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LETTER TO THE EDITOR

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Transpulmonary pressures in obese and non-obese COVID-19 ARDS

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Abstract

Background: Data on respiratory mechanics of COVID-19 ARDS patients are scarce.Respiratory mechanics and response to positive expiratory pressure (PEEP) may bedifferent in obese and non-obese patients.

Methods: We investigated esophageal pressure allowing determination oftranspulmonary pressures (PL) and elastances (EL) during a decremental PEEP trialfrom 20 to 6 cm H_2O in a cohort of COVID-19 ARDS patients.

Results: Fifteen patients were investigated, 8 obese and 7 non-obese patients. PEEP ≥ 16 cm H_2O for obese patients and PEEP ≥10 cm H_2O for non-obese patients were necessary to obtain positive expiratory P_L. Change of PEEP did not alter significantly ΔP_L or elastances in obese patients. However, in non-obese patients lung EL and ΔP_L increased significantly with PEEP increase. Chest wall EL was not affected by PEEP variations in both groups.

Background

Obesity, which is usually associated with better outcome for acute respiratory distress syndrome (ARDS) patients, is considered as a risk factor of acquiring a severe form of SARS COV-2-associated ARDS for SARS-CoV-2 [1]. Impact of obesity on respiratory mechanics of SARS-CoV-2-associated ARDS has not been investigated.

We hypothesized that respiratory mechanics including esophageal pressure (*Pes*) measurements might be different in obese and non-obese patients.

Therefore, the first objective of this study was to investigate transpulmonary pressures (P_L) in intubated SARS-CoV-2 patients according to their body mass index (BMI) during a decremental PEEP trial. Secondary objective was to assess lung and chest wall elastances ($EL_L$and $EL_{CW,}$ respectively).

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Methods

Patients

We conducted a prospective observational study in two intensive care units both in tertiary university hospitals (Hôpital de la Croix-Rousse, Hospices Civils de Lyon and Hôpital Nord, Assistance Publique-Hôpitaux de Marseille).

Patients were included in the study from 15 March to 15 April 2020 if they fulfilled inclusion criteria: adult admitted into the ICU for SARS-CoV-2, intubated and mechanically ventilated with moderate-to-severe ARDS criteria, sedated and paralyzed for clinical purpose and monitored by *Pes* catheter. As part of routine clinical management, we performed a decremental PEEP trial from 20 to 6 cm H_2O by 2 cm H_2O-steps in each patient during volume-controlled ventilation while other parameters were kept constant.

Esophageal pressure monitoring, transpulmonary pressures and elastances calculations

Pes catheter (Nutrivent TM, Sidam, Mirandola, Italy, or C7680U (Marquat, Boissy-St-Leger, France) was in place. The correct placement of esophageal catheter was confirmed by presence of cardiac artifacts on the esophageal curve and by an occlusion test (expiratory hold on the ventilator) in passive conditions with gentle chest compression. The occlusion test was considered as positive when the correlation between ΔP_{es} and Δ airway pressure (Paw) was 0.8–1.2. To avoid overestimation or underestimation of esophageal pressures, we inflated the esophageal balloon with the minimal filling volume among the recommended range for each catheter which was within the flat portion of the volume–pressure curve of the balloon [2, 3].

At each PEEP step, 2-s end-inspiratory occlusion pause allowed measurement of respiratory system (RS) and esophageal plateau pressure (Pplat and $P_{es,\ insp}$, respectively), whereas 5-s end-expiratory occlusion pause allowed, respectively, measurement of RS and esophageal total PEEP ($PEEP_{tot}$ and $P_{es,exp}$ respectively). RS driving pressure (ΔP_{RS}) was calculated as Pplat minus $PEEP_{tot.}$ RS, chest wall and lung elastances (EL_{RS}, EL_{CW}, and EL_L, respectively) and elastance ratio were computed according standard formula.

P_L absolute values were calculated as airway pressures minus esophageal pressures during inspiration ($P_{L,insp} = P\text{plat} - P_{es,insp}$) and expiration ($P_{L,\ exp} = PEEP_{tot} - P_{es,exp}$), transpulmonary driving pressure (ΔP_L) $= P_{L,insp} - P_{L,exp}$. Elastance ratio derived P_L ($P_{L,ER}$) was calculated as Pplat x (EL_L/EL_{RS}).

Statistics

Obesity was defined by a BMI ≥ 30. Results are reported as medians [interquartile range] or count (percentage) and compared between groups by Mann–Whitney U. Friedman test was used for repeated variables. p value < 0.05 was considered as significant.

Results

Fifteen patients were included in the study, 8 in the obese group (median BMI 34 [33–41]) and 7 in the non-obese group (mean BMI 26 [25–29]). Patient's characteristics were comparable between groups except for age (66 [53–73] years for non-obese group vs. 44 [39–49] years for obese group, $p = 0.04$). Table 1 compares respiratory mechanics for each BMI group according to the PEEP levels. Figure 1a represents Pplat and ΔP_{RS} for each BMI group according to the PEEP levels. Figure 1b represents transpulmonary pressures and ΔP_L.

PEEP ≥ 16 cm H_2O for obese patients and PEEP ≥ 10 cm H_2O for non-obese patients were necessary to obtain positive $P_{L,\ exp}$ (Fig. 1b). At 16 cm H_2O of PEEP, 71% of non-obese patients had $P_{L,\ insp} \geq 20$ cm H_2O and 0% of obese patients, whereas with $P_{L,\ ER}$ was ≥ 20 cm H_2O in, respectively, 86% of non-obese patients and 75% of obese patients. Change of PEEP did not alter significantly ΔP_Lor elastances in obese patients (Table 1). However, in non-obese patients EL_{RS} and EL_L increased significantly with PEEP increase. EL_{CW} was not affected by PEEP variations in both groups.

Differences between obese and non-obese groups were significant at 18–20 cm H_2O of PEEP with higher Pplat, ΔP_{RS}, $P_{L,insp}$, ΔP_L in non-obese patients.

Discussion

During decremental PEEP trial, we found differences in transpulmonary pressures and respiratory mechanics in COVID-19 ARDS patients according to the presence of obesity. First, $P_{L,insp}$, ΔP_Lwere higher in non-obese patients at high PEEP (≥ 18 cm H_2O), as Pplat and ΔP_{RS}. Second, EL_{CW} and EL_L were not statistically different between groups. However, increase of PEEP was significantly associated with an increase of EL_L in non-obese patients. Third, high PEEP levels (i.e., 16 cm H_2O) were associated with potential injurious $P_{L,ER}$(≥ 20 cm H_2O).

Preliminary studies with CT-scan have reported diffuse and bilateral pulmonary lesions during COVID-19 ARDS, which is usually associated with recruitability by PEEP in ARDS [4].

Recent studies using the same method to assess recruitability (recruitment-to-inflation ratio) reported conflicting data in those patients [5–7] with range from 17 to 56% of highly recruitable patients and possible less recruitable patients at a more advanced time point of the disease [5].

However, the lower driving pressures (ΔP_{RS} and (ΔP_L) observed for obese patients cannot discriminate lung recruitment from less lung overdistension without appropriate evaluation (CT-scan or electrical impedance tomography for instance).

We did not check for airway flow limitation in all patients that could have led to overestimate lung and respiratory system elastances, in particular in obese patients.

Finally, we were not able to compare respiratory mechanics of this cohort with non COVID-19 ARDS patients.

In conclusion, assessment of respiratory mechanics of COVID-19 ARDS patients with transpulmonary pressure monitoring might be useful when targets of protective lung ventilation could not be reached. The characteristics of obesity on respiratory mechanics airway opening pressure, recruitability of COVID-19 ARDS patients need further investigations.

Abbreviations

ARDS: Acute respiratory distress syndrome; BMI: Body mass index; ΔP_L: Transpulmonary driving pressure; ΔP_{RS}: Respiratory system driving pressure; EL_{CW}: Chest wall elastance; EL_L: Lung elastance; EL_{RS}: Respiratory system

Table 1 Respiratory mechanics according to BMI group and PEEP level

VPariable	BMI group	PEEP (cm H_2O)							
		6	8	10	12	14	16	18	20
*P*plat (cm H_2O)	Non-obese[$]	15 [13.6–17.7]	16.3 [16.2–18.4]	18 [17.7–21.1]	21.8 [21.1–22.6]	25.8 [23.8–25.9]	29.9 [28.6–30.7]	_34 [32.6–35.4]_	_38 [35.4–40.9]_
	Obese[$]	16.5 [15.1–17.3]	17.5 [16.5–18.5]	20.5 [19–21]	22.5 [21–23.3]	24.5 [23.8–26.3]	27 [25.8–28.5]	_29.5 [27–30.5]*_	_31.5 [28.8–32.8]*_
Total PEEP (cm H_2O)	Non-obese[$]	6.8 [6.8–6.9]	9 [8.4–9.5]	10.9 [10.9–11]	12.2 [12.2–13.3]	15 [15–15]	16.3 [16.3–16.7]	19 [19–19]	20.4 [20.4–21.4]
	Obese[$]	6.9 [6.7–6.9]	8.7 [8.3–8.9]	10.5 [10–11]	13 [12.2–13]	15 [14–15]	16.7 [16–17]	18.5 [18–19]	20 [20–20.6]
ΔP_{RS} (cm H_2O)	Non-obese[$]	8.2 [6.8–10.2]	6.8 [6.8–8.9]	7 [6.8–9.6]	8.2 [8.2–10.5]	10.8 [8.8–11.4]	13.6 [11.6–14.5]	_15 [13.6–16.9]_	_18 [14.3–20.2]_
	Obese	9.6 [7.6–10.5]	8.15 [7.7–9.9]	10 [8–11]	9 [8–12]	10 [8.8–12.3]	11 [8.8–12.3]	_10.5 [8.1–12.5]*_	_11.5 [8–13.3]*_
$P_{es. insp}$ (cm H_2O)	Non-obese[$]	8.6 [6.9–10.2]	9.4 [7.6–10.9]	10 [7.6–11.6]	10.9 [8.8–11.6]	10.9 [8.8–12.8]	10.9 [9.3–12.8]	12 [9.5–12.9]	13 [10.9–14.3]
	Obese[$]	11.5 [9.1–14.5]	11.5 [9.5–15.3]	11.5 [9.5–16.3]	12 [9.5–16]	12.5 [10.5–16.3]	12.5 [10.6–16.5]	13 [11.4–17.3]	13.5 [12.8–17.5]
$P_{es. exp}$ (cm H_2O)	Non-obese[$]	7.1 [5.2–8.9]	7.5 [5.9–8.9]	7.8 [6.4–10.2]	8.3 [7.1–10.2]	9.1 [7.1–10.9]	9.5 [7.6–11]	10 [8.1–11.6]	11 [8.8–12.2]
	Obese[$]	9.9 [8.1–12.3]	10.5 [8.2–13]	10.5 [8.5–13.3]	11 [8.7–14]	11 [8.7–15]	11.5 [9.3–14.5]	11.5 [10.3–15.3]	12.5 [11–16]
$P_{L. insp}$ (cm H_2O)	Non-obese[$]	6.8 [6.4–9.3]	8.2 [6.8–10.3]	9.6 [9.5–11.5]	10.9 [10.9–15]	14.9 [12.9–16.4]	20.4 [17.7–20.7]	_24.5 [21.1–24.8]_	_28 [23.1–28.3]_
	Obese[$]	5.5 [2.8–9]	7 [4.3–9.3]	9 [6.5–11.3]	10 [8.5–12.4]	12.6 [9.5–15]	14.8 [12.3–17]	_16.2 [13–18.5]*_	_17.15 [14.8–19]*_
$P_{L, ER}$ (cm H_2O)	Non-obese[$]	10.8 [9.4–15.4]	11.9 [10.6–14.3]	15.4 [14.1–17.3]	17.6 [15.9–19.2]	20.5 [18.5–22.1]	25.7 [23.3–27.7]	31.1 [26–32.4]	33.8 [28.6–37.4]
	Obese[$]	13 [11.8–14.2]	13.8 [12.8–15.7]	17.2 [14.5–19.1]	18.4 [15.7–20.9]	21.7 [18.3–22.8]	24 [20.3–25.9]	25.3 [21.3–27.4]	27.8 [23.8–29.4]
$P_{L. exp}$ (cm H_2O)	Non-obese[$]	0 [− 1.9 to 1.7]	1.4 [− 0.2 to 3.4]	3.2 [1.4–4.6]	4.1 [2.7–5.4]	5.9 [4.2–7.4]	7.3 [5.5–8.6]	9 [7.5–10.4]	_10 [8.9–11.5]_
	Obese[$]	− 3.1 [− 5.4 to − 1.3]	− 1.9 [− 4.2 to 0.5]	0 [− 3 to 1.8]	1 [− 1 to 3.8]	3.9 [− 0.3 to 5.8]	5 [1.8–7]	7 [3.5–7.6]	_7 [4.8–9]*_
ΔP_L	Non-obese[$]	5.5 [4.8–8.9]	5.4 [4.6–6.8]	6 [5.4–7.8]	6.9 [6.2–8.8]	9.1 [6.8–9.4]	12 [9.5–13]	13.7 [10.9–15.5]	_16 [11.5–18.5]_
	Obese	7.6 [5.9–8.7]	6.7 [5.9–8.2]	8 [6.5–10]	7.5 [5.8–10.3]	9 [6.8–10.4]	9.4 [7.5–11.3]	9 [6.6–11.3]	_10.5 [6.8–11.3]*_
EL_{RS} (cm $H_2O.L^{-1}$)	Non-obese[$]	20 [17.4–23.8]	18.3 [15.6–23.2]	18.3 [17–23.3]	24.1 [18.4–26.4]	24 [22.7–28.9]	33.3 [27.4–38.3]	39.3 [32–43]	47.1 [33.5–54.1]
	Obese	27.3 [18.5–38.1]	26.3 [18–38.3]	25.1 [17.6–53.7]	26.7 [18–49.1]	30.1 [18.6–48.5]	31.4 [19.9–53.4]	29.2 [23.3–45.9]	31.4 [22.9–45.9]
EL_{CW} (cm $H_2O.L^{-1}$)	Non-obese	4.6 [3.8–5.7]	5.8 [4.7–6.2]	3.2 [3.1–5.2]	5.2 [3.5–6.3]	5.2 [3.6–6.3]	5.2 [3.6–6.3]	3.8 [3.2–6.2]	6.2 [4.7–6.3]
	Obese	4.2 [4–5.7]	4.2 [3.5–7.1]	4.8 [2.7–7.8]	4.9 [2.7–8.2]	4.8 [4.2–8.4]	5.7 [2.7–8.2]	4.2 [3.5–6.7]	3.9 [2.7–6.7]
EL_L(cm $H_2O.L^{-1}$)	Non-obese[$]	15.9 [11.6–20.7]	13.1 [10.9–17.8]	15.7 [13.7–19.6]	20.3 [13.8–22.2]	20.9 [17.7–24.6]	30.2 [22.5–33.8]	36.4 [25.7–39.8]	41.9 [27.2–48.7]
	Obese	23.3 [14.6–32.4]	22.3 [15.3–30.7]	22.6 [14.9–42]	23.2 [12.8–39.8]	26.4 [14.2–42.5]	28.9 [16.1–43.6]	25.2 [19.9–36.6]	28.9 [20.3–38.8]
EL ratio	Non-obese[$]	0.79 [0.67–0.87]	0.75 [0.66–0.80]	0.8 [0.79–0.84]	0.81 [0.74–0.84]	0.83 [0.74–0.85]	0.86 [0.8–0.9]	0.9 [0.79–0.92]	0.89 [0.81–0.9]
	Obese[$]	0.8 [0.77–0.85]	0.80 [0.78–0.85]	0.84 [0.74–0.89]	0.82 [0.72–0.89]	0.85 [0.77–0.86]	0.87 [0.79–0.9]	0.85 [0.8–0.9]	0.88 [0.79–0.91]

Variables are reported as medians [interquartile range]

BMI body mass index, *PEEP* positive end-expiratory pressure, *Pplat* plateau pressure, ΔP_{RS} respiratory system driving pressure, $P_{es. insp}$ esophageal inspiratory pressure, $P_{es. exp}$ esophageal expiratory pressure, $P_{L. insp}$ inspiratory transpulmonary pressure, $P_{L, ER}$ transpulmonary pressure calculated with the elastance ratio, EL ratio, $P_{L. exp}$ expiratory transpulmonary pressure, ΔP_L driving transpulmonary pressure, EL_{RS} respiratory system elastance, EL_{CW} chest wall elastance, EL_L lung elastance, *EL* ratio, ratio of lung elastance to elastance of the respiratory system.

*$p < 0.05$ between obese and non-obese group for a given PEEP by Mann–Whitney *U* test; [$]$p < 0.05$ for PEEP effect by Friedman test. Computed for each group

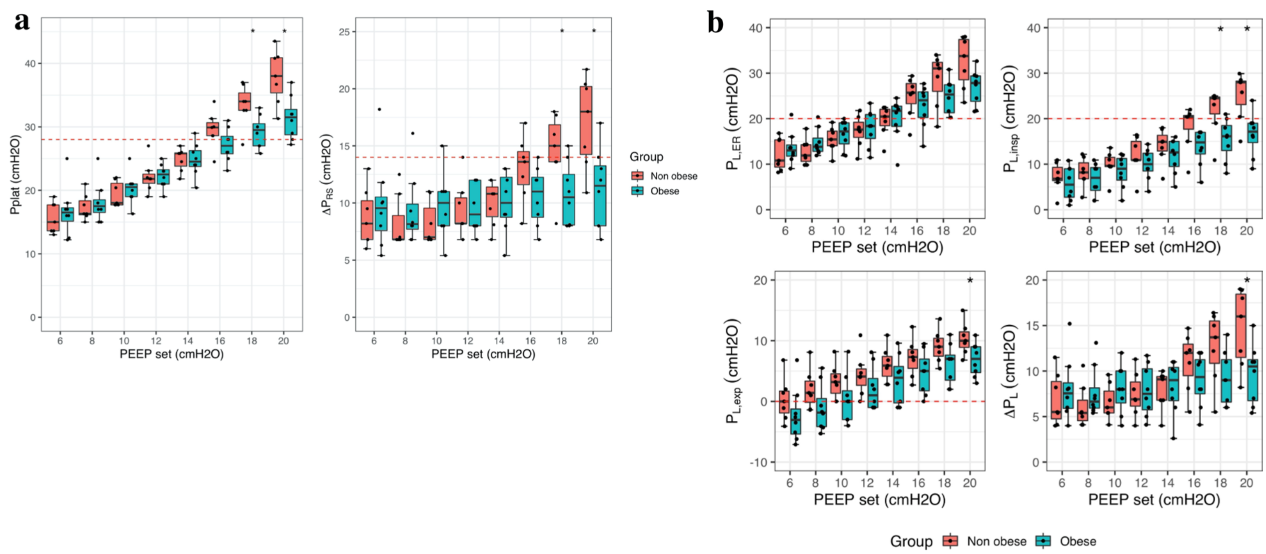

Fig. 1 **a** Boxplots of respiratory system plateau pressures (Pplat) according to set PEEP and group. Black dots represent individual values. Red dashed line denotes 28 cm H_2O. *$p<0.05$ between obese and non-obese group for a given PEEP by Mann–Whitney U test. Boxplots of respiratory system driving pressures (ΔP_{RS}) according to set PEEP and group. Black dots represent individual values. Red dashed line denotes 14 cm H_2O. *$p<0.05$ between obese and non-obese group for a given PEEP by Mann–Whitney *U* test. **b** Boxplots of end-inspiratory elastance-ratio derived ($P_{L, ER}$), end-inspiratory absolute method ($P_{L, insp}$) and end-expiratory ($P_{L, exp}$) transpulmonary pressures according to set PEEP and group. Black dots represent individual values. Red dashed lines denote 20 cm H_2O for $P_{L, ER}$and $P_{L, insp}$ plots, and 0 cm H_2O for $P_{L, exp}$ plot. *$p<0.05$ between obese and non-obese group for a given PEEP by Mann–Whitney *U* test

elastance; ICU: Intensive care unit; PEEP: Positive end-expiratory pressure; *Pes*: Esophageal pressure; $P_{L, ER}$: Inspiratory transpulmonary pressure (elastance ratio); $P_{L, exp}$: Expiratory transpulmonary pressure; $P_{L, insp}$: Inspiratory transpulmonary pressure (absolute value); P_L: Transpulmonary pressure; *P*plat: Plateau pressure; SARS-CoV-2: Severe acute respiratory syndrome coronavirus.

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Authors' contributions
MM and CG were responsible for the concept, revision and approval of this manuscript. MM, SH and CG participated in the design and drafted the manuscript. LP and JCR helped to revise the manuscript. MM, FD, PC, SH, LB, JMF, HY, IG, FD, LP, JCR and CG contributed to the data analysis and interpretation. All authors read and approved the final manuscript.

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Availability of data and materials
The datasets analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate
All patients admitted for SARS-CoV-2 or their relatives in case of unable to be informed patients, received non-opposition information to be part of the French clinical data base (COVID-ICU). The study was approved by an Ethic Committee, through the French national registry COVID-ICU for patients included in Marseille and through the Lyon University for patients included in Lyon (#20–41).

Consent for publication
All authors reviewed the manuscript and approved the publication of the manuscript. The corresponding author has completed the "Consent for publication".

Competing interests
The authors have no competing interests to declare.

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