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Advanced respiratory monitoring in COVID-19 patients: Use less PEEP!

Lisanne Roesthuis[1], Maarten van den Berg[1], Hans van der Hoeven[1]

[1] Department of Intensive Care Medicine, Radboud University Medical Center, Nijmegen, The Netherlands

Correspondence:

Lisanne Roesthuis, MSc

Geert Grooteplein-Zuid 10

6525 GA Nijmegen, The Netherlands

Lisanne.Roesthuis@Radboudumc.nl

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Introduction

With the emergence of Coronavirus disease 2019 (COVID-19) we are confronted with a new clinical picture of acute respiratory distress syndrome (ARDS) in the intensive care unit (ICU). Although patients with COVID-19 who are admitted to the ICU respond well to ventilation with high positive end-expiratory pressure (PEEP), we see in the majority of patients, that respiratory mechanics are very different from the "normal" ARDS patient (1). In patients with COVID-19 plateau pressures and driving pressures are often low and respiratory system compliance relatively normal compared to the ARDS patient (2). Many physicians use high PEEP for patients with COVID-19 although the potential for recruitment is often low (3). We fear that the high compliance of the respiratory system in combination with high PEEP will lead to hyperinflation, high dead space and potentially right ventricular failure. We have implemented the following strategy for all our COVID-19 patients (N = 45): after intubation we use a tidal volume of 6 ml/kg predicted body weight and immediately prone our patients for at least 3 days. We use the lowest possible PEEP to obtain adequate oxygenation with a FiO_2 of 50%. We increase PEEP according to the low PEEP/FiO_2 table when FiO_2 has to increase. We measured transpulmonary pressure and dead space ventilation to assess the effects of high and low PEEP levels on lung compliance and ventilation-perfusion mismatching.

Methods

Respiratory mechanics was assessed in COVID-19 patients admitted to the Radboud University Nijmegen Medical Center as part of standard patient care. Brief occlusions were performed to assess end-inspiratory and end-expiratory airway and transpulmonary pressures and to calculate driving pressures and respiratory and lung compliances as previously described (4, 5). In supine position the relative end-inspiratory transpulmonary pressure was

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calculated using the elastance ratio method, in prone position absolute transpulmonary pressures were used (6). Dead space ventilation was assessed using two methods:

1) The Bohr equation using partial pressure of carbon dioxide in alveolar air ($PACO_2$) and mixed expired air ($PeCO_2$): ($PACO_2 - PeCO_2$) / $PACO_2$. Both parameters were obtained by measuring flow and carbon dioxide tension (PCO_2) using the NICO capnograph (Philips Respironics, Murrysville, PA, USA). See our previous work for detailed description (7). Offline analysis was performed using MATLAB 2018a (MathWorks, Natick, MA, USA) using a method developed by Tusman and colleagues (8).

2) The Enghoff modification of Bohr's equation using partial pressure of carbon dioxide in arterial blood ($PaCO_2$) instead of $PACO_2$: ($PaCO_2 - PeCO_2$) / $PaCO_2$. Therefore, shunt and diffusion limitations are taken into the equation. $PeCO_2$ was obtained with volumetric capnography.

In addition, the ventilatory ratio was assessed as a simple bedside measure of ventilation correlating with physiological dead space fraction. It was computed as: (minute ventilation * $PaCO_2$) / (predicted body weight * 100 * 37.5) (9). In a few patients we assessed the effects of different positive end-expiratory pressure (PEEP) levels on these parameters.

Results

Advanced respiratory mechanics was assessed in 14 patients (8 males and 6 females, age (mean ± SEM) 67 ± 2 years, body mass index 28.0 ± 0.9 kg/m^2) between the 19th of March and 2nd of April. Respiratory parameters are shown in Table 1. Compliance of the respiratory system was low (42 ± 3 mL/cmH_2O) due to a lower than normal lung compliance (61 ± 5 mL/cmH_2O). However, compared to ARDS patients lung compliance was relatively high, resulting in low end-inspiratory transpulmonary pressures (12 ± 1 cmH_2O). COVID-19 patients

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had high dead space ventilation and gas exchange impairment (Bohr 52 ± 3%; Enghoff modification 67 ± 2%; ventilatory ratio 2.24 ± 0.23). Patient 14 had very high dead space ventilation, underwent CT-a and turned out to have pulmonary embolism.

Reducing PEEP resulted in an increase in lung compliance and decrease in dead space ventilation, except for patient 1 (Figure 1).

Discussion

We demonstrate that mechanically ventilated patients with COVID-19 have a relatively high lung compliance, high dead space ventilation and gas exchange impairment. In almost all patients lung compliance decreased with increasing PEEP levels. Dead space ventilation according to Bohr increased in all patients and according to Enghoff modification increased in 6/9 patients with increasing PEEP levels, albeit by a small amount.

The decrease in lung compliance and increase in dead space ventilation in response to higher PEEP levels indicate that COVID-19 lesions were not recruited and that higher PEEP levels cause hyperinflation of the more compliant parts of the lung. These results are in accordance with recent findings in COVID-19 patients. Pan et al. (3) found that the majority of patients had low recruitability with high PEEP levels. Recruitability seemed to improve with alternating body position (i.e. from supine to prone position). Liu et al. (10) computed the ventilatory ratio as a measure of ventilatory efficiency. They found a high ventilatory ratio in hypercapnic COVID-19 patients, which decreased when tidal volume was increased from 7 ± 0.6 to 7.7 ± 0.6 mL/kg. We found that the ventilatory ratio increased in accordance with Enghoff modification (not Bohr) in response to higher PEEP levels.

When lung compliance increases in response to higher PEEP levels (patient 1), recruitment is likely and PEEP should be set accordingly.

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Conclusions

In conclusion, we show that higher PEEP levels decrease lung compliance and in most cases increase dead space ventilation, indicating that high PEEP levels probably cause hyperinflation in patients with COVID-19. We suggest using prone position for an extended period of time (e.g. 3-5 days) and apply lower PEEP levels as much as possible.

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Figure legends

Figure 1 The effects of increasing positive end-expiratory pressure (PEEP) on lung compliance (N = 9) and dead space ventilation (N = 9). **A** Lung compliance decreased with increasing PEEP levels in 8 patients. **B** Dead space ventilation according to Bohr increased in all patients with increasing PEEP levels. **C** In response to higher PEEP levels dead space ventilation according to Enghoff modification (global gas exchange impairment) increased in 3 patients, first decreased and then increased in 3 patients, decreased in 2 patients and had no effect in 1 patient. **D** The ventilatory ratio could be determined in 8 patients and showed a similar trend as Enghoff modification.

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Tables

Table 1

Table 1 Respiratory mechanics

Patient No.	MV days	FiO_2	PaO_2/FiO_2 (mmHg)	$PaCO_2$ (mmHg)	$P_{plateau}$ (cmH_2O)	P_{drive} (cmH_2O)	$P_{L,e-i}$	$P_{L,drive}$ (cmH_2O)	C_{rs} (mL/cmH_2O)	C_L (mL/cmH_2O)	Enghoff (%)	Bohr (%)	Ventilatory ratio	Position
1	7	0.50	156	87	22	8	9	5	55	82	-	-	3.41	P
2	2	0.45	208	56	24	7	17	18	54	79	-	-	1.98	S
	3	0.55	124	57	26	8	-	-	48	-	66	47	2.04	S
3	0	0.50	228	44	23	9	17	16	47	62	66	56	1.42	S
4	1	0.60	123	44	-	-	-	-	-	-	71	58	1.83	P
5	0	0.40	214	48	23	13	9	9	40	54	55	42	1.47	P
	1	0.40	278	44	18	10	7	8	50	64	48	38	1.29	P
6[#]	1	0.45	143	49	-	-	-	-	-	-	63	40	-	P
7	1	0.55	183	55	23	14	11	10	36	50	60	42	1.55	P
8	1	0.40	176	52	16	8	7	5	56	95	64	51	1.65	P
9	0	0.95	98	61	29	12	14	9	38	50	-	-	2.63	P
	5	0.60	143	89	27	12	14	9	35	45	72	60	3.27	P
10	1	0.80	125	53	21	10	11	7	36	49	66	52	2.07	P
11	2	0.55	147	49	21	12	11	10	40	51	69	47	1.92	P
12	2	0.75	113	59	25	11	11	8	26	37	69	57	2.28	P
	3	0.65	111	47	26	12	11	8	27	40	71	60	2.16	P
13	1	0.50	192	67	24	12	10	7	47	76	82	74	4.22	P
14	6	0.70	150	62	28	15	15	11	31	43	65	52	2.65	S

C_{rs} = compliance of respiratory system; C_L = lung compliance; MV days = days of mechanical ventilation at time of measurement; $P_{L,e-i}$ = end-inspiratory transpulmonary pressure; $P_{L,drive}$ = transpulmonary driving pressure; P = prone position; S = supine position.

[#]Patient ventilated in pressure support mode, therefore the ventilatory ratio could not be determined.

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Figure 1