and that we detected microbubbles in 83% of the patients in our study, we believe the contribution of PFO to the microbubble detection in our study is minimal. We agree that it would have been useful to perform the contrast-enhanced TCD in patients with equally severe non–COVID-19 ARDS as a control group. However, Boissier and colleagues performed contrast-enhanced transesophageal echocardiography, a technique that is equally sensitive to contrast-enhanced TCD, on 216 patients with classical ARDS who were also ruled out for the presence of PFO (3). The severity of disease in their cohort was similar to ours, with median Pa_{O_2}:FI_{O_2} ratios of 121 mm Hg and 127 mm Hg, respectively. In their study, 96 patients (44%) demonstrated TPBT, but unlike in our study, neither the presence nor the degree of TPBT correlated with Pa_{O_2}:FI_{O_2} or other markers of gas exchange. This suggests that pulmonary vascular dilatations (or intrapulmonary arterial–venous anastomoses) are not a major mechanism of hypoxemia in classical ARDS but may be significant contributors to hypoxemia in COVID-19 respiratory failure. In the future, it will be important to better characterize the gas exchange abnormalities in COVID-19 respiratory failure using more sophisticated techniques, such as the multiple inert gas elimination technique. ■

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Assessment of Airway Closure and Expiratory Airflow Limitation to Set Positive End-Expiratory Pressure in Morbidly Obese Patients with Acute Respiratory Distress Syndrome

To the Editor:

We read the study by De Santis Santiago and colleagues with great interest (1). They demonstrated, in a very elegant crossover study that included morbidly obese patients with acute respiratory distress syndrome (ARDS) (mean body mass index of 57 kg/m^2), physiological respiratory and hemodynamics benefits of a ventilator strategy including a high positive end-expiratory pressure (PEEP) as compared with a strategy with a low PEEP–FI_{O_2} table. The high PEEP strategy was determined with a lung recruitment maneuver with increased stepwise of PEEP until 50 cm H_2O of plateau pressure while keeping constant driving pressure of 10 cm H_2O, followed by a decreasing stepwise of 2 cm H_2O of PEEP until 5 cm H_2O allowing the determination of optimal PEEP (PEEP level for best compliance of the respiratory system + 2 cm H_2O). This strategy was associated with improvement of respiratory mechanics (decrease of driving pressure, increase of respiratory system compliance) and oxygenation through reduction of atelectasis. Interestingly, this was not accompanied by impairment in right and left ventricular functions. Moreover, a very similar swine model confirmed these results.

Besides these findings, we are surprised that some important points of respiratory mechanics in morbidly obese patients are not discussed. First, complete airway closure is a very frequent phenomena in those patients (up to 65% for class III obesity) (2). It can be easily identified as the inflection point on the initial portion of a low-flow inflation pressure–volume when volume started to increase. The lack of consideration of complete airway pressure (by using a PEEP lower than the opening airway pressure) induces an overestimation of driving pressure, respiratory system, and lung elastances (2). Second, the association of low V_T and supine position in obesity may induce consequent expiratory airflow limitation, which can be easily visualized and measured as intrinsic PEEP (3). Therefore, if intrinsic PEEP is not considered, it could mislead correct values of expiratory transpulmonary pressure (total PEEP minus

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expiratory esophageal pressure). Regarding electrical impedance tomography results, we are surprised that the authors reported regional compliance only for 10 patients, whereas electrical impedance tomography measurements were made on 18 patients.

Furthermore, the authors report good hemodynamic tolerance of high levels of PEEP in class III obese patients. We are then surprised that the authors did not report $\dot{Q}$ variations, easily measured during transthoracic echocardiography, which was performed on 17 patients. Lack of variation of vasoactive-inotropic score or mean arterial pressure does not exclude that high PEEP did not decrease $\dot{Q}$. To support this comment, in the ARDS swine study, the authors report a trend to lower $\dot{Q}$ (−13%, $P = 0.053$) and higher venous O_2 saturation (Sv_{O_2}) with higher PEEP, despite similar mean arterial pressure and vasoactive-inotropic score. The authors conclude that higher Sv_{O_2} reflects adequate systemic perfusion. However, because $\dot{Q}$ tends to be lower and V_{O_2} stable, it is more likely that higher Sv_{O_2} is explained by the rise of Sa_{O_2} due to higher PEEP.

In patients with class III obesity, we advocate that the strategy of high pleural pressures should be compared with *1*) complete evaluation of respiratory mechanics, which include checking for possible airway closure and expiratory airflow limitation, and *2*) complete evaluation of hemodynamics, including $\dot{Q}$, to set a sufficient level of PEEP. ■

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Reply to Mezidi *et al.*

From the Authors:

We appreciate the thoughtful letter of Dr. Mehdi Mezdi and colleagues addressing our recent manuscript (1). The authors have raised several key pulmonary and hemodynamic questions on the ventilation of patients with obesity that should be investigated further. Our discussion here is limited and is focused on the apparent paradoxical hemodynamic response to lung recruitment in patients with severe obesity with an average body mass index (BMI) of 57 ± 12 kg/m^2 and an average esophageal pressure range of 17–20 cm H_2O. To address this point, we present novel data, documenting the hemodynamic effects of a lung-recruitment maneuver in two patients who were hemodynamically unstable, had severe obesity, and were treated by the Massachusetts General Hospital Lung Rescue Team (2).

Case 1

A 59-year-old woman with a BMI of 59 kg/m^2 (predominantly gynoid in distribution) was intubated because of aspiration pneumonia. The Lung Rescue Team was consulted in the setting of worsening hypoxemia (Pa_{O_2}/FI_{O_2} of 55 mm Hg with positive end-expiratory pressure [PEEP] of 15 cm H_2O) in septic shock requiring infusion of four inotropic-vasopressor medications. Before the recruitment maneuver was performed, the patient had a mean arterial pressure (MAP) of 70 mm Hg and a heart rate of 126 beats/min (bpm). After the recruitment maneuver and PEEP titration were performed and a best PEEP of 23 cm H_2O was found, the patient's MAP increased to 84, and her heart rate was 132 bpm. During the ventilatory procedure, inotropic-vasopressor agents were not adjusted. Figure 1 (case 1) shows that increased positive airway pressures translated into a progressive increase in arterial pressure. In the following hours at a PEEP of 23 cm H_2O, inotropic-vasopressor requirements were reduced by more than 50% (no fluid challenges were administered).

Case 2

A 58-year-old man with a BMI of 40 kg/m^2 (predominantly android in distribution) was intubated in the setting of pneumothorax and pulmonary contusions after a high-velocity motor-vehicle accident. The Lung Rescue Team was requested because of worsening oxygenation (Pa_{O_2}/FI_{O_2} of 99 mm Hg with

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