

LETTER



Mechanism of airway closure in acute respiratory distress syndrome: a possible role of surfactant depletion

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Dear Editor,

We recently reported the presence of airway closure in patients with acute respiratory distress syndrome (ARDS), evidenced by a low-flow inflation pressure–volume (P – V) curve [1]. We noticed that the initial slope of the respiratory system P – V curve was extremely low in some patients and corresponded to the compliance of the circuit, therefore suggesting complete airway closure. Respiratory system compliance (C_{rs}) suddenly increased above a threshold, named airway opening pressure (AOP) [1]. We concluded that 1) AOP have been missed in the past, and 2) mechanisms leading to airway closure are unknown. Some data suggest that the air–liquid interface creates high surface tension in the small airways and could cause their closure. Surfactant depletion, as often observed in ARDS, could play a role.

Using previously published data, we conducted a post hoc analysis of a study investigating the relationship between P – V curves and bronchoalveolar lavage (BAL) in ARDS [2]. Our aims were 1) to reassess the existence of AOP on P – V curves using our new approach [1] and 2) to look for a correlation with the level of type IIA secretory phospholipase A2 activity (sPLA2), an indirect marker of surfactant depletion [3]. For each patient, a tracheal P – V curve was plotted and compared to that of the ventilator circuit (Fig. E1). BAL biomarkers were compared considering AOP. AOP was defined as the tracheal pressure at which gas volume delivered to a patient became 15 ml

greater than the volume compressed in an occluded circuit (Electronic Supplemental Material).

Among the 23 patients analysed, 11 (48%) presented airway closure (Fig. 1), with a median AOP of 9.3 (7.1–12) cmH₂O. Characteristics and respiratory mechanics were similar between the two groups, except for higher sPLA2 levels in patients with airway closure [416 (28–1407) vs. 21 (21–31) UI/ml, $p=0.03$] (Supplemental Table E1). In airway closure patients, driving pressure decreased from 19 (12–20) to 12 (10–18) cmH₂O ($p=0.04$) when it was corrected for AOP being the minimal pressure value, leading to a ‘corrected’ C_{rs} increasing from 29 (26–38) to 40 (29–50) ml/cmH₂O ($p=0.04$). sPLA2 levels were correlated with AOP levels with a logarithmic relationship ($Rho=0.52$, $y = 0.099 + 1.410 \times \ln(x)$, $p=0.01$, see Supplemental Fig. E1). Similarly, markers of lung inflammation (neutrophil count and tumour necrosis factor alpha) and markers of collagen turnover (matrix metalloproteinase 2 and N-terminal peptide of type 3 procollagen) were correlated as previously reported [2] (Supplemental Fig. E1).

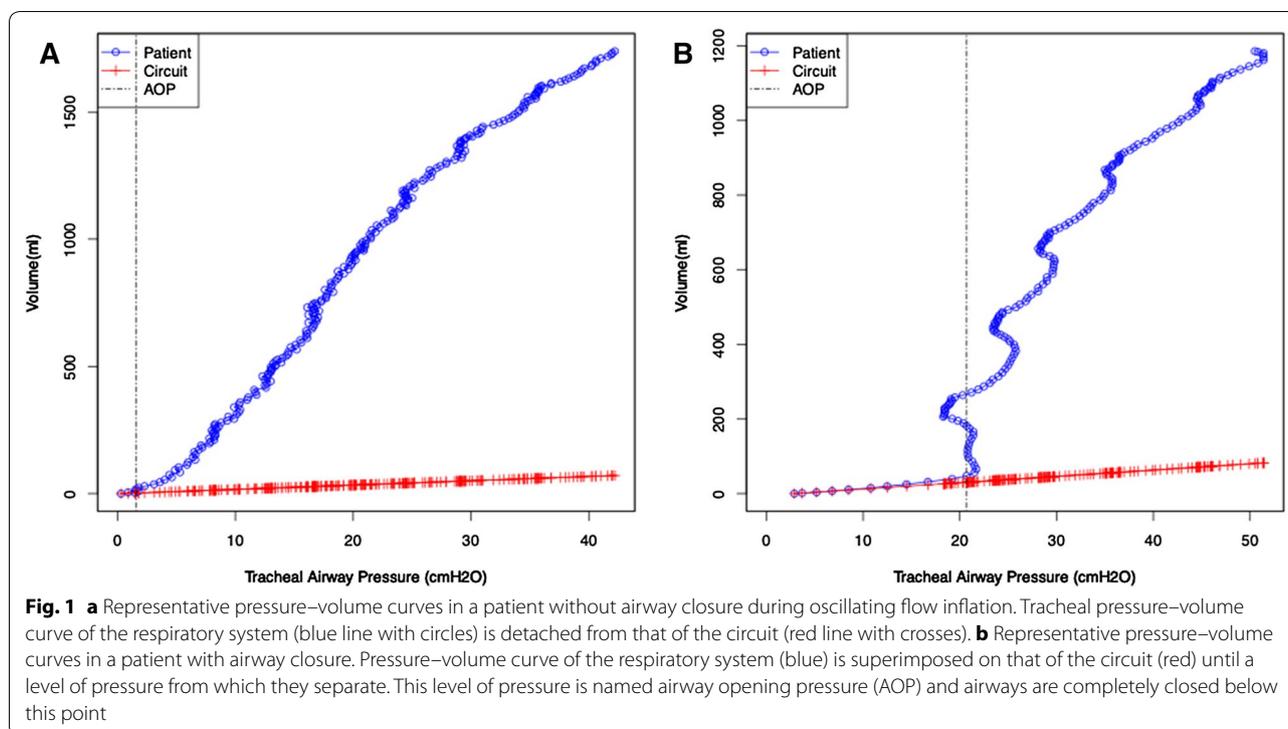
For the first time, we report a correlation between sPLA2 and AOP levels in a cohort of patients with ARDS having a high prevalence of airway closure. Almost 50 years ago, Hughes and colleagues reported airway closure in distal bronchioles in an ex vivo lung model [4]. Our results suggest that surfactant depletion could participate in airway closure by modifying surface tension forces in small airways. This finding is in keeping with an estimation based on Laplace’s law, suggesting that terminal bronchioles could close as a result of surface tension modification at the liquid–gas interface.

Altogether, these results show that airway closure in ARDS is a frequent phenomenon [5] and our findings are

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compatible with surface tension modifications in terminal bronchioles favoured by surfactant depletion. This deserves to be confirmed in further studies.

Electronic supplementary material

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Compliance with ethical standards

Conflicts of interest

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