

Lung Mechanics in Type L CoVID-19 Pneumonia: A Pseudo-Normal ARDS.

Lorenzo Viola (✉ lorenzo.viola@auslromagna.it)

Ospedale Maurizio Bufalini <https://orcid.org/0000-0002-8959-8357>

Emanuele Russo

Ospedale Maurizio Bufalini

Marco Benni

Ospedale Maurizio Bufalini

Emiliano Gamberini

Ospedale Maurizio Bufalini

Alessandro Circelli

Ospedale Maurizio Bufalini

Luca Bissoni

Ospedale Maurizio Bufalini

Domenico Pietro Santonastaso

Ospedale Maurizio Bufalini

Giovanni Scognamiglio

Ospedale Maurizio Bufalini

Giuliano Bolondi

Ospedale Maurizio Bufalini

Luca Mezzatesta

Ospedale Maurizio Bufalini

Vanni Agnoletti

Ospedale Maurizio Bufalini

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Abstract

Background.

This study was conceived to provide systematic data about lung mechanics during early phases of CoVID-19 pneumonia, as long as to explore its variations during prone positioning.

Methods.

We enrolled four patients hospitalized in the Intensive Care Unit of “M. Bufalini” hospital, Cesena (Italy); after the positioning of an esophageal balloon, we measured mechanical power, respiratory system and transpulmonary parameters and arterial blood gases every 6 hours, just before decubitus change and 1 hour after prono-supination.

Results.

Both respiratory system and transpulmonary compliance and driving pressure confirmed the pseudo-normal respiratory mechanics of early CoVID-19 pneumonia (respectively, C_{RS} 40.8 ml/cmH₂O and DP_{RS} 9.7 cmH₂O; C_L 53.1 ml/cmH₂O and DP_L 7.9 cmH₂O). Interestingly, prone positioning involved a worsening in respiratory mechanical properties ($C_{RS,SUP}$ 56.3 ml/cmH₂O and $C_{RS,PR}$ 41.5 ml/cmH₂O – P 0.37; $C_{L,SUP}$ 80.8 ml/cmH₂O and $C_{L,PR}$ 53.2 ml/cmH₂O – P 0.23).

Conclusions.

Despite the severe ARDS pattern, respiratory system and lung mechanical properties during CoVID-19 pneumonia are pseudo-normal and tend to worsen during pronation.

Trial registration.

Restrospectively registered.

Background

Since its outbreak, in January, 2020, it has been clear that CoVID-19 pneumonia is atypical. Despite a full concordance to Berlin criteria for Acute Respiratory Distress Syndrome (ARDS), respiratory system mechanics is preserved [1]. Mechanical ventilation and muscular paralysis are recommended in worsening respiratory insufficiency [2]; in a substantial number of cases, prone positioning significantly improves oxygenation.

Little is known about isolated lung behavior in CoVID-19 pneumonia. Hence, the aim of this study is to analyze lung mechanical properties in the first hours after the beginning of mechanical ventilation and in prone and supine position.

Methods

A retrospective observational study was performed at Maurizio Bufalini hospital (Cesena, Italy). Patients hospitalized in the Intensive Care Unit (ICU) from 03/23/2020 to 04/10/2020 were enrolled. The inclusion criteria were: age > 18 years, need of mechanical ventilation, need of muscular paralysis and < 48 hours of tracheal intubation.

After admission in ICU, a naso-gastric tube with an esophageal balloon (Nutrivent® - SEDA S.p.A., Mirandola, Italy) was positioned; the correct positioning and insufflation volume were tested with the occlusion method and measures were recorded with a multiparametric monitor connected to esophageal balloon and ventilator circuit (Optivent® – SEDA S.p.A., Mirandola, Italy).

Protective ventilation, defined as tidal volume (V_t) of 5–7 ml/kg predicted body weight (PBW), was used. Respiratory rate (RR) was set to tolerate mild hypercarbia ($p_a\text{CO}_2 < 60$ mmHg) and/or $\text{pH} > 7.25$.

Measures were performed at admission, then every six hours or just before placing patients in prone or supine position and one hour after the change of decubitus. An arterial blood gas sample was collected along with every evaluation. We stopped measuring when muscular paralysis was suspended. Ventilator settings were recorded; static parameters were obtained through a 3 seconds inspiratory and expiratory hold. Airway (P_{AW}) and esophageal (P_{ES}) pressure values were recorded and the latter was used to calculate transpulmonary pressure (P_L), as the result of the real-time subtraction of P_{ES} to P_{AW} . Subsequently, compliance (C_{RS} , C_L), driving pressure (DP_{RS} , DP_L) and mechanical power (MP_{RS} , MP_L) related both to respiratory system and lung were calculated [3].

Results

We report data of four consecutive patients who fulfilled the inclusion criteria; two more patients were enrolled and excluded from the analysis – one died and the other was suspended myoresolution after enrollment. In all patients, chest computed tomography (CT) showed interstitial pneumonia without loss of parenchymal aeration; patients were put on mechanical ventilation within 24 hours of hospital admission. In Table 1 are summarized the main clinical and ventilatory features for every patient.

Table 1

Clinical features, ventilator settings and mechanical measurements of individual patients, in supine and prone position. BMI: Body Mass Index; I:E: inspiratory-to-expiratory ratio; PEEP: Positive End-Expiratory Pressure; P_{plat} : plateau pressure; $PEEP_{tot}$: total PEEP; DP_{RS} : Respiratory System Driving Pressure; C_{RS} : Respiratory System Compliance; MP_{RS} : Respiratory System Mechanical Power; $P_{L,end\ insp}$: Transpulmonary Pressure at end inspiration; $P_{L,end\ exp}$: Transpulmonary Pressure at end expiration; DP_L : Transpulmonary Driving Pressure; C_L : Transpulmonary Compliance; MP_L : Transpulmonary Mechanical Power; p_aO_2 : oxygen arterial partial pressure; $F_{I}O_2$: inspired fraction of oxygen; p_aCO_2 : carbon-dioxide arterial partial pressure; A-a O_2 gradient: alveolar-to-arterial oxygen gradient; EtCO $_2$ /p $_a$ CO $_2$ ratio: end-tidal CO $_2$ to p $_a$ CO $_2$ ratio.

	<i>Patient 1</i>		<i>Patient 2</i>		<i>Patient 3</i>		<i>Patient 4</i>	
	Supine	Prone	Supine	Prone	Supine	Prone	Supine	Prone
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
<i>Clinical features</i>								
Age	67		43	75		65		
Sex	M		M	F		M		
BMI (kg/m ²)	24.5		28,4	31,3		24,8		
Comorbidities	No		No	BPCO		No		
<i>Ventilator settings</i>								
Tidal volume (ml/PBW)	5.9 (0)	6.2 (0.04)	6.1 (0.3)	5.9 (0)	7.4 (0.1)	7,4 (0)	5.6 (0.2)	5.6 (0)
Respiratory rate (bpm)	22 (4.5)	19.5 (2.5)	20 (0.3)	20 (0)	20 (0)	20 (0)	28 (5)	25 (8)
I:E (sec)	0.51 (0.2)	0.48 (0.11)	0.56 (0.11)	0.64 (0.13)	0.5 (0)	0.5 (0)	0.43 (0.07)	0.53 (0.07)
PEEP (cmH ₂ O)	12 (3)	12 (0)	10 (1)	11 (1)	14 (0)	14 (0)	10 (2)	12 (0)
<i>Respiratory system mechanics</i>								
P_{plat} (cmH ₂ O)	19 (3)	20 (2.1)	21.8 (2.3)	21.5 (1.5)	23.6 (0.6)	24.7 (0.3)	23 (2.3)	27 (3)
$PEEP_{tot}$ (cmH ₂ O)	12.4 (2.5)	12.7 (0.4)	10.9 (0.9)	11.7 (1.3)	14.9 (0.2)	14.9 (0.1)	11 (3.7)	13 (2)
DP_{RS} (cmH ₂ O)	7 (0.7)	7.8 (1.4)	10.9 (1.4)	9.8 (0.2)	8.7 (0.7)	9.8 (0.3)	12 (1.8)	13.8 (1)

	<i>Patient 1</i>		<i>Patient 2</i>		<i>Patient 3</i>		<i>Patient 4</i>	
C_{RS} (ml/cmH ₂ O)	60.1 (6.3)	57.2 (17.7)	38.3 (3.6)	39.8 (0.8)	44.6 (4.2)	40 (1)	35.4 (4.7)	33.1 (2.3)
MP_{RS} (J/min)	16.9 (4.8)	16.4 (2)	15.7 (3.3)	15.8 (2.3)	17.9 (0.1)	18.2 (0)	25.6 (7.2)	27.6 (8.8)
<i>Lung mechanics</i>								
P_L , end insp (cmH ₂ O)	8.2 (3.2)	7.9 (3)	13.5 (2.2)	16 (1.9)	11.4 (2.6)	15.3 (0.2)	14.3 (1.5)	19.6 (7.6)
P_L , end exp (cmH ₂ O)	4.4 (2.2)	3 (1.5)	4.4 (2)	7.6 (1.6)	6.1 (2.1)	7.7 (0.5)	5.4 (1.7)	7.9 (5.8)
DP_L (cmH ₂ O)	4.4 (2.4)	5.2 (2.1)	9.2 (1.5)	8.4 (0.3)	5.4 (0.6)	7.6 (0.6)	8.8 (2.3)	11.5 (1.4)
C_L (ml/cmH ₂ O)	100.4 (54.5)	81.5 (23.3)	45.2 (7.4)	46.5 (1.7)	72.8 (8.4)	51.6 (4.1)	47.7 (9.6)	39.3 (4.6)
MP_L (J/min)	11.8 (2.5)	12.4 (1.2)	12.2 (1.6)	11.6 (0.9)	12.6 (0)	13.6 (0.2)	16.6 (4)	20.1 (6.8)
<i>Blood gas analysis</i>								
P_aO_2 (mmHg)	90.6 (13.3)	84.6 (53.6)	75.3 (16.8)	82.3 (12.4)	141.8 (54)	164.6 (16.9)	64.5 (17.8)	75.9 (16.9)
F_{IO_2} (%)	80 (22.5)	75 (17.5)	50 (2.5)	50 (0)	77.5 (22.5)	70 (0)	80 (10)	80 (5)
P_aCO_2 (mmHg)	68 (12.1)	58.1 (10.1)	50.4 (1.5)	40.6 (0.2)	53 (5.6)	45.3 (5.3)	52.1 (7.7)	53 (10.3)
pH	7.23 (0.05)	7.28 (0.06)	7.38 (0.03)	7.41 (0.01)	7.35 (0.04)	7.37 (0)	7.22 (0.05)	7.24 (0.06)
A-aO ₂ gradient (mmHg)	386.6 (153.1)	325.7 (47.1)	219.5 (5.3)	223.5 (12.2)	344.6 (113.4)	277.9 (35.2)	372.5 (71)	433.9 (82.3)
EtCO ₂ /p _a CO ₂ ratio	0.51 (0.09)	0.68 (0.25)	0.84 (0.03)	0.84 (0)	0.64 (0.05)	0.74 (0.19)	0.58 (0.06)	0.57 (0.01)

The median time of observation was 54.5 hours. Patients underwent 1.5 median cycles of pronosupination, for a median pronation time of 30 hours. Median V_t was 5.9 ml/kg PBW and median RR was 20 breaths per minute; MP_{RS} was 17.9 J/min, while MP_L was 13.1 J/min. Median C_{RS} and DP_{RS} were,

respectively, 40.8 ml/cmH₂O and 9.7 cmH₂O. The same parameters, calculated using the transpulmonary pressure, led to a median C_L of 53.1 ml/cmH₂O and a median DP_L of 7.9 cmH₂O.

No statistically significant variation was observed in respiratory system (C_{RS,SUP} 56.3 ml/cmH₂O; C_{RS,PR} 41.5 ml/cmH₂O – P 0.37) and lung (C_{L,SUP} 80.8 ml/cmH₂O; C_{L,PR} 53.2 ml/cmH₂O – P 0.23) mechanics during prone positioning.

Discussion

CoVID-19 pneumonia is peculiar: despite a severe hypoxemia, respiratory system mechanics is pseudo-normal [1]. Gattinoni *et al.* described a biphasic trend of the CoVID-19 pneumonia: in the initial phase – type L pneumonia – elastance is low, as well as recruitability, ventilation/perfusion ratio (V/Q ratio) and lung weight on CT scan. Conversely, in the second phase – type H pneumonia (20–30% of cases) – elastance, recruitability and lung weight are high and right-to-left shunt predominates [4, 5], thus framing in a classical form of ARDS. However, data regarding isolated lung mechanical properties in type L pneumonia are partial and disorganized.

We present preliminary data of a series of patients affected by type L pneumonia. Through the systematic evaluation of transpulmonary pressure, our findings seem to confirm the pseudo-normality of lung mechanics during the first days of mechanical ventilation and in different clinical settings. Even if lungs were severely damaged, the transpulmonary pressures remained below the thresholds commonly referred to as harmful [6], confirming a preserved lung aeration.

Another proof of the pseudo-normality of the respiratory system comes from the calculation of mechanical power [3]. Serpa Neto and coworkers found that risk for ventilation-induced lung injury (VILI) starts to increase from a value above 17 J/min [7]. Despite high ventilatory requests for maintaining acceptable p_aCO₂ and pH, in our series MP_{RS} remained at a borderline value of 17.9 J/min. In an experimental study, Cressoni *et al.* found that VILI occurs with a MP_L above 12 J/min [8]; our data show a median MP_L of 13.1 J/min, that is slightly above the harmful value. Therefore, while standard protective ventilation is unlikely to lead to VILI, we cannot clearly define whether the ventilatory demands in type L pneumonia are injurious to the lung.

Type L pneumonia is characterized by a profound hypoxemia, in most cases dramatically responsive to pronation. Prone positioning involves a redistribution of transpulmonary pressure throughout the lung and an inflation improvement in well perfused dorsal areas, leading to an amelioration of ventilation/perfusion ratio (V/Q ratio) [9]. We evaluated the V/Q ratio through alveolar-to-arterial oxygen gradient (A-aO₂ gradient) and end-tidal CO₂/p_aCO₂ ratio (EtCO₂/p_aCO₂ ratio) [5, 10] both in prone and supine positioning, just before the decubitus change. As expected, pronation entails a reduction of V/Q mismatch (A-aO₂ gradient_{SUP} 419 mmHg; A-aO₂ gradient_{PR} 310 mmHg – P 0.29; EtCO₂/p_aCO₂ ratio_{SUP} 0.6; EtCO₂/p_aCO₂ ratio_{PR} 0.71 – P 0.63); of note, C_{RS} and C_L worsen throughout pronation time (Fig. 1). In previous studies on primary ARDS, prone positioning did not substantially affect C_{RS} nor C_L [9]; although

this finding seems to further confirm the peculiarity of CoVID-19 pneumonia with respect to ARDS, its statistical and physio-pathological significance is limited by the small amount of data and a more targeted research is needed.

Conclusion

Our data underline the differences between classical ARDS and type L pneumonia, characterized by a pseudo-normal lung mechanics that deteriorates during prone positioning. Further research is needed to confirm this peculiar trend.

Abbreviations

A-aO₂ gradient: Alveolar-to-arterial Oxygen gradient

ARDS: Acute Respiratory Distress Syndrome

C_{RS}: Respiratory System Compliance

C_{RS,SUP}: Respiratory System Compliance, Supine

C_{RS,PR}: Respiratory System Compliance, Prone

C_L: Transpulmonary Compliance

C_{L,SUP}: Transpulmonary Compliance, Supine

C_{L,PR}: Transpulmonary Compliance, Prone

CoVID-19: Coronavirus Infectious Disease-19

CT: Computed Tomography

DP_{RS}: Respiratory System Driving Pressure

DP_L: Transpulmonary Driving Pressure

EtCO₂/p_aCO₂ ratio: end-tidal CO₂/p_aCO₂ ratio

ICU: Intensive Care Unit

MP_{RS}: Respiratory System Mechanical Power

MP_L: Transpulmonary Mechanical Power

p_aCO₂: carbon dioxide arterial partial pressure

P_{AW} : Airway Pressure

PBW: Predicted Body Weight

P_{ES} : Esophageal Pressure

P_L : Transpulmonary pressure

RR: Respiratory Rate

V/Q ratio: Ventilation/Perfusion ratio

VILI: Ventilation-Induced Lung Injury

V_t : Tidal Volume

Declarations

- Ethics approval and consent to participate: this study was approved by the Ethical Committee of AUSL Romagna.
- Consent for publication: not applicable.
- Availability of data and materials: the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
- Competing interests: the authors declare that they have no competing interests.
- Funding: not applicable.
- Authors' contributions: LV: study design, data collection, writing of the manuscript; ER: study design, writing of the manuscript; MB: study design, data collection; EG: data collection; AC: data collection; LB: data collection; DPS: data collection; GS: data collection; GB: data collection; LM: data collection; VA: study design, writing of the manuscript. All authors read and approved the final manuscript.
- Acknowledgements: not applicable.

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Figures

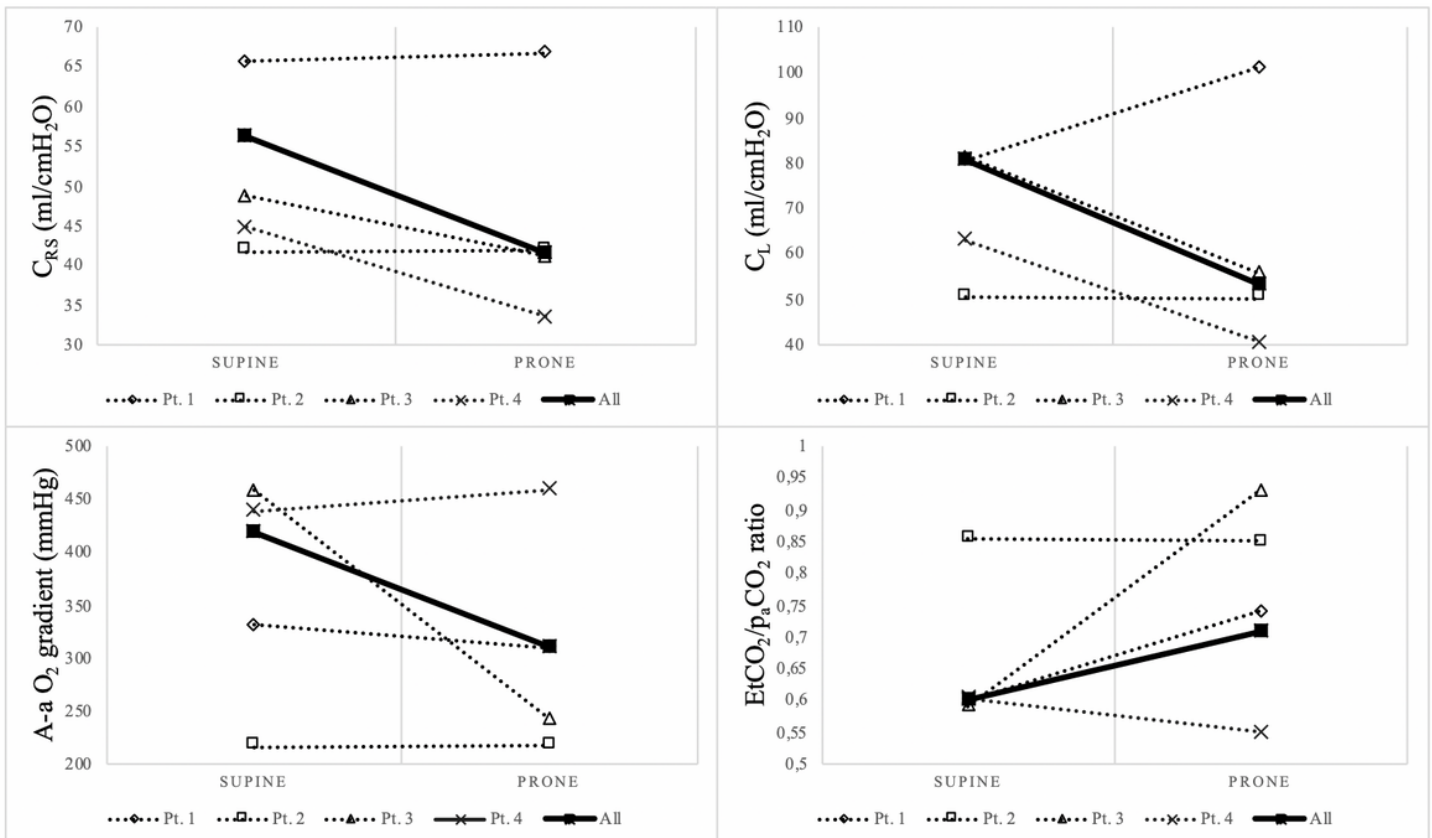


Figure 1

Mechanical and Ventilation/Perfusion ratio variations in supine and prone positioning, just before decubitus change. CRS: Respiratory System Compliance; CL: Transpulmonary Compliance; A-aO₂ gradient: alveolar-to-arterial oxygen gradient; EtCO₂/paCO₂ ratio: end-tidal CO₂ to paCO₂ ratio.