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Positive end-expiratory pressure in COVID-19-related ARDS: Do not forget the airway closure

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ABSTRACT

Airway closure is a physiological phenomenon in which the distal airways are obstructed when the airway pressure drops below the airway opening pressure. We assessed this phenomenon in 27 patients with coronavirus disease 2019-related acute respiratory distress syndrome. Twelve (44%) patients had an airway opening pressure above 5 cmH_2O. The median airway opening pressure was 8 cmH_2O (interquartile range, 7–10), with a maximum value of 17 cmH_2O. Three patients had a baseline positive end-expiratory pressure lower than the airway opening pressure.

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1. Introduction

The optimal positive end-expiratory pressure (PEEP) in acute respiratory distress syndrome (ARDS) is subject to debate - especially for ARDS related to coronavirus disease 2019 (COVID-19). Some clinicians argue that a high PEEP optimizes alveolar recruitment, while others suggest that a low PEEP avoids alveolar overdistention and reduces the dead space [1,2].

Airway closure is a physiological phenomenon in which the distal airways are obstructed when the airway pressure drops below a given threshold during expiration [3]. Consequently, the alveoli do not communicate with the airways when the pressure is below the airway opening pressure (AOP). This obstruction can be extrinsic (due to lung compression) or intrinsic (due to liquid-filled bronchi and qualitative or quantitative abnormalities in the surfactant) [4]. Airway closure interferes with the assessment of airway pressure at end-expiration (causing errors in driving pressure measurements) and exhaled tidal volume (causing errors in the interpretation of the recruitment to inflation ratio used to assess lung recruitability) [4]. Moreover, repeated opening and closure movements lead to bronchiolar damage (leading to ventilator-induced lung injury) and promote ventilation-perfusion mismatch [5]. Given that airway closure is common in classical (i.e. non-COVID-19-related) ARDS, we decided to assess this phenomenon in COVID-19-related ARDS [6].

2. Methods

Here, we report on an ancillary analysis of an ongoing, prospective, single-center study of lung recruitability in ARDS, conducted in the intensive care department of Amiens university hospital (Amiens, France). All participants had tested positive in a real-time PCR assay for SARS-CoV-2. The partial pressure of oxygen to inspired oxygen fraction (P_aO_2/F_iO_2) ratio was always below 150 mmHg at a PEEP of 5 cmH_2O. All patients received continuous infusion of sedatives and neuromuscular blocking agents.

In supine position, we measured AOP during low-flow (5 L/min) insufflation starting at a PEEP of 0 cmH_2O, within 72 h prior orotracheal intubation. We defined airway closure as the presence of an inflection point on the time-pressure curve, and considered that the AOP was the pressure at the inflection point. An AOP above 5 cmH_2O was considered to be clinically significant [3,4] (Fig. 1). We compared the AOP with the baseline PEEP (premeasurement), and PEEP recommended in the PEEP-F_iO_2 table (lower PEEP/Higher F_iO_2) published by the ARDS Network or that recommended in the ExPress study as a function of the plateau pressure (to reach 28–30 cmH_2O).

3. Results

We included 27 patients with COVID-19-related ARDS, of whom 12 (44%) had an AOP above 5 cmH_2O. Among them, 8 (67%) were men and the median age was 67 years (interquartile range (IQR), 53–77). Eight study participants (67%) were obese, with a median body mass index

Abbreviations: AOP, Airway opening pressure; ARDS, Acute respiratory distress syndrome; COVID-19, Coronavirus disease 2019; IQR, Interquartile range; P_aO_2/F_iO_2, partial pressure of oxygen to inspired oxygen fraction; PEEP, Positive end-expiratory pressure.

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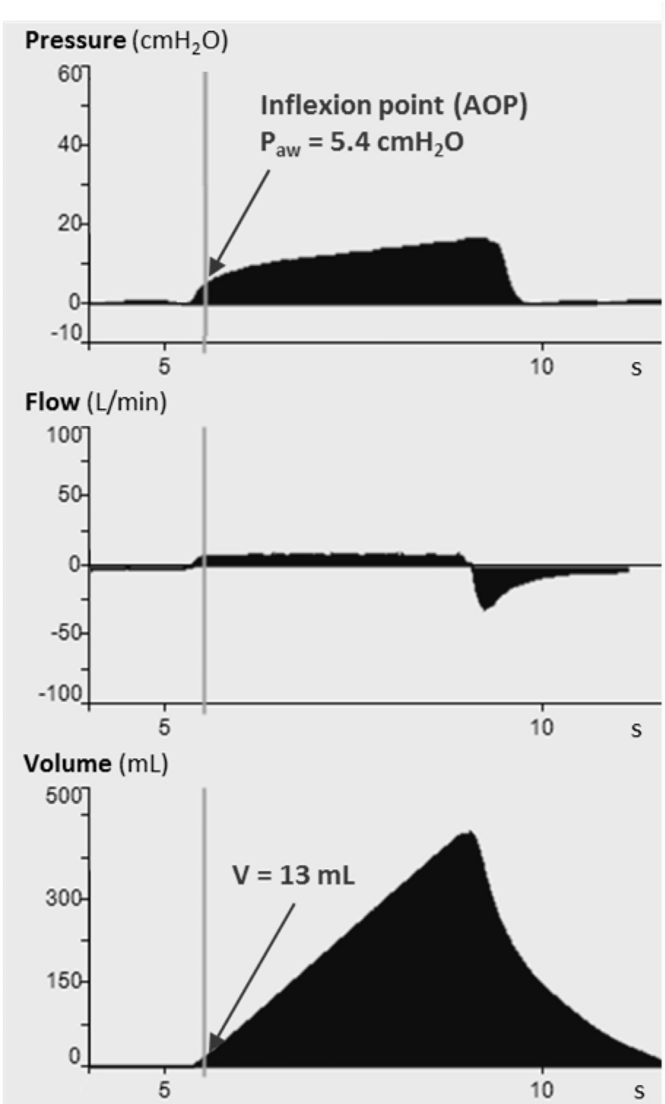

Fig. 1. Pressure-time curve during a low-flow insufflation in a patient with airway closure (Patient #10). At the beginning of the insufflation, airway pressure (P_{aw}) increases rapidly from 0 cmH_2O to the inflection point (5.4 cmH_2O, corresponding to the AOP) while only a small part of tidal volume is delivered (13 mL). The very low compliance of this short period (calculate as the change in volume divided by the change in airway pressure) corresponds to the circuit compliance (generally less than 5 mL/cmH_2O). In this example, the circuit compliance is 13/5.4 = 2.4 mL/cmH_2O. When airway pressure exceeds the AOP, compliance suddenly increases in relation with alveolar inflation.

of 35 kg/m^2 (IQR, 28–39). The median P_aO_2/F_iO_2 ratio was 94 mmHg (IQR 69–107), and 8 (67%) patients had a severe ARDS. The most common features on a CT scan of the chest were diffuse ground-glass opacity (in 100% of the patients) and consolidation (75%). Posterior or basal predominance was found in 6 patients (50%), and the median lung involvement was 67% (IQR, 44–71) (Table 1).

The median AOP was 8 cmH_2O (IQR, 7–10), with a maximum value of 17 cmH_2O. Four patients (33%) had an AOP of 10 cmH_2O or more. Before measurement, 3 patients (#1, #3, and #8) had a baseline PEEP lower than AOP. The optimal PEEP was 21 cmH_2O (IQR, 19–21) according to the ARDS network protocol and 17 cmH_2O (IQR, 15–18) according to the Express protocol. One patient (#3) had a PEEP level (according to the Express protocol) that was below the AOP and would have led to airway closure (Table 1).

4. Discussion

Airway closure is a common phenomenon in COVID-19 related ARDS; in the literature, the prevalence ranges from 0% to 40% (Table 2) [7-9]. The occurrence of airway closure is still poorly understood but can be partially explained by the high prevalence of obesity in COVID-19 patients; this leads to a positive pleural pressure in dependent regions and thus to lung compression. The pathogenesis of COVID-19 involves conducting airways, and distal bronchiolar injury can be severe. When combined with the frequent loss of surfactant, this damage increases the likelihood of airway closure [10].

The use of a low PEEP suggested by some clinicians exposes the patients to the above-mentioned consequences of airway closure. It is therefore essential to maintain the PEEP above the AOP. In some patients, the AOP may be high (up to 17 cmH_2O, in our cohort) and so the PEEP recommended by the ARDS Network or the ExPress study might not be sufficient. However, one must to bear in mind that airway occlusion is not always complete and may only concern some lung areas (due to ARDS-induced lung inhomogeneity) [4]. That is why increasing the PEEP to stop airway occlusion might lead to alveolar overdistention.

5. Conclusion

The routine monitoring of airway closure and AOP is essential for the choice of an individualized PEEP in ARDS. The optimal PEEP will be the best compromise between (i) maintaining lung recruitment, (ii) avoiding alveolar hyperinflation, and (iii) keeping the airways open.

Ethical approval and consent to participate

Compliance with ethical standards. The study was approved by our local independent ethics committee (CPP Nord-Ouest II, Amiens, CEERNI 110).

Consent for publication

Informed consent was obtained from all patients or their families.

Availability of supporting data

The dataset supporting the conclusions of this article is included within the article.

Competing interest

The authors report no disclosures of relevance to the manuscript.

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Author contributions

CB, YZ and MC collected data.
CB, YZ and JM wrote the manuscript.
LK and MS critically reviewed the manuscript.
All authors approved the final version of the manuscript.

Table 1
Demographic, radiographic and respiratory data for the study population.

Patient	Age (y)	Sex	BMI (Kg/m^2)	PaO2/FiO2 ratio	Lung involvement on CT (%)	AOP (cmH_2O)	PEEP (cmH_2O)		
							Baseline	Express protocol	ARDSnet protocol*
1	77	F	27.06	98	50	13	10	20	18–24
2	50	M	23.67	94	50–75	7	12	18	10–14
3	29	M	48.22	83	50–75	17	14	15	18–24
4	79	F	38.50	70	50	8	15	15	18–24
5	43	M	32.68	63	NA	10	15	22	18–24
6	66	M	36.90	67	75	7	10	18	14
7	54	M	27.68	93	25–50	7	10	16	18–24
8	77	F	20.57	130	25–50	8	5	12	18–24
9	79	M	41.00	60	75	7	15	15	18–24
10	68	M	35.60	124	25–50	5	5	19	18–24
11	56	M	34.00	104	75	8	15	17	10–14
12	71	F	41.50	117	50–75	10	15	15	18–24
Median [IQR]	67 [53–77]	8 M / 4F	35 [28–39]	94 [69–107]	67 [44–71]	8 [7–10]	13 [10–15]	17 [15–18]	21 [19–21]

AOP: airway opening pressure; ARDS: acute respiratory distress syndrome network; BMI: body mass index; IQR: interquartile range; NA: not available; P_aO_2/F_iO_2: partial pressure of oxygen to inspired oxygen fraction; PEEP: positive end-expiratory pressure.
* the lower PEEP/Higher F_iO_2 table.

Table 2
Literature review of airway closure in classical ARDS (i.e. not related to Covid-19) and COVID-19-related ARDS.

References	Covid-19-related ARDS	Prevalence	Detection method	AOP (cmH_2O)
Chen et al. [3]	No	8/30 (27%)	P-V curves	Mean ± SD: 13 ± 5
Chen et al. [4]	No	15/45 (33%)	P-V curves	Range: 5–20
Guérin et al. [6]	No	13/25 (52%)	P-V curves	Median [IQR]: 9 [8–15]
Haudebourg et al. * [7]	No	3/30 (10%)	P-V curves	Median [IQR]: 5 [5–9]
Haudebourg et al. * [7]	Yes	12/30 (40%)	P-V curves	Median [IQR]: 8 [5–10]
Pan et al. [8]	Yes	0/12 (0%)	P-V curves	NA
Beloncle et al. [9]	Yes	6/25 (24%)	P-T curves	Median [IQR]: 8 [7–10]
The present report	Yes	12/27 (44%)	P-T curves	Median [IQR]: 8 [7–10]

AOP: airway opening pressure; ARDS: acute respiratory distress syndrome network; IQR: interquartile range; NA: not available; P-T: pressure-time; P-V: pressure-volume; SD: standard deviation.
* This study included both COVID-19-related and non-COVID-19-related ARDS.

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