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Reply to Chalkias and Xanthos

To the Editor:

We are very grateful to Dr. Chalkias and Dr. Xanthos for their thoughtful comments regarding the description of the phenomenon of intrathoracic airway closure reported in the *Journal* (1).

These authors recently reported an impressive series of 300 out-of-hospital patients with cardiac arrest who were resuscitated with a strategy combining rapid intubation, continuous chest compression (CC), and positive pressure ventilation delivered via a ventilator (2). The unexpectedly high percentage of return of spontaneous circulation reported in this study was significantly associated with highest mean airway pressure (Paw) measured after 3 minutes of resuscitation via an external monitor. CO_2 measured via a mainstream monitor was similar between survivors and nonsurvivors. The authors concluded that a mean Paw above 42.5 mbar was associated with a higher chance of return of spontaneous circulation.

Interestingly, the apparent negative effect of a low mean Paw during CC could be related to (or associated with) the intrathoracic airway closure we recently reported (1). In fact, the transmission of pressure generated by CC at the airway opening is limited or absent in the case of intrathoracic airway closure. Conversely, the expected beneficial effect of positive pressure delivered by the ventilator (which refers to the thoracic pump effect) can be effective only if the positive airway pressure applied at the airway opening is transmitted to the intrathoracic compartment, although this transmission will be limited by intrathoracic airway closure. The methodological difficulty of capturing the highest value of CO_2 that seems the best surrogate of alveolar CO_2 during resuscitation limits the interpretation of the lack of difference reported in their study.

Therefore, if we accept that the association between a mean Paw below 42.5 mbar and a worse prognosis reported in the study of Chalkias and colleagues might be explained by intrathoracic airway closure, several different mechanisms could still be at play. First, intrathoracic airway closure could simply be a marker of poor prognosis that also limits transmission of pressure generated by CC at the airway opening, making the calculated mean airway pressure at the mouth lower. Second, intrathoracic airway closure may have impaired the transmission of positive pressure generated by ventilation to the intrathoracic compartment, thus limiting its expected beneficial effect on the thoracic pump effect. By overcoming intrathoracic airway closure, higher mean airway pressure could be beneficial on both circulation and ventilation. Finally, one cannot exclude that the lower mean Paw associated with the lower chance of return of spontaneous circulation in the abovementioned study could be simply the reflection of less effective CC, independent of intrathoracic airway closure. These fascinating physiological discussions deserve additional observations to better understand the mechanisms at play and the evolution of airway closure along the time of resuscitation. The use of the capnogram during CC, based on the description of Grieco and colleagues, may permit us to adapt ventilator settings according to intrathoracic airway closure to balance both the beneficial and potential harmful effects of positive airway pressure during resuscitation. ■

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Mechanical Ventilation during Extracorporal Support: The Relevance of V_T

To the Editor:

In cases in which pulmonary gas exchange is mainly guaranteed by extracorporeal support, the optimal ventilation strategy to protect the lung remains unclear. It is generally accepted that the ventilator should be set to prevent further ventilator-associated lung injury. Nevertheless, even a lung-protective approach with low V_Ts may still aggravate lung injury. Thus, an ultraprotective approach with very low V_Ts (<6 ml/kg) is frequently used in patients undergoing extracorporeal support to facilitate the healing of the injured lung (1). A very interesting concept is the reduction of the V_Ts to near apneic oxygenation, as done by Araos and colleagues (2). These researchers examined three different ventilation strategies in a swine acute respiratory distress syndrome model over the course of 24 hours, using extracorporeal membrane oxygenation to examine nonprotective, conventional, and near-apneic ventilation. The researchers found that histopathologic lung injury was lower in the conventional and especially the near-apneic group. However, wet-dry lung weight ratio and expression of most genes indicating fibroproliferation were not different between the groups. As remarked in the editorial by Fan (3), there was no comparison of ultraprotective strategies, and the three strategies differed not only in their V_Ts but also in positive end-expiratory pressure (PEEP) level and respiratory rate. Fan raised the question whether ventilation is needed at all during extracorporeal lung support. This was primarily described by Kolobow in an animal study (4).

Our group also conducted a study using a similar acute respiratory distress syndrome model (5). In the conventional group, protective mechanical ventilation with 6 ml/kg V_T was used. Unlike Araos and colleagues, we used arteriovenous extracorporeal lung assist to reduce V_Ts to 3 ml/kg body weight, and apneic oxygenation with V_Ts set to zero in further experimental groups. Moreover, an "open lung concept" was used in all groups by using PEEP levels above the lower inflection point of the lung. This strategy resulted in continuous airway pressure above 20 cm H_2O, even in the apneic group. Mean respiratory rate was similar in the 6 ml/kg and the 3 ml/kg group, with 20 and 17–18 breaths/min, respectively. After 24 hours, a histopathologic examination of the dependent lung showed more inflammation, alveolar exudation, and atelectasis with 3 ml/kg or no V_Ts. In contrast, alveolar overdistension was reduced with apneic oxygenation in the nondependent lung areas (5).

Hence, our study addressed several of the shortcomings of the data presented by Araos and colleagues and may help to answer the questions raised by Fan (3). Ventilation with protective V_Ts led to overdistension in the nondependent lung. Nevertheless, despite using high positive airway pressures, the dependent lung in the apneic group showed a worse lung injury score compared with protective V_Ts. Thus, the combination of both strategies as "near apneic ventilation with low respiratory rates" and higher PEEP levels might be very appealing. This strategy might prevent derecruitment of the dependent lung via repeated recruitment at a low rate set above higher PEEP levels. Overdistension of the nondependent lung may be prevented because of lower peak pressures and minimized shear stress resulting from a low respiratory rate. Another point is that using lower airway, and thus intrathoracic, pressures might reduce hemodynamic compromise. This is enabled by lower respiratory rates and lower V_Ts. Theoretically, a strategy with sufficient PEEP, low respiratory rates, and very low V_Ts individually adapted to the size of the residual nonconsolidated lung parts combined with prone positioning might be optimal to protect the lung during extracorporeal lung support.

We strongly agree with Fan that the optimal ventilator strategy during extracorporeal gas exchange should now be addressed in clinical studies. ■

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