biventricular dysfunction, respectively. Need for ECMO for patients with normal function, RV dysfunction, and biventricular dysfunction were 8.5%, 41.8%, and 80.3%, respectively. In patients with RV and biventricular dysfunction, mortality and need for ECMO were significantly higher, with an $RV_D/LV_D \geq 1.1$.

Discussion

Early postnatal ventricular disproportion ($RV_D/LV_D \geq 1.1$) occurs frequently in neonates with CDH and is associated with increased mortality and the need for ECMO. Although neonates with CDH with an $RV_D/LV_D \geq 1.1$ were born at a lower gestational age and with worse CDH severity, RV_D/LV_D remained independently associated with mortality and need for ECMO after multivariate analysis. In neonates with and without CDH, RV_D and LV_D correlate with body weight and gestational age. However, RV_D/LV_D was not affected by gestational age, and the prognostic utility was similar in term and preterm neonates with CDH.

Echocardiography is commonly used in neonates, although the diagnosis of PH and cardiac dysfunction has challenges and limitations. Postnatal phenotypes observed in neonates with CDH ranged from normal size and function to impaired RV function with dilated RV, to a small, dysfunctional LV. Although RV enlargement likely results from high pulmonary vascular resistance, LV hypoplasia may derive from developmental impairment during fetal life, reduced LV filling in the context of right-to-left shunting by means of the ductus arteriosus, and displacement of the intraventricular septum compressing the LV (5). The association of fetal LV hypoplasia with adverse outcomes in patients with CDH has been previously confirmed (6). Abnormal ductus venosus streaming, mechanical compression, and reduced pulmonary venous return may contribute to fetal LV hypoplasia (7). Few postnatal studies have reported an association of a small LV and mortality in neonates with CDH (8–10). RV_D/LV_D is a reliable and reproducible echocardiographic parameter, incorporating important features of PH and cardiac dysfunction, which can be, contrary to the assessment of cardiac function, easily obtained from a four-chamber view without the need for advanced training, extensive experience, or postprocessing. Concomitant therapies (e.g., vasopressors, inotropes, prostaglandin E1), differences in loading conditions, and ventilation strategy might also affect RV_D/LV_D and require investigation in prospective studies.

Limitations include the retrospective single-center design with offline analysis of echocardiographic data and associated risk of bias by timing of echocardiography and center-specific treatment preferences. Nonetheless, the large cohort size and the blinded assessment support the value of RV_D/LV_D measurements to predict outcome in neonates with CDH. ■

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Specific Respiratory System Compliance in COVID-19 and Non–COVID-19 Acute Respiratory Distress Syndrome

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To the Editor:

The specific respiratory system compliance is defined as the ratio between the compliance of the respiratory system and the absolute resting volume of the lung, usually at FRC, and reflects the elastic characteristics of the pulmonary units. We previously found that the specific compliance in patients undergoing mechanical ventilation for acute respiratory distress syndrome (ARDS) was similar regardless of disease severity (1) and, at least in the early stages of disease, similar to that of normal lungs. This is the basis of the baby lung model: the ARDS lung is not stiffer but smaller (i.e., the compliance adjusted for the FRC is unmodified) (2). As lung volume and respiratory mechanics in early coronavirus disease (COVID-19) ARDS (C-ARDS) are different from those in the baby lung of typical ARDS, we wanted to investigate whether its intrinsic elasticity is also different and, if so, the potential underlying mechanisms.

Methods

This is a retrospective, observational study including 253 patients with early ARDS (intubated for <7 d): 221 (87%) with typical ARDS (136 [62%] with pulmonary and 85 [38%] with extrapulmonary ARDS) and 32 (13%) with C-ARDS. Lung volumes were measured in all patients in the supine position using whole-lung computed tomography at 5 cm H_2O of airway pressure. The potential for lung recruitment was measured only in patients with typical ARDS (3). Partitioned respiratory mechanics were measured in all patients in standardized conditions—in the supine position, with positive end-expiratory pressure (PEEP) of 5 cm H_2O, a respiratory rate of 16 (interquartile range, 14–19) beats/min, and V_T of 8 (interquartile range, 7–9) ml/kg predicted body weight—and computed using standard formulas. Specific respiratory system and lung compliances were calculated as the ratio of respiratory and lung compliance to lung gas volume at a PEEP of 5 cm H_2O, rather than at zero PEEP, for safety reasons.

Results

In Table 1, we present respiratory system and lung specific compliances, as well as their determinants (i.e., compliances and lung volumes), in the patient cohort on the basis of ARDS etiology. As shown, specific compliance and its components were similar between pulmonary and extrapulmonary ARDS, except for a small difference in specific respiratory system compliance. In contrast, all mechanical variables were significantly different between patients with C-ARDS and those with pulmonary and extrapulmonary ARDS. Notably, lung volumes and respiratory system and lung compliances were significantly higher in patients with COVID-19, whereas specific compliances were significantly lower.

In Figure 1, we report respiratory system specific compliance for each quintile of end-expiratory volumes. As shown, specific respiratory system compliance sharply decreases when lung volume increases. Within each quintile, we report the proportion of patients with potential for lung recruitment higher or lower than the median value (14.7% [interquartile range, 7.1–24.9%]), as well as the proportion of patients with C-ARDS, in whom the potential for lung recruitment was not assessed. The proportion of patients with higher potential for lung recruitment steadily decreases with increasing end-expiratory lung volume, whereas the proportion of patients with lower potential for lung recruitment increases. Patients with C-ARDS are more frequent in upper quintiles of lung volume and lower respiratory system specific compliance.

Discussion

The main finding of this study is that respiratory mechanics were similar between pulmonary and extrapulmonary ARDS, whereas they were markedly different in patients with C-ARDS. This notion has been repeatedly reported (4, 5) although it is still debated (6). What has never been reported, however, is the difference in respiratory system specific compliance between C-ARDS (lower) and typical ARDS (higher). We must emphasize, however, that all the data presented refer to early phases of the disease, as in later stages, the intrinsic elasticity of the pulmonary unit may change because of structural alterations of the lung parenchyma.

As respiratory system specific compliance is an indicator of the intrinsic elasticity of lung parenchyma, it appears surprising that a patient with higher lung volume, and therefore compliance (e.g., in early C-ARDS), exhibits a lower intrinsic elasticity than the baby

Table 1. Respiratory Mechanics in Pulmonary, Extrapulmonary, and Coronavirus Disease Acute Respiratory Distress Syndrome

	Typical ARDS			
	Pulmonary ($n = 136$)	Extrapulmonary ($n = 85$)	COVID-19 ARDS ($n = 32$)	*P* Value
Weight, kg	73 (60–85)	75 (62–85)	85 (75–90)	0.231
BMI, kg/m^2	25 (22–28)	25 (22–28)	27 (25–29)	0.467
Time from intubation to study day, d	2 (1–3)	2 (1–3)	1 (1–3)	0.678
$C_{RS\ Specific}$, cm H_2O^{-1}	0.042 (0.030–0.049)	0.045 (0.033–0.058)*	0.032 (0.026–0.041)*†	<0.001
$C_{L\ Specific}$, cm H_2O^{-1}	0.066 (0.048–0.085)	0.059 (0.043–0.079)	0.049 (0.036–0.057)*	0.029
C_{RS}, ml cm H_2O^1	39.9 (31.8–51.6)	42.2 (35.1–51.0)	49.5 (40.5–60.3)*†	0.044
C_L, ml cm H_2O^1	54.4 (42.5–68.5)	52.6 (42.3–77.0)	75.1 (55.1–89.4)*	<0.001
$EELV_5$, L	0.87 (0.62–1.30)	1.08 (0.73–1.60)	1.5 (1.2–2.1)*†	<0.001
Recruitment potential, %	17.8 (9.0–27.9)	10.0 (4.6–15.6)*	N/A	<0.001

Definition of abbreviations: ARDS = acute respiratory distress syndrome; BMI = body mass index; C_L = lung compliance; $C_{L\ Specific}$ = lung specific compliance; COVID-19 = coronavirus disease; C_{RS} = respiratory system compliance; $C_{RS\ Specific}$ = respiratory system specific compliance; $EELV_5$ = end-expiratory lung volume measured by computed tomography scan at 5 cm H_2O; N/A = not applicable.
Data are reported as median (interquartile range). Differences among groups were evaluated using one-way ANOVA or the Kruskal-Wallis test, as appropriate; multiple comparisons were performed using Bonferroni correction.
*Different from pulmonary ARDS.
†Different from extrapulmonary ARDS.

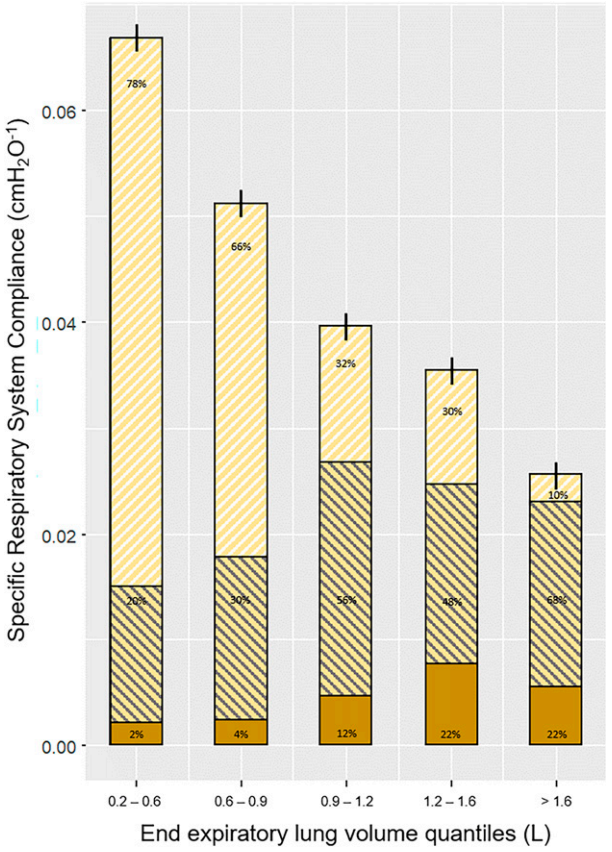

Figure 1. Respiratory system specific compliance as a function of five end-expiratory lung volume quantiles. The first quantile includes 51 patients, while the others include 50 patients each. In each quantile, gold hatching represents the fraction of patients with higher potential for lung recruitment, brown hatching represents the fraction of patients with lower potential for lung recruitment, and plain brown represents the fraction of patients with coronavirus disease (COVID-19), in whom potential for lung recruitment was not assessed.

lung of typical ARDS. These findings, however, become easily understandable if we examine in more detail the interaction between specific compliance and intratidal recruitability (i.e., a measure of alveolar opening and closing during tidal breathing). We may assume that in a simplified model (2), lung gas volume is the sum of the gas volume content of open pulmonary units with the same specific compliance (normal range, 0.025–0.040 cm H_2O^{-1}). Accordingly, the primary reason for a different lung gas volume between healthy and acutely injured lung is the number of open pulmonary units, each one with similar intrinsic elasticity (with the obvious exceptions of chronic lung diseases).

If, during inflation, atelectatic pulmonary units reopen, the same V_T at end inspiration will be distributed in more pulmonary units, resulting in a lower airway pressure than expected in the absence of intratidal recruitment and, therefore, in higher respiratory system compliance (i.e., the system appears softer). The resulting respiratory system specific compliance would be also increased, as the higher respiratory system compliance (caused by intratidal recruitment) will be normalized to the original resting volume (i.e., fewer pulmonary units than in the presence of intratidal recruitment). Tidal recruitment can influence how strongly end-expiratory lung volume and compliance are related to each other. This means that the amount of variance in the relationship between end-expiratory lung volume and compliance can be in part explained by the potential for lung recruitment. In summary, in the early phase of C-ARDS, specific respiratory system compliance is not lower than normal but more similar to its ideal value, whereas, in pulmonary and extrapulmonary ARDS, specific respiratory system compliance is higher depending on greater recruitability (7).

Therefore, the ratio between measured specific compliance and an ideal specific compliance could be an indicator of the degree of intratidal recruitment, which is associated with overall recruitability (Figure 1).

We must realize, however, that the term *recruitment* may include both opening of previously collapsed lung areas, as detected by (static) computed tomography, or a possible mechanical improvement of already open units, as detected by (dynamic) gas-based methods (8, 9). In both models, however, the greater the ratio between measured and ideal specific compliance, the greater intratidal recruitment should be. ■

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