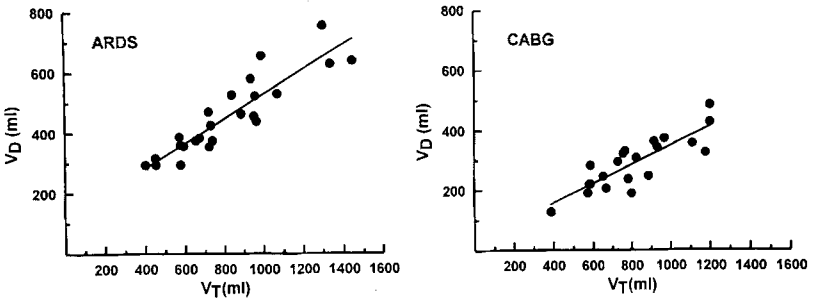

Fig. 2 The relationship between V_T and V_D. In ARDS, $V_D = 0.41 * V_T + 119$; r^2 0.82 ($P < 0.001$). In CABG, $V_D = 0.32 * V_T + 31$; r^2 0.70 ($P < 0.001$)

Table 4 Oxygen transport ($\dot{Q}$ cardiac output, $\dot{D}O_2$ oxygen delivery, PaO_2, PvO_2 O_2 partial pressure in arterial and mixed venous blood, $\dot{Q}_S/\dot{Q}_T$ fraction of venous admixture, $\dot{V}O_2$ oxygen consumption)

	$\dot{Q}$ ($l\,m^{2-1}\,min^{-1}$)	$\dot{D}O_2$ ($ml\,kg^{-1}\,min^{-1}$)	PaO_2 (kPa)	PvO_2 (kPa)	$\dot{Q}_S/\dot{Q}_T$ (fraction)	$\dot{V}O_2$ ($ml\,kg^{-1}\,min^{-1}$)
ARDS						
Baseline	4.7 ± 0.3[b]	15.5 ± 1.3[b]	8.1 ± 0.5[c]	5.2 ± 0.3	0.48 ± 0.02[c]	3.8 ± 0.2[a]
1.25 V_T	4.5 ± 0.4[b]	14.9 ± 1.3[a]	8.5 ± 0.5[b]	5.2 ± 0.3	0.46 ± 0.03[c]	3.7 ± 0.2[a]
0.75 V_T	4.9 ± 0.3[b]	15.4 ± 1.1[b]	7.9 ± 0.5[c]	5.3 ± 0.3	0.51 ± 0.03[c]	3.8 ± 0.2[a]
CABG						
Baseline	3.0 ± 0.3	10.6 ± 0.9	15.1 ± 1.2	4.7 ± 0.2	0.18 ± 0.03	3.3 ± 0.2
1.25 V_T	3.1 ± 0.3	10.8 ± 0.9	14.7 ± 1.7	4.7 ± 0.2	0.18 ± 0.03	3.2 ± 0.1
0.75 V_T	3.1 ± 0.3	11.0 ± 0.8	14.4 ± 1.0	4.7 ± 0.2	0.19 ± 0.03	3.3 ± 0.1

Analysis of variance: effect of V_T: not significant for any variable; difference between patient groups: P_aO_2 and $\dot{Q}_S/\dot{Q}_T$, $P < 0.001$, Q, $P < 0.01$, $\dot{D}O_2$ and $\dot{V}O_2$, $P < 0.05$; post hoc t-tests: difference between diagnostic groups: [a]$P < 0.05$, [b]$P < 0.01$, [c]$P < 0.001$

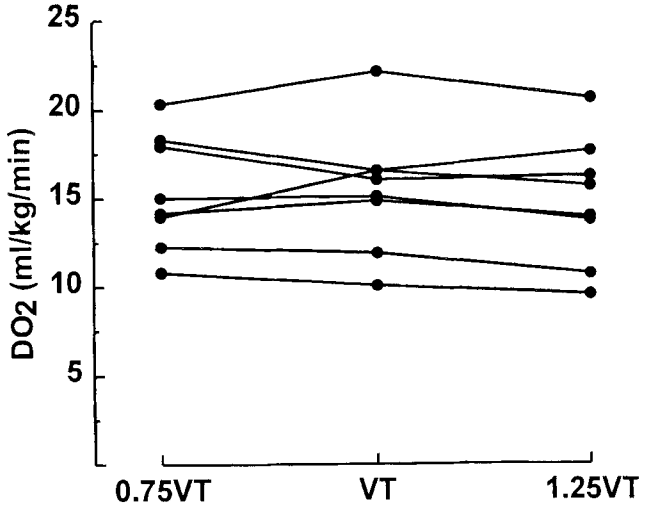

Fig. 3 Individual responses of oxygen delivery to changes in V_T in ARDS. V_T baseline ventilator settings; 0.75 V_T V_T decreased by 25% from baseline settings; 1.25 V_T V_T increased 25% from baseline settings

O_2 contents throughout the study (110 ± 4 ml/l in ARDS and 109 ± 7 ml/l in CABG at baseline, respectively). There were no significant changes in P_aO_2 during the experiment in either group. Arterial oxygen saturation (S_aO_2) tended to increase marginally in ARDS with the large V_T (86 ± 1%, 88 ± 2%, and 86 ± 1%, for baseline, and the large and the small V_T, respectively, NS), whereas it remained unchanged at 97 ± 1% in the CABG patients. This was associated with minor but consistent changes in arterial pH at the different V_T levels ($P < 0.05$; for ARDS: 7.384 ± 0.016, 7.395 ± 0.021, and 7.370 ± 0.014; for CABG: 7.469 ± 0.019, 7.470 ± 0.017, and 7.461 ± 0.018, for baseline and the large and the small V_T, respectively; $P < 0.01$ for ARDS vs CABG, and $P < 0.05$ for large V_T vs baseline in ARDS).

Intrinsic PEEP ($PEEP_i$) was 2.4 ± 1.2 cm H_2O in ARDS, and 0.3 ± 0.3 cm H_2O in CABG ($P < 0.05$). No changes were observed during the study in either group.

Discussion

The main observations following large changes in V_T with a constant $\dot{V}_E$ and inspiratory flow were a well-maintained gas exchange and oxygen transport at the low V_T, and that the V_T can be changed over a wide range without detrimental effect on arterial oxygenation.

In our earlier study, where V_T changes were accompanied by concomitant changes in $\dot{V}_E$ and inspiratory flow, $\dot{Q}$ and $\dot{D}O_2$ were inversely related to V_T [7]. In contrast, in the present study, $\dot{Q}$ and $\dot{D}O_2$ did not change despite substantial changes in V_T. However, a trend to improved $\dot{D}O_2$ at the low V_T was observed: five ARDS patients had the highest $\dot{D}O_2$ at the lowest V_T, and the lowest $\dot{D}O_2$ at the large V_T. The hemodynamic effects of mechanical ventilation are largely determined by the effect on mean airway pressure (P_{aw}mean) [16]. Since respiratory mechanics were not measured, we estimated the effects of a V_T change on the P_{aw}mean by the formula presented by Marini: $P_{aw}\text{mean} = (R_I^*\dot{V}/60 + V_T/2C + \text{PEEP})^*T_I/T_{TOT} + \text{PEEP } ^*T_E/T_{TOT}$, where R_I $\dot{V}$, C and PEEP represent inspiratory resistance, flow, compliance and end-expiratory pressure. Assuming R_I and C values typical of ARDS (e.g. $R_I = 4.5$ cm H_2O/L/s, C = 25 ml/cm H_2O, PEEP = 10, $T_I/T_{TOT} = 0.35$, baseline $V_T = 800$ ml, and a frequency of 19 breaths/min), changes in V_T such as in the present study can be expected to alter P_{aw}mean by only 6% in either direction. This probably explains the lack of significant hemodynamic alterations. In contrast, when the $\dot{V}_E$ is altered in parallel with V_T, changes in P_{aw}mean are much larger, and most likely explain the difference between the present findings and the quite substantial hemodynamic changes found in our previous study. Similarly, Leatherman and coworkers [17] found an increase in cardiac output, when V_T together with $\dot{V}_E$ and T_I was decreased at high PEEP levels.

When V_T is increased, a proportional increase in $\dot{V}_A$ may be expected. However, the change in $\dot{V}_A$ is attenuated by the concomitant change in V_D. No significant effect on $\dot{V}_A$ was observed in the current study, whereas $\dot{V}_A$ followed the changes in V_T when $\dot{V}_E$ was concomitantly changed [7]. We have previously shown a correlation between V_D and V_I in ARDS with changing $\dot{V}_E$ and inspiratory flow.

The V_D/V_T ratio was unchanged over a wide range of V_Ts [7]. A similar relationship between V_D and V_T has been shown by Cooper in mechanically ventilated anesthetized patients with normal lungs [18]. Also, Severinghaus and Stupfel, in a study on anesthetized dogs showed that V_{Dphys} correlates with V_T [19]. In their study, the relative contribution of alveolar $V_D(V_{Dalv})$ to the physiological V_D increased with increasing V_T, but V_D/V_T was affected little by V_T changes. In the present study, V_{Dphys} increased markedly with increasing V_T, but the V_D/V_T was slightly reduced in ARDS, indicating that the V_{Dphys} increased somewhat less than the V_T. Similarly, when V_T was decreased to the lowest level, the small increase in the V_D/V_T demonstrates that the V_{Dphys} decreased slightly less than the V_T. The full effect of the consequent decrease in $\dot{V}_A$ on P_aCO_2 at the small V_T was not evident in the 30-min observation period, as a steady state was not achieved in the gas exchange. At this point, the P_aCO_2 was marginally higher than at baseline (6.2 at 0.75 V_T vs 5.9 kPa at baseline), and no untoward hemodynamic effects were observed. However, if the metabolic CO_2 production is assumed to remain unchanged from baseline, the P_aCO_2 at a steady state would have reached 6.4 ± 0.3 kPa, still only slightly higher than with the baseline V_T. Thus, an increase in P_aCO_2, secondary to the reduced V_T, is counteracted by the concomitant reduction in V_D.

Large V_Ts (12–15 ml/kg), previously in common use, also increase the risk of barotrauma in the lung. Kolobow and coworkers demonstrated the connection of large V_Ts and high transpulmonary pressures with worsening of lung injury [2]. In ARDS, normoventilation can be maintained only at alveolar pressure that could damage the lung. Several studies have suggested that in ARDS, decrease of peak airway pressure and minimizing lung overdistention should be the primary goals. This may be accomplished by decreasing $\dot{V}_E$ and V_T, and consequently also $\dot{V}_A$. In retrospective studies, moderate, permissive hypercapnia has been associated with lesser lung injury and has enhanced survival in status asthmaticus [20] and ARDS [21]. According to the findings in the present study, a substantial decrease in V_T will induce only a modest increase in P_aCO_2. V_T can be decreased without impairing arterial oxygenation and $\dot{D}O_2$.

In conclusion, our results indicate that tidal volumes can be reduced in the treatment of severe hypoxemia without impairing oxygenation. The reduction in V_D together with V_T will minimize the effect of V_T reduction on $\dot{V}_A$.

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