Comparing lung mechanics of patients with COVID related respiratory distress syndrome versus non-COVID acute respiratory distress syndrome: a retrospective observational study

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Abstract

Background

Most patients admitted to the intensive care unit with coronavirus disease (COVID-19) develop severe respiratory failure. Understanding lung mechanics helps to guide protective mechanical ventilation, improve oxygenation, and reduce the ventilator induce lung injury. This study aims to describe lung mechanics characteristics of patients with COVID -19 related acute respiratory distress syndrome (CARDS) and to compare them with non-COVID-19 associated ARDS.

Methods

We performed a retrospective observational study of lung mechanics: plateau pressure (Pplat), Driving pressure (DP), Mechanical power (MPw), Elastic (dynamic) power (EdPw), Total ventilatory power (TPw), and oxygenation parameters (ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO_2/FiO_2), the ratio of arterial oxygen partial pressure to fractional inspired oxygen multiplied by PEEP [$PaO_2/(FiO_2$ x PEEP)], arterial and venous carbon dioxide partial pressure ($PaCO_2$, $PvCO_2$), and Ventilation dead space (VD) were measured and compared between the two groups after initiation of mechanical ventilation.

Results

30 CARDS and 10 ARDS patients fulfilled the study requirements. We observed a significant higher MPw in the CARDS group (29.17 ± 8.29 J/min vs 15.78 ± 4.45 J/min, P 0.007), similarly observed with EdPw (256.7 ± 84.06 mJ/min vs 138.1 ± 39.15 mJ/min, P 0.01) and TPw (289.1 ± 84.51 mJ/min vs 161.5 ± 45.51, P 0.007). Inside the CARDS group, we found 2 subgroups, a low shunt subgroup and a higher shunt (Qs/Qt (%): 6.61 ± 2.46 for vs 40.3 ± 20.6, P 0.0009), however, between these two subgroups we didn't find statistical differences on lung mechanic parameters but only in oxygenation parameters (PaO_2/FiO_2 and PaO_2/FiO_2*PEEP). When comparing these two subgroups with ARDS patients, we found more similarity between the low shunt CARDS and the ARDS patients on MP (R^2 0.99, P 0.001), EdPw (R^2 0.89, P 0.05) and TPw (R^2 0.99, P 0.0009).

Conclusions: Our study suggests important differences between CARDS and ARDS regarding mechanical parameters that could lead to more complicated management of CARDS patients and a higher prevalence of VILI. However due to the study limitations, a bigger study is necessary to corroborate our findings.

Keywords: COVID-19, CARDS, ARDS, lung mechanics, VILI.

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Introduction

Most patients admitted to the intensive care unit (ICU) with coronavirus disease (COVID-19) develop severe respiratory failure; however, some reports may disagree if the COVID-19 associated respiratory syndrome (CARDS) shares or not the same pathophysiology and lung mechanic characteristics of the "classic" acute respiratory distress syndrome (ARDS) non-associated to COVID-19.[1] To date, several groups studied aspects of lung mechanics in patients with CARDS finding a high heterogeneity between patients, some more likely ARDS patients, some identifying different phenotypes.[2] Gattinoni and et al proposed reconciliation and proposed two phenotypes according to the interaction between the time course and severity of the disease, and the patient's ventilatory response, the early L-type phenotype was characterized with low lung elastance and low recruitability and a late H-type phenotype with high lung elastance and high recruitability.[3]

According to the equation of motion of the respiratory system, the energy applied to the respiratory system depends on the elastic and resistive mechanical properties of the lung to an applied tidal volume, inspiratory flow, and positive end expiratory pressure (PEEP) level.[1] By this means, the driving pressure (DP) represents just the pressure amount of pressure applied to the system to a given tidal volume (V_T) and is strongly affected by lung compliance, but on the other hand, the mechanical power (MP) integrates the elastic and resistive components in a period and to a given PEEP making it possibly a method better to predict ventilator induced lung injury (VILI).

In today's healthcare, the practice of precision medicine has become a standard of care by applying personalized therapy guided by physiological measurements. In 2020, Rocco et al proposed in an experimental model that some other lung mechanic parameters that may play an important role in VILI; they proposed that elastic power (dynamic power) parallels total power as a VILI risk indicator when PEEP is the primary tidal variable used to influence cumulative stress exposure,[4] however, these parameters have not been studied on ARDS or CARDS patients.

The systematic assessment of lung mechanics helps to understand the severity of the patient condition to guide protective mechanical ventilation settings to improve oxygenation and reduce possible (VILI).[5] However, despite the great effort to understand the pathophysiology of CARDS and its difference/similarity to the classical ARDS, there are still some questions in the understanding of CARD pathophysiology. This study aims to describe the oxygenation, and respiratory mechanics such as compliance, DP, tidal, elastic, mechanical and total ventilation power characteristics of patients with CARDS and to compare it with non-COVID-19 associated ARDS.

Methods

This is a single center retrospective study performed at the Péterfy Sándor Hospital in Budapest, Hungary from 1st January 2021 to December 30th, 2021. We recruited the data from patients with positive RE-PCR for COVID-19 and patients with ARDS with negative RE-PCR for COVID-19, admitted in the intensive care unit (ICU) and treated with mechanical ventilation.

Patients with history of chronic obstructive pulmonary disease, acute or chronic heart failure, circulatory shock (mean arterial pressure <65 mmHg or in vasopressors/inotropes treatment), pregnancy, recent pulmonary embolism, pneumothorax, chronic kidney disease (eGFR < 60mL/min/1.73m^2), body mass index >30 and older than 65 years old were excluded from the study, as well those patients were all the necessary data required for the study was not written at the 1st hour after initiation of invasive ventilatory support.

After the approval by the institution ethical committee and with waiver of informed consent, we extracted the demographic data and the first data after intubation regarding lung mechanics, oxygenation, and perfusion. Initial ventilatory parameters were set at the discretion of the treating intensivist in Pressure-regulated volume control mode (PRVC) with a PEEP of 10 cmH_2O, and the goal to optimize oxygenation (PaO_2 > 60 mmHg) with the lowest V_T per Kg of predicted body weight, plateau pressure (Pplat) <30 cmH_2O, DP <14 cmH_2O. As a part of routine clinical care, all patients were sedated, and neuromuscular blockade.

The data was extracted from the electronic medical records at the first measurements after intubation. Set fraction of inspired oxygen (FiO_2), Pplat, PEEP, respiratory rate (RR), peak pressure (Ppeak), V_T, dynamic and static compliance (DC = V_T/Ppeak-PEEP, SC=V_T/Ppl-PEEP), arterial and venous oxygen partial pressure (PaO_2, PvO_2), arterial and oxygen saturation (SaO_2, SvO_2), arterial and venous carbon dioxide partial pressure ($PaCO_2$, $PvCO_2$) and hemoglobin concentration.

Derived from these parameters we calculated the ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO_2/FiO_2), the ratio of arterial oxygen partial pressure to fractional inspired oxygen multiplied by PEEP [$PaO_2/(FiO_2$xPEEP)], DP (inspiratory hold pressure (Pplat) - expiratory hold pressure (total PEEP), MP (MPw = minute ventilation (MV) in liters/minute, the inspiratory flow (F) in liters/minute, and Ppeak and PEEP in centimeter of water), MP normalized by respiratory system compliance [MP/Crs = MPw/(V_T/DP)], elastic (dynamic) power (EdPw = V_T × RR × [(Pplat + PEEP)/2], Total ventilatory power (TPw = ((MV/2) × [2 (Ppeak) − Pplat + PEEP]), Physiologic shunt (Qs/Qt = capillary oxygen content (CcO_2) - arterial oxygen content (CaO_2) / CcO_2 - mixed venous oxygen content (CvO_2) x 100), Physiologic dead space (PhyD = (V_T x ($PaCO_2$-$PECO_2$))/$PaCO_2$) and Ventilation dead space (VD = PhyD x RR).

Each variable was tested for normality using the Kolmogorov–Smirnov test. Data are presented as mean ± SD unless otherwise specified. Comparisons among lung functional data between CARDS and ARDS were performed using nonparametric tests. All tests were performed in GraphPad Prism v9.0.0 (GraphPad software San Diego, CAUSA). Significance was established at p value less than 0.05.

Results

From an initial population of 286 patients, a total of 30 CARDS and 10 ARDS patients were included fulfilling all the necessary data for this study. There were no significant differences between the two groups in pre-intubation oxygenation (PaO_2/FiO_2 CARDS 80.33 ± 20.39 vs ARDS 70.5 ± 21.0, P 0.41), age (CARDS 54 ± 10,1 years vs ARDS 48.5 ± 13.22 years, p = 0.28), or gender (CARDS males 45.16% vs ARDS 40%). We did not find differences between VT settings between the two groups (CARDS VT 4.8 ± 0.83 ml/Kg/PBW vs ARDS 4.75 ± 0.95 ml/Kg/PBW, P 0.81).

From lung mechanics only three parameters were significantly different between CARDS and ARDS, MP was significantly higher on the CARDS group (29.17 ± 8.29 J/min vs 15.78 ± 4.45 J/min, P 0.007) as well the normalized MP/Crs (0.75 ± 1.81 J/min/cmH_2O for CARDS vs 0.3 ± 0.08 J/min/cmH_2O for ARDS with P <0.0001), , the elastic (dynamic) power was higher on CARDS compared to ARDS (256.7 ± 84.06 mJ/min vs 138.1 ± 39.15 mJ/min, P 0.01) as the total ventilation power as well (289.1 ± 84.51 mJ/min vs 161.5 ± 45.51 mJ/min, P 0.007).

Concerning the other mechanical parameters, there was no significant difference between the two groups (table 1).

One interesting result was that, even when the physiologic shunt between CARDS and ARDS was not statistically significant (P 0.13), we found that inside CARDS two subgroups, one with a lower shunt (n=17) and one with a higher shunt (n=13) where the physiologic shunt Qs/Qt (%) was 6.61 ± 2.46 vs 40.3 ± 20.6, P 0.0009. However, inside these two subgroups we didn't find more differences than shunt level and oxygenation, were PaO_2 (95.13 ± 29.9 mmHg vs 57.65 ± 8.44 mmHg, P 0.005), PaO_2/FiO_2 (109.00 ± 38.98 ps 73.13 ±22.25, p = 0.04) and PaO_2/FiO_2 x PEEP (90.13 ± 52.57 vs 224.8 ± 61.94, P 0.0004) were significantly higher on the low shunt subgroup vs the higher one (Table 2)

When comparing the two CARDS subgroups between ARDS lung mechanics we observed similarity between ARDS and low shunt CARD patients in MP (R^2 0.99, P 0.001), normalized MP/Crs (R^2 0.96, P 0.04), Elastic (dynamic) power (R^2 0.89, P 0.05) and Total ventilatory power (R^2 0.99, P 0.0009). (Table 3).

Discussion

Since the introduction of COVID-19 pandemic started the controversy that if COVID-19 leads or not to a typical ARDS. Gattinoni and colleagues supported the idea that CARDS is not a typical ARDS based in a study on 16 patients with CARDS where during severe hypoxemia those patients had a relative preserved respiratory system compliance and a good lung aeration level on the CT scan.[6] In our study we also found that in patients with severe hypoxia (PaO_2/FiO_2 <150 before intubation), the compliance was relative non-compromised (Static compliance 96.1 ± 133 cmH_2O and dynamic compliance 57.2 ± 49.5 cmH_2O) with no statistical differences between CARDS and ARDS.

However, the same group of Gattinoni and colleagues, in a different publication, also described two CARDS phenotypes and named L and H.[3] The L type was characterized by a low elastance, low ventilation-to-perfusion ratio, low lung weight and low lung recruitability contrary to the H type. The importance of determining the mechanical differences is crucial to avoid VILI and select the most appropriate strategy to improve oxygenation and ventilation.

	CARDS (n=30)		ARDS (n=10)		
	mean	**SD**	**mean**	**SD**	**P value**
PaO_2 (mmHg)	75.1	28.1	104.2	23.11	0.076
PaO_2/FiO_2	90.7	35.47	203	58.35	***< 0.0001***
$PaO_2/(FiO_2$*PEEP)	90.13	52.57	224.8	61.94	***0.0004***
Plateau pressure (cmH_2O)	25.8	9.76	21.5	4.79	0.41
Driving pressure (cmH_2O)	14.6	8.26	14	4.24	0.89
Mechanical power (J/min)	29.17	8.29	15.78	4,45	***0.007***
MP/Crs (J/min/cmH_2O)	0.75	1.81	0.3	0.08	***< 0.0001***
Tidal power (J/min)	18.59	11.27	10.55	3.46	0.18
Dynamic compliance (cmH_2O)	57.21	49.52	42.45	12.3	0.56
Static compliance (cmH_2O)	96.13	13.4	53.38	16.72	0.53
Elastic dynamic power (mJ/min)	256.7	84.06	138.1	39.15	***0.01***
Total ventilation power (mJ/min)	289.1	84.51	161.5	45.51	***0.007***
Physio dead space (ml/Kg)	6.24	2.04	4.07	2.4	0.08
Alveolar ventilation (ml/Kg/min)	134.6	48.9	56.38	28.15	***0.007***
Physiologic shunt Qs/Qt (%)	24.58	22.76	6.32	4.04	0.13

Table 1. Oxygenation and lung mechanic parameters from CARDS and ARDS patients.

	Low shunt (n=17)		High shunt (n=13)		P value
	mean	SD	mean	SD	
Physiologic shunt Qs/Qt (%)	6.61	20.6	40.2	20.6	***0.0009***
PaO_2 (mmHg)	95.13	29.9	57.65	8.44	***0.005***
PaO_2/FiO_2	109	38.98	73.13	22.25	***0.04***
$PaO_2/(FiO_2$*PEEP)	100.7	57.19	80.88	50.15	0.48
Plateau pressure (cmH_2O)	22.57	6.21	28.63	11.75	0.24
Driving pressure (cmH_2O)	10.57	4.23	18.13	9.52	0.07
Mechanical power (J/min)	25.84	5.65	32.09	9.46	0.15
MP/Crs (J/min/cmH_2O)	0.41	0.22	1.04	0.06	0.24
Tidal power (J/min)	13.09	6.81	23.4	12.55	0.07
Dynamic compliance (cmH_2O)	65.46	51.85	50	49,73	0.56
Static compliance (cmH_2O)	128.8	179.6	67.51	76.92	0.39
Elastic dynamic power (mJ/min)	225.7	56.04	283.8	98.17	0.19
Total ventilation power (mJ/min)	264.1	58.06	327.8	96.47	0.15
Physio dead space (ml/Kg)	6.44	1.46	6.06	2.54	0.73
Alveolar ventilation(ml/Kg/min)	134.1	37.05	135.1	60.04	0.96

Table 2. Oxygenation and lung mechanic parameters from low and high physiologic shunt CARDS patients.

	Low shunt CARDS				High shunt CARDS				ARDS	
	mean	SD	R^2 vs ARDS	P	mean	SD	R^2 vs ARDS	P	mean	SD
PaO_2 (mmHg)	95.13	29.9	0.36	0.39	57.65	8.44	0.01	0.88	104.2	23.11
PaO_2/FiO_2	109	38.98	0.12	0.64	73.13	22.25	0.04	0.78	203	58.35
$PaO_2/(FiO_2$*PEEP)	100.7	57.19	0.06	0.73	80.88	50.15	0.02	0.85	224.8	61.94
Plateau pressure (cmH_2O)	22.57	6.21	0.4	0.36	28.63	11.75	0.33	0.42	21.5	4.79
Driving pressure(cmH_2O)	10.57	4.23	0.41	0.35	18.13	9.52	0.37	0.38	14	4.24
Mechanical power (J/min)	25.84	5.65	***0.99***	***0.001***	32.09	9.46	0.29	0.46	15.78	4.45
MP/Crs (J/min/cmH_2O)	0.4.	0.22	***0.95***	***0.04***	1,04	0.06	0.72	0.28	0.31	0.09
Tidal power (J/min)	13.09	6.81	0.04	0.79	23.4	12.55	0.81	0.1	10.55	3.46
Dynamic compliance(cmH_2O)	65.46	51.85	0.25	0.49	50	49.73	0.5	0.29	42.45	12.3
Static compliance(cmH_2O)	128.8	179.6	0.09	0.69	67.51	76.92	0.21	0.53	53.38	16.72
Transp. driving pressure (cmH_2O)	21.01	13.23	0.18	0.57	23.95	8.87	0.42	0.34	16	4.08
Elastic dynamic power (mJ/min)	225.7	56.04	***0.89***	***0.05***	283.8	98.17	0.36	0.39	138.1	39.15
Total ventilation power (mJ/min)	264.1	58.06	***0.99***	***0.0009***	327.8	96.47	0.28	0.46	161.5	45.51
Physio dead space (ml/Kg)	6.44	1.46	0.05	0.77	6.06	2.54	0.007	0.91	4.07	2.4
Alveolar ventilation (ml/Kg/min)	134.1	37.05	0.00002	0.99	135.1	60.04	0.42	0.34	56.38	28.15
Physiologic shunt Qs/Qt (%)	6.61	2.46	0.34	0.41	22.58	20.62	0.15	0.61	6.32	4.09

Table 3 Oxygenation and lung mechanic parameters from low and high physiologic shunt CARDS Vs ARDS patient

In our study, we did not find differences in elastance inside our COVID group but between CARDS and ARDS, but we found a significant difference in MP (29.17 ± 8.29 in CARDS vs 15.78 ± 4.45 in ARDS, P 0.007) and the normalized MP/Crs (0.75 ±1.81 J/min/cmH_2O for CARDS vs 0.3 ± 0.08 J/min/cmH_2O for ARDS with P <0.0001), being higher on the CARDS group. Normalization of MP to several components such as body weight, well-inflated tissue, compliance, and lung gas volume has been investigated recently, and from those, MP/Cr as well MP/well-inflated tissue were the only ones independently associated with ICU mortality in ARDS patients (RR 1.79, 95% CI 1.16 - 2.76) by Coppola and colleagues in 2020.[7] Unfortunately, one limitation of our study was not having access to the final outcomes of the patients, to observe this effect in our sample.

The elastic component was also compromised more in the CARDS patient's vs ARDS patients, we

observed an Elastic dynamic power (256.7 ± 84.06 CARDS vs 138.1 ± 39.15 ARDS, P 0.01) higher in the CARDS group vs ARDS group, as well in the total ventilation power (289.1 ± 84.51 CARDS, 161.5 ± 45.51 ARDS, P 0.007).

The tidal energy delivered during mechanical ventilation is determined by the product of the applied stress and the resulting incremental strain in the lung. Recent literature has demonstrated that all component of the energy interacts with one another with the potential of developing VILI,[8,9] regarding this concept, Rocco and colleagues[4] dissected these components in three main parameters: the driving power the (V_T x DP × RR), which is the energy applied to the lung parenchyma without taking into account the PEEP, the elastic dynamic power which is the dynamic power but taking into account the energy applied by PEEP and total power which includes all dynamic and static pressures that influence strain during V_T delivery and accounts for the rate at which tidal energy is repeated.

Roccoo and colleagues observed an important correlation between the elevation of these parameters, in special the elastic dynamic power and the development of VILI.[4] The significative higher values in CARDS patients compared with ARDS patients corresponds to the higher prevalence of VILI found in CARDS patients in the last years, this can be due to the lower elastance and as observed in our cases, higher power required to ventilate the lungs.[10,11]

The alveolar ventilation is defined as the volume of air that reaches the alveoli in a unit of time, this parameter provides information about the volume of gas that takes part in gas exchange at the alveolar-capillary interface and its reduction results in hypercapnia.[12] We found that CARDS patients had a significant higher alveolar ventilation than ARDS patients (134.6 ± 48.9 CARDS vs 56.38 ± 28.15 ARDS, P 0.0076). Alongside this finding, CARDS patients had higher physiological dead space that ARDS patients, however, this difference was not statistically significant (6.24 ± 2.04 CARDS vs 4.07 ± 2.41 ARDS, P 0.08).

A study reported by Diehl and colleagues [13] in 2020 found that severe CARDS patients at the initial hours observed high physiological dead space, hypothesizing that it can be a result of alveolar overdistention with compression of intra-alveolar vessels in some pulmonary territories in relation to a high-PEEP, however, in patients with low PEEP this phenomenon was still observed. In our study we also observed a high physiological shunt, however, we also found that some patients had higher shunt that other leading to worsening of oxygenation, they hypothesized that this phenomenon the COVID-19 unusual diffuse microcirculatory dysfunction, strongly associated with ACE-2 receptor mediated endothelial disfunction may lead to activation of the hypercoagulation state observed in COVID-19 patients leading to this increase in pulmonary shunt.

Limitations

Due to uncomplete data from admission notes, from an initial population of 286 patients, the sample included in this study was limited to 30 COVID patients and 10 non-COVID patients. A larger more standardized study may be necessary to corroborate our findings. All the measurements were done at one time immediately after intubation with no repeated measures included in the analysis. We did not have access to the outcome of this patients like mortality, ventilation days or duration of mechanical ventilation.

Conclusions

Our study suggests important differences between severe CARDS and ARDS regarding mechanical parameters what could lead to the more complicated management of CARDS patients and higher prevalence of VILI. CARDS patients with lower shunt may share more lung mechanic similarities to ARDS patients.

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