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ORIGINAL ARTICLE

Lung mechanics in pediatric acute respiratory distress syndrome associated to acute COVID-19 and MIS-C: implications for therapies and outcomes

Mecánica pulmonar en el síndrome de distrés respiratorio agudo pediátrico asociado a COVID-19 aguda y MIS-C: implicaciones para las terapias y los resultados

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What do we know about the subject matter of this study?

Pulmonary involvement caused by SARS-CoV-2 in children has different clinical manifestations that could be categorized as pulmonary phenotypes and their recognition could have a potential impact on clinical management.

What does this study contribute to what is already known?

Differences in pulmonary mechanics between MIS-related PARDS and C-related PARDS could contribute to the application of more appropriate ventilation strategies in both groups of critically ill patients.

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EDITORIAL IKU

Abstract

Objective: To describe lung mechanics in Pediatric Acute Respiratory Distress Syndrome (PARDS) associated with acute COVID-19 and MIS-C with respiratory failure. **Methods:** A concurrent multicenter observational study was performed, analyzing clinical variables and pulmonary mechanics of PARDS associated with COVID-19 in 4 Pediatric intensive care units (PICU) in Peru. The subgroup analysis included PARDS associated with multisystem inflammatory syndrome in children (MIS-C), MIS-PARDS, and PARDS with COVID-19 primary respiratory infection, C-PARDS. In addition, receiver operating characteristic (ROC) curve analysis for mortality and lung mechanics was performed. **Results:** 30 patients were included. The age was 7.5 (4-11) years, 60% were male, and mortality was 23%. 47% corresponded to MIS-PARDS and 53% to C-PARDS groups. C-PARDS had positive RT-PCR in 67% and MIS-PARDS none ($p < 0.001$). C-PARDS group had more profound hypoxemia (P/F ratio < 100, 86% vs. 38%, $p < 0.01$) and higher driving-pressure [14(10-22) vs 10(10-12) cmH_2O], and lower compliance of the respiratory system (CRS) [0.5 (0.3-0.6) vs 0.7(0.6-0.8) ml/kg/cmH_2O] compared with MIS-PARDS (all $p < 0.05$). The ROC analysis for mortality showed that driving pressure had the best performance [AUC 0.91(95%CI0.81-1.00), with the best cut-off point of 15 cmH_2O (100% sensitivity and 87% specificity). Mortality in C-PARDS was 38% and 7% in MIS-PARDS ($p = 0.09$). MV-free days were 12(0-23) in C-PARDS and 23(21-25) in MIS-PARDS ($p = 0.02$). **Conclusion:** Patients with C-PARDS have lung mechanics characteristics similar to classic moderate to severe PARDS. This was not observed in patients with MIS-C. As seen in other studies, a driving pressure ≥ 15 cmH_2O was the best discriminator for mortality. These findings may help guide ventilatory management strategies for these two different presentations.

Keywords:
PARDS;
COVID-19;
MIS-C;
Pulmonary Mechanics;
Driving Pressure

"Take-home message"

- PARDS associated with acute COVID-19 and MIS-C respiratory failure are two different entities with different lung mechanics.
- C-PARDS group was characterized as a classic moderate to severe PARDS. MIS-PARDS presented a higher gradient between peak pressures and plateau pressures.
- Clinical outcomes revealed that C-PARDS had less VFD and a trend toward higher mortality.
- Data from the quasi-static calculations were associated with mortality; DP ≥ 15 cmH_2O was the best discriminator.

Background

Respiratory failure has been the leading cause of hospital admission and death during the COVID-19 pandemic. Patients develop pneumonia leading to severe acute respiratory distress syndrome (ARDS) which is a frequent cause of admission to intensive care for advanced respiratory support, especially in adult populations[1]. However, since the first cohorts' description in China and Europe, many authors reported discrepancies between the severity of the oxygenation and the relatively spared pulmonary mechanics in a subgroup of patients[2,3]. In addition, atypical lung imaging in chest CT scan and histopathology with lung microvascular involvement raises questions about whether the underlying pathophysiology in COVID-19 is like that of ARDS in other etiologies2,4,5,6. Thus, a new entity called C-ARDS (COVID-19-associated ARDS) is proposed by some researchers[7-9].

Pediatric COVID-19 critical illness is heterogeneous and infrequent[10-12]. The most common causes of admission to the pediatric intensive care unit (PICU) are respiratory failure in acute COVID-19 and severe multisystem inflammatory syndrome in children (MIS-C)[10-15]. The latter has been associated with different presentations and a large group of patients with MIS-C also have predominantly respiratory failure [6,16]. While the low morbidity and mortality in the general pediatric population are reassuring, there is a significant gap in knowledge in identifying high-risk subgroups, such as those who develop pediatric ARDS (PARDS) or multiorgan failure[11,12,17].

Invasive mechanical ventilation (MV) for pediatric COVID-19 at PICU has been reported between 30% to 70% in different cohorts[11,13,15,18-20]. For patients with MIS-C and respiratory failure the need for MV has been reported around 15%-18%[12]. Surprisingly, specific information on PARDS related to COVID-19 and MIS-C is scarce. The heterogeneous nature of lung involvement generated the hypothesis of distinctive phenotypes in adult C-ARDS based on pulmonary mechanics[2]. Although still controversial, different phenotypes might have implications for therapy and outcomes[21,22]. This principle also applies to respiratory failure and PARDS secondary to acute COVID-19 and MIS-C. A better description of PARDS characteristics

is urgently needed to improve guidelines and recommendations and ultimately improve outcomes for critically ill children.

This study aimed to describe lung mechanics in critically ill children with PARDS due to COVID-19, analyzing patients with MIS-C with respiratory failure (MIS-PARDS) and severe COVID-19-related PARDS (C-PARDS) and their correlation to clinical outcomes.

Methods

An observational study was conducted in four PICU of pediatric referral hospitals in Perú: *Hospital Nacional Hipolito Unanue, Hospital de Emergencias de Villa El Salvador, Hospital Regional del Cusco, and Hospital Edgardo Rebagliati Martins*. Institutional review boards' approval for data collection was obtained at each hospital, waiving informed consent. The participating sites hospitals included general units with 6-12 beds pr unit, one attending for every 6 beds and 1 nurse for every 2 patients. These units did not have a high-frequency oscillatory ventilator, nitric oxide, extracorporeal membrane oxygenation or renal replacement therapy.

Patients and diagnosis definitions

The study included patients between 1 month and 17 years of age from the pediatric intensive care unit (PICU) Registry of COVID-19 admitted between April 1 and August 31, 2021. Briefly, this observational registry recorded the treatment and the management of critical COVID-19 patients admitted to participating centers. De-identified data were collected from administrative and clinical databases for comparison analysis, including demographics, clinical and physiological parameters, therapeutic interventions, and outcomes. Critical COVID-19 definition included patients with SARS-CoV-2 rt-PCR in respiratory airways or antibody profile compatible with acute COVID-19 infection diagnosed with positive antigen test and CT scan with characteristics of acute COVID-19 infection. In addition, patients who met the case definition for MIS-C according to the United States of America Center for Disease Control were also considered to, to include all the causes of pediatric critical COVID-19, requiring PICU admission, as previously defined[11,12,23,24].

Patients with a clinical and microbiological profile of SARS-CoV-2 infection at PICU admission, receiving MV, and meeting the Pediatric Acute Lung Injury Consensus Conference (PALICC) criteria for PARDS[25], were included in the analysis. Pneumonia severity was defined based on the Pan American Health Organization (PAHO) definition[26]. Patients were excluded if they had uncorrected congenital heart disease, pre-existing lung or airway disease, chronic respiratory failure requiring long-term MV and tracheostomy, left ventricular dysfunction failure with ejection fraction less than 50%[27] and COVID-19 with primary neurological involvement. In addition, patients with spontaneous breathing effort and endotracheal tube air leak were excluded due to possible interference data collection and unreliable quasi-static lung mechanics measurements and calculations. Patients were classified into two groups: MIS-PARDS and C-PARDS. All patients with MIS-C diagnostic criteria were classified as MIS-PARDS[31-33]. The C-PARDS group consisted of PARDS patients fulfilling acute COVID-19 pneumonia criteria according to the modified case definitions of the World Health Organization (WHO)[3]. Supplementary Table 1 shows detailed patient classifications according to diagnostic tests.

Variables and outcomes

During the first 72 hrs after initiation of MV, all patients were screened at 8 AM and 8 PM. PARDS severity was determined following PALICC criteria, according to the oxygenation index, classified as mild (4 to < 8), moderate (8 to < 16), and severe (≥ 16)[25]. When hypoxemia was the lowest, all the parameters were recorded. Organ dysfunction was assessed by the treating physician based on definitions by the International Pediatric Sepsis Consensus Conference[28], and multiorgan dysfunction was defined as ≥ 3 organ dysfunctions. Vasoactive support was quantified through Vasoactive-Inotropic Score (VIS)[29]. Cardiac function

Table 1. Demographic and clinical characteristics of pediatric respiratory distress syndrome associated with COVID-19 according to the clinical phenotypes and outcome.

	All n. 30	MIS-PARDS n. 14	C-PARDS n. 16
Age, years	7.5 (4-11)	7 (6-9)	10 (2-13)
Male sex	18 (60)	12 (67)*	6 (33)
Weight, kg	30 (21-45)	32 (21-45)	28 (13-57)
Signs and Symptoms			
SpO2, %	87 (82-90)	89 (86-95)*	85 (78-88)
Respiratory distress	24 (80)	12 (86)	12 (75)
Chest Retractions	7 (23)	4 (29)	3 (19)
Oxygen desaturation	21 (70)	7 (50)*	14 (88)
Rhinorrhea	3 (10)	0 (0)	3 (19)
Cough	7 (23)	0 (0)*	7 (44)

Data are n (%) or median (IQR). *p < 0.05 using Fisher's exact test or Mann-Whitney U test. Abbreviations: SpO2, pulse oximetry saturation; MV, mechanical ventilation; PARDS, Pediatric Acute Respiratory Distress Syndrome; C-PARDS, PARDS associated with COVID-19 pneumonia; MIS-PARDS, PARDS associated with multisystem inflammatory syndrome in children.

was evaluated in all patients with transthoracic echocardiography performed by an experienced clinician, defining cardiac dysfunction as any alteration in systolic and diastolic function, and severe dysfunction was defined as an ejection fraction less than 40%[27, 30]. In assessing organ dysfunction, we consider the worst value in the first 72 h after admission.

Analyzed outcomes were duration of MV, Ventilator-free days at day 30 (VFD), Length of PICU stay, length of hospital stay, multiorgan failure and PICU mortality. VFD was defined as the number of days between weaning off the MV and day 28 after intubation. If the patient dies before day 28 or if the patient requires MV for more than 28-days, the value VFD value was 0. Multiorgan failure was defined as ≥ than 3 organ dysfunctions.

Ventilations parameters

Lung mechanics were measured with volume-controlled ventilation (VCV) mode[34,35]. Ventilator parameters included peak inspiratory pressure (PIP), plateau pressure (Pplat), positive end-expiratory pressure (PEEP), exhaled tidal volume (VTE), and inspiratory time (IT). The arterial blood gases values registered and, additionally, PaO_2/FiO_2 ratio and Oxygenation Index (OI) were calculated. The components of working pressure measured were calculated for each subject, as follows: resistive component (PIP - Pplat) and elastic component, or driving pressure, (DP, Pplat-PEEP). Respiratory system compliance (C_{RS}, $mL \cdot cmH_2O^{-1} \cdot kg^{-1}$) was calculated according to the standard equation, VTE divided by DP.

Statistical analysis

The data obtained were entered in a database on Microsoft® Excel (version for Windows 2016), reviewed, cleaned, and analyzed in STATA v.16 (StataCorp LP, Texas, USA). Frequencies and percentages were used to describe the categorical variables, while median and interquartile range (IQR) were used for quantitative data since the assumption of normality was not met. As a secondary analysis we evaluated the lung mechanics parameters and their association with mortality. A p-value less than 0.05 was considered statistically significant. Finally, receiver operator characteristic (ROC) curves were built for DP, $C_{RS,}$ and Pplat, to evaluate their accuracy as discriminators for mortality as an outcome.

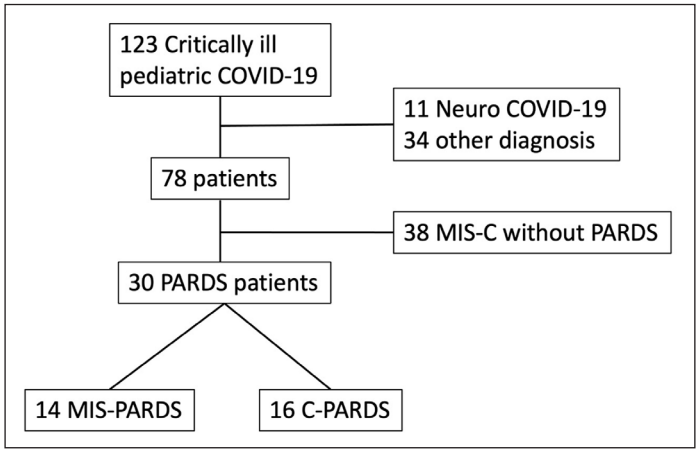

Figure 1. Study patient flow diagram. (PARDS: Pediatric Acute Respiratory Distress Syndrome; C-PARDS, PARDS associated with COVID-19 pneumonia; MIS-PARDS, PARDS associated with multisystem inflammatory syndrome in children).

Results

During the study period, 123 critically ill COVID-19 children were admitted to the participating units, and 30 of those patients had PARDS and met the selection criteria (figure 1). The median age was 7.5[4-11] years, 63% were intubated before PICU admission and there was a similar distribution between groups, 50% of the patients presented moderate PARDS and 30% severe PARDS (table 1).

Clinical characteristics by diagnosis

According to their COVID-19 diagnosis, 14 (47%) were MIS-PARDS and 16 (53%) were C-PARDS. (Supplementary Table 3). Hemodynamic compromise was seen in all the patients with MIS-PARDS and, in patients with C-PARDS, all but one patient (94%). The oxygen saturation on admission was higher in MIS-PARDS with 89% (86-95) compared with 85% (78-88) in C-PARDS. More patients with MIS-PARDS had some degree of cardiac dysfunction compared with patients within the C-PARDS group (71 vs. 25%, p = 0.03), and no other differences were found in organ failures and vasoactive support (Table 2). Mild left ventricular dysfunction was observed in 42% of MIS-PARDS and 6% of C-PARDS (Supplementary Table 2), but no severe dysfunction was observed.

PARDS and Lung mechanics

Severe PARDS was diagnosed in 6 (37%) of patients with C-PARDS compared with 3 (21%) in MIS-PARDS, both groups had 50% of moderate PARDS. The oxygenation index (OI) in MIS-PARDS was 7.5 (4.2-13.6) and in C-PARDS was 11.9 (7.8-23). The tidal volumes, peak pressures and PEEP were slightly higher in C-PARDS compared with MIS-PARDS. The Pplat and the DP were higher in the C-PARDS group. However, the C_{RS} was worst. In the MIS-PARDS group the was a had a higher PIP to Pplat gradient (table 3 and figure 2).

Table 2. Organ failure, vasoactive support and clinical outcomes in pediatric respiratory distress syndrome associated with COVID-19 according to the clinical phenotypes and outcomes

	All n. 30	MISC-PARDS n. 14	C-PARDS n. 16
Organ dysfunction			
Pulmonary	30 (100)	14 (100)	16 (100)
Hemodynamic	29 (96)	14 (100)	15 (94)
Another organ (any)	17 (57)	6 (43)	11 (69)
Hematological	10 (33)	3 (21)	7 (44)
Renal	3 (10)	1 (7)	2 (13)
Neurological	6 (20)	3 (21)	3 (19)
GI/Hepatic	3 (10)	2 (14)	1 (6)
Number of organ dysfunctions			
1	5 (17)	2 (14)	3 (19)
2	16 (53)	7 (50)	9 (56)
≥ 3	9 (30)	5 (36)	4 (25)
Vasoactive support			
Any vasoactive	29 (96)	14 (100)	15 (94)
Vasopressor	19 (63)	10 (71)	9 (56)
Inotropes	24 (80)	13 (93)	11 (69)
Median VIS	22 (12-50)	31 (19-50)	18 (10-45)
Outcomes			
Ventilator free days	22 (7-24)	23 (21-25)*	12 (0-23)
PICU length of stay, days	7 (5-9)	6 (5-9)	7 (5-10)
Hospital length of stay, days	11 (7-16)	13 (8-14)	9 (7-18)
ICU death	7 (23)	1 (7)	6 (38)

Data are n (%) or median (IQR). Abbreviations: GI, gastrointestinal; VIS, vasoactive inotropic scale; PARDS: Pediatric Acute Respiratory Distress Syndrome; C-PARDS, PARDS associated with COVID-19 pneumonia; MIS-PARDS, PARDS associated with multisystem inflammatory syndrome in children. PICU: Pediatric Intensive Care Unit.

Clinical outcomes

There was no statistically significant difference in mortality, but there was a higher number of patients that died in the C-PARDS group compared with MIS-PARDS (38% vs. 7%, p = 0.09). In both groups, the primary cause of death was refractory shock and multiorgan failure. All the patients had negative cultures for bacterial infection except two patients from the C-PARDS group that died due to bacteremia. One of them had a positive blood culture for viridans streptococci group and the other patient had *Pseudomonas aeruginosa*. The patient with the *Pseudomonas* bacteremia had severe PARDS. Ventilator free days were significantly lower in C-PARDS than MIS-PARDS (p = 0.02). C-PARDS had 4 (35%) patients that developed multiorgan failure compared with MIS-PARDS with 5 (36%) patients. The PICU length of stay was $7^{5\text{-}10}$ days in C-PARDS and 6 (5.9) in MIS-PARDS.

Secondary analysis: Lung mechanics and mortality

There were no significant differences in V_T and PEEP between survivors and no-survivors, but C_{RS} was significantly lower in non-survivors; thus, PIP, Pplat, and DP were higher (all $p < 0.05$). ROC of DP and mortality showed an AUC of 0.91 (95% CI 0.81-1.00), and the best cut point was 15 cmH_2O (100% sensitivity and 87% specificity). AUC for Elastance (1/C_{RS}) was 0.89 (95% CI 0.77-1.00), with a best cut-off point was 15 cmH_2O (100% sensitivity and 87% specificity). AUC for Elastance (1/CRS) was 0.89 (95% CI 0.77-1.00), with the best cut-off point of 2.7 (CRS 0.37) (85.7% sensibility and 91.3% specificity). AUC for Pplat was 0.89 (95% CI 0.76-1.00), with the best

Table 3. Gas exchange, mechanical ventilation settings, and lung mechanics in pediatric respiratory distress syndrome associated with COVID-19 according to the clinical phenotypes and outcome

	All n. 30	MIS-PARDS n. 14	C-PARDS n. 16
Oxygenation			
FiO_2	60 (45-100)	53 (40-60)	60 (48-100)
PaO_2, mmHg	80 (60-100)	92 (70-129)	77 (55-83)
PaO_2/FIO_2	130 (85-228)	163 (129-252)*	96 (74-150)
$PaO_2/FIO_2 < 100$	12 (40)	6 (38)*	12 (86)
P(A-a) O_2, mmHg	246 (165-399)	235 (141-305)	336 (175-564)
Oxygenation index	9.7 (6.1-19.9)	7.5 (4.2-13.6)*	11.9 (7.8-23.0)
PARDS severity			
Mild (4 to < 8)	6 (20)	4 (29)	2 (13)
Moderate (8 to < 16)	15 (50)	7 (50)	8 (50)
Severe (≥ 16)	9 (30)	3 (21)	6 (37)
Prone Position	9 (30)	3 (21)	6 (38)
Prone duration, hours	48 (48-48)	96 (48-96)	48 (48-48)
Neuromuscular blockade	13 (43)	4 (29)	9 (56)
Arterial Blood Gas			
pH	7.33 (7.19-7.39)	7.30 (7.22-7.39)	7.37 (7.2-7.44)
PaCO2, mmHg	44 (33-51)	38 (33-51)	47 (34-56)
Bicarbonate, mmol/L	21 (17-24)	20 (17-23)	22 (17-26)
Hemoglobin, g/dL	10.3 (9.6-11.0)	10.0 (10.0-11.0)	10.6 (9.0-11.5)
Lactate, mmol/L	1.6 (1.0-3.0)	1.7 (1.2-3.4)	1.4 (0.9-2.6)
Lung mechanics			
PIP, cmH_2O	28 (24-32)	27 (22-30)	29 (25-33)
Pplat	20 (16-30)	18 (15-20)*	26 (19-30)
PEEP, cmH_2O	7 (6-11)	7 (5-10)	8 (7-12)
Paw	12.7 (11.0-16.4)	11.5 (10.0-16.0)	14.1 (11.6-17.5)
V_T, ml/kg	7 (6-8)	7.0 (6.5-8.0)	6.5 (6.0-7.5)

Data are n (%) or median (IQR); *p < 0.05 using Fisher's exact test or Mann-Whitney U test. Abbreviations: FiO_2: Fraction of inspired oxygen; PaO_2: Arterial oxygen partial pressure; PaO_2/FIO_2: PaO_2 to FiO_2 ratio; P(A-a) O_2: Alveolar–arterial oxygen gradient; PEEP: Positive end-expiratory pressure; $PaCO_2$: Partial pressure of carbon dioxide; PIP: Peak inspiratory pressure; Vt/Kg: Tidal volume per kilogram; Pplat: plateau pressure; Paw: mean airway pressure; C-ARDS, Coronavirus associated acute respiratory distress syndrome; PARDS: Pediatric Acute Respiratory Distress Syndrome; C-PARDS, PARDS associated with COVID-19 pneumonia; MIS-PARDS, PARDS associated with multisystem inflammatory syndrome in children

cut-off point of 28 (CRS 0.37) (100% sensibility and specificity 87%). (Supplementary Table 4 and supplementary figures).

Discussion

SARS-CoV-2 infection in pediatric patients has two different presentations: acute COVID-19 infection and MIS-C. We examine and describe the lung mechanics in patients that required mechanical ventilation, with any of these two presentations and PARDS. The lung mechanics parameters were different between subgroups, with a higher elastic component in C-ARDS and a higher resistive component in patients with MIS-ARDS.

The physiopathology of acute COVID-19 and MIS-C is different. However, studies have described overlapping characteristics in MIS-C patients that develop respiratory failure with those with acute COVID-19. These two presentations of respiratory failure secondary to SARS-CoV-2 infection have different physio-

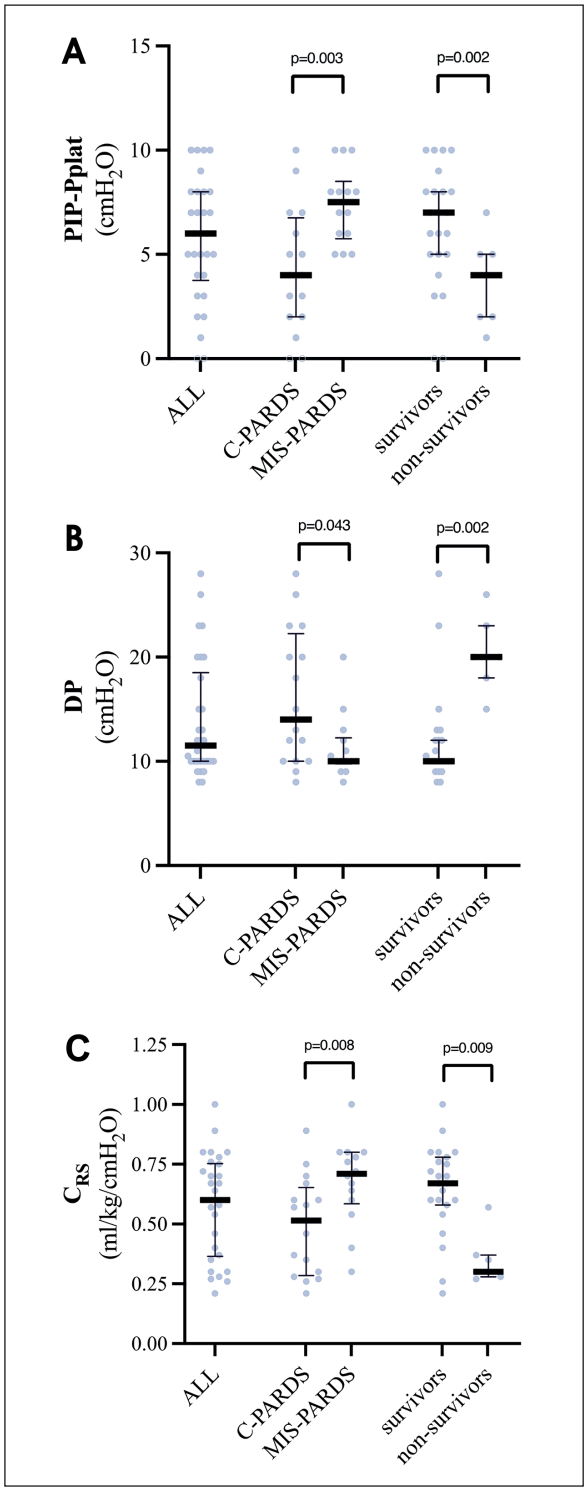

Figure 2. Boxplot graph of calculated parameters of lung mechanics of Children with PARDS associated with COVID-19, according to the clinical phenotypes and outcome. (**A**) The resistive component of work of breathing (Peak Inspiratory Pressure minus Plateau Pressure subtraction, [PIP-Pplat]); (**B**) the viscoelastic component of the work of breathing (Driving Pressure, DP); (**C**) compliance of the respiratory system (C_{RS}). (PARDS: Pediatric Acute Respiratory Distress Syndrome; C-PARDS, PARDS associated with COVID-19 pneumonia; MIS-PARDS, PARDS associated with multisystem inflammatory syndrome in children).

pathology, where the C-PARDS group's features were like a classic moderate to severe primary ARDS. 46 The inherent clinical differences between MIS-C and acute COVID-19 pneumonia may be seen in the presentation of these entities. There is a well-defined group of patients with MIS-C that have a predominantly respiratory presentation as opposed to shock, myocarditis, or Kawasaki-like symptoms. Our inclusion criteria aimed to include patients with MIS-C with such respiratory phenotype and to see if they overlap in lung mechanic characteristics with acute COVID-19. Even excluding patients with moderate and severe left ventricular failure to exclude pulmonary edema caused by left ventricle dysfunction as described in the PARDS criteria, we noticed that the use of vasopressors and mild cardiac dysfunction was more frequent in MIS-C. Both groups had similar length of stay in the PICU, but C-PARDS had lower ventilator free days and higher mortality. Furthermore, the differences in the lung mechanics described point that the possibility that the patients with MIS-C with a predominantly respiratory component are an overlap between acute COVID and MIS-C is unlikely. The C-ARDS numbers with higher driving pressure are consistent with PARDS mechanics and pathophysiology as described by other authors for non-COVID PARDS. However, the MIS-C patients with PARDS had measurements on the ventilator with wider difference between plateau and peak pressure. Remarkably, the DP and C_{RS} of C-PARDS were close to the values reported in other pediatric cohorts of viral PARDS[32] and other restrictive lung diseases[39,11,12,15]. We noticed that the PEEP utilized in C-ARDS seems to be lower than the current recommendations of pediatric ARDS management. Lower PEEP has been associated with higher mortality in ARDS as seen in the study by Khemani et al.[56]. The correlation between physiopathology and this lung mechanics findings needs to be further investigated.

As a secondary analysis we performed a mortality analysis associated with lung mechanics. Our participating centers recorded a historical PARDS mortality of 10% before the the SARS-CoV-2 pandemic. A possible explanation for the trend toward higher mortality is the low C_{RS} of the C-PARDS group, resulting in higher DP, a previous parameter associated with mortality in ARDS patients. In an exploratory analysis, we found that DP was close to the ideal clinical discriminator for mortality. Interestingly, the best cut-off point was 15 cmH_2O, a number mentioned by different authors in other studies. In 2 retrospective studies of children children with MV due to acute hypoxemic respiratory failure, high DP ($\geq$ 15 cmH_2O) was associated with less VFD but not mortality. This threshold has been described in adults as well. Amato et al, in a meta-analysis that included nine prospective trials and more than

3,500 patients, Amato et al. showed that DP was the best variable correlated with survival, even in patients within the usual thresholds of a lung-protective MV strategy[51]. Furthermore, interventions that resulted in a decrease in DP were associated with a greater survival rate. Other authors have confirmed the association between DP and ARDS outcomes, and a threshold of 15 cmH_2O, which has been incorporated into most lung-protective protocols[51,52] and can help understanding the physiopathology, thus leading to a change in the ventilation strategy management when facing these presentations. The mortality of our cohort may seem high when analyzing survival, many studies report a mortality between 10 and 70% in PARDS.37 Our study is a small cohort with critical care patients with COVID-19 or MIS-C and PARDS. It is difficult to draw conclusions regarding mortality compared to other studies. Also, the value of DP associated to mortality needs to be confirmed with larger studies. In addition, there are reports regarding differences in mortality between high and low-middle-income countries[40,41].

Our study has some limitations. We report respiratory mechanics in quasi-static conditions in VCV mode; thus, they cannot be extrapolated to other modes of MV with a deaccelerating flow, which is frequently used in pediatrics[45]. Presented data is the worst during the first 72h of admission, so time-dependent variables are not analyzed[44]. We did not investigate other parameters associated with PARDS severity or outcomes, i.e., dead space or mechanical power, because it was not part of our objective[54-56]. As in many multicenter studies, there might be differences in ventilatory strategy between hospitals, and comparisons were not possible given the heterogeneity of cases per center. The lack of consistency, especially PEEP titration, might influence some calculations of of lung mechanics. The small number of patients in each group might lead to type II statistical errors in some analyzed variables. There is also a risk of type I statistical errors, given the absence of statistical correction for multiple comparisons. Finally, the small number of cases probably influenced the lack of a statistical difference in mortality between C-PARDS and MIS-PARDS groups, although the difference was clinically relevant (38 vs. 7%). Nonetheless, we consider our results important to define high-risk groups of children with critical COVID-19 and as hypothesis-generating data for PARDS in the general PICU population.

Conclusions

Patients with acute COVID-19 and PARDS have lung mechanics characteristics similar to classic moderate to severe PARDS. Patients with MIS-C and PARDS presented lung mechanics similar to obstructive pulmonary failure. As seen in other studies, a driving pressure ≥ 15 cmH_2O was the best discriminator for mortality. The differences seen help making a clear discrimination between acute COVID-19 and MIS-C with respiratory failure. These findings can help guide ventilation management strategies for these two different presentations.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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