6. Cosgrove JF. 'Speaking in tongues'—fixation on a non-native language at induction of anaesthesia. *Anaesthesia* 2000; **55**: 728
7. Akpek EA, Sulemanji DS, Arslan G. Effects of anaesthesia on linguistic skill—can anaesthesia cause language switches? *Anesth Analg* 2002; **95**: 1127
8. Frizelle HP. Transient fixation on a non-native language associated with anaesthesia. *Anaesthesia* 2005; **60**: 713
9. Ivashkov Y, Hui C, Bhananker SM. Transient post-anaesthetic foreign language fixation: two cases. *Anaesth Cases* 2016; **4**: 53–7
10. Webster CS. Transient fixation on a non-native language associated with anaesthesia. *Anaesthesia* 2001; **56**: 908
11. Webster CS. A reply. *Anaesthesia* 2005; **60**: 713–4
12. Kim KHS, Relkin NR, Lee K-M, et al. Distinct cortical areas associated with native and second languages. *Nature* 1997; **388**: 171–4
13. Alkire MT, Hudetz AG, Tononi G. Consciousness and anesthesia. *Science* 2008; **322**: 876–80
14. Watts DJ, Strogatz SH. Collective dynamics of 'small-world' networks. *Nature* 1998; **393**: 440–2
15. Anonymous, Foreign accent syndrome. Available from: https://en.wikipedia.org/wiki/Foreign_accent_syndrome (Accessed 19 Feb 2020).

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Identification of lung overdistension caused by tidal volume and positive end-expiratory pressure increases based on electrical impedance tomography

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Editor—Overdistension can occur after an increase in PEEP even under lung-protective ventilation. It is unknown if such overdistension is caused by PEEP itself or by tidal breathing at higher PEEP. Lung-protective ventilation requires low tidal volume (V_T) (6–8 ml kg^{-1} ideal body weight) and adequate PEEP. Ultra-protective lung ventilation with very low V_T (e.g. 4 ml kg^{-1}) is usually limited to patients receiving extracorporeal membrane oxygenation (ECMO). Whether V_T is low enough to avoid lung overdistension is unknown. An increase in PEEP may also introduce regional overdistension.[1] A bedside tool to identify overdistension is warranted.

Electrical impedance tomography (EIT) is used to optimise PEEP at the bedside to avoid regional lung overdistension and collapse.[2] Here we introduce a simple EIT-based method to identify (1) whether lung tissue is overdistended after PEEP increase and (2) whether the overdistension is caused by V_T or PEEP changes.

In the scenario of PEEP increase (e.g. recruitment manoeuvre, PEEP titration, or assessment of lung recruitability),[3,4] tidal impedance variation and the changes in end-expiratory lung impedance (ΔEELI) were normalised to volume for all pixels of the lung regions (regions with tidal impedance variation >20% of the maximum). Regional compliance was calculated according to Eq. (1).

$$C_{\mathrm{EIT},i} = \mathrm{TV}_i / \Delta P \,, \tag{1}$$

where TV_i corresponds to tidal impedance variation for pixel i (ml) and ΔP is the driving pressure (mbar).

Step 1. Confirm if C_{EIT} at high PEEP is higher or lower than C_{EIT} at low PEEP

For any lung regions with $\Delta C_{\mathrm{EIT}}<0$ (high PEEP minus low PEEP), regional overdistension occurs. $\Delta C_{\mathrm{EIT}}>0$ represents regional recruitment. This assessment can be performed

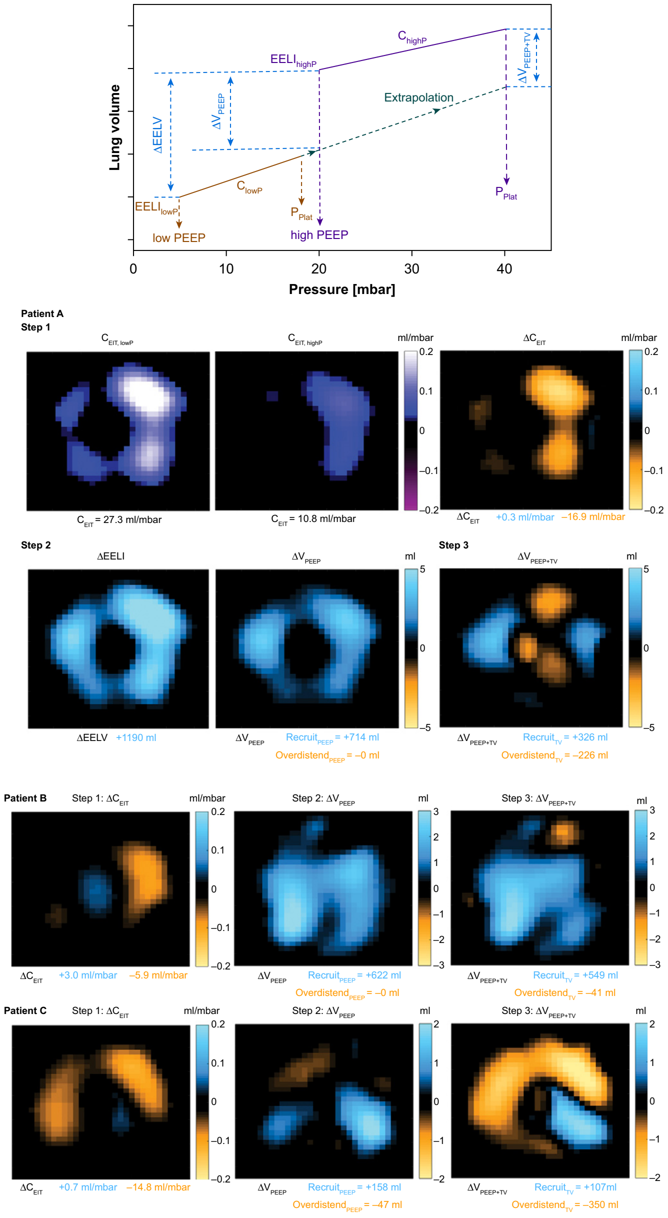

Fig 1. Illustration of the electrical impedance tomography (EIT)-based method for discriminating lung overdistension caused by PEEP from overdistension induced by tidal volume. Different nomenclatures in the equations are illustrated in the top figure. EELV, end-expiratory lung volume; ΔV_{PEEP}, lung volume changes introduced by PEEP increase; C, compliance; P_{Plat}, plateau pressure; lowP and highP represent low and high PEEP levels; $\Delta V_{PEEP+TV}$, lung volume changes introduced by PEEP increase and tidal breathing at high PEEP. After calculating the regional compliance C_{EIT} at each PEEP level, the changes caused by PEEP increase (ΔC_{EIT}) are calculated (Step 1). Significant decrease of C_{EIT} is confirmed (in this case orange regions, −16.9 ml $mbar^{-1}$). The light blue number is the sum of all positive pixel values and the orange one the sum of all negative ones. Volume changes caused by PEEP (ΔV_{PEEP}) are calculated (Step 2). In this patient there was no sign of overdistension. Next, volume changes caused by PEEP and tidal breathing at high PEEP ($\Delta V_{PEEP+TV}$) are assessed (Step 3). Overdistension introduced by tidal breathing at high PEEP ($Overdistend_{TV}$=−226 ml) was observed (orange regions in Step 3), although the pre-set tidal volume (6 ml kg^{-1}) was supposed to be lung protective. Low and high PEEP levels in this patient were 5 and 20 mbar, respectively. Patient B: PEEP was increased from 8 to 20 mbar. Adequate recruitment through the PEEP increase (Step 2, ΔV_{PEEP}, blue regions 622 ml) and limited overdistended volume in addition to tidal volume (Step 3, $\Delta V_{PEEP+TV}$, orange regions, −41 ml) was observed, compared to recruited volume (blue regions, 549 ml). For Patient C (bottom), recruitment manoeuvre was performed with PEEP of 24 mbar (from the clinical PEEP of 14 mbar). Overdistension at the level of end-expiration was noticeable in the non-dependent region (Step 2, ΔV_{PEEP}, orange regions, −47 ml). Through tidal breathing at the high PEEP, overdistension deteriorated (Step 3, $\Delta V_{PEEP+TV}$, orange regions, −350 ml).

directly during the examination. If no overdistension is observed, Step 2 and Step 3 are not needed.

Step 2. Confirm if the overdistension is caused by PEEP increase

When overdistension is observed in Step 1, the cause needs to be further clarified. The recruited ($\mathrm{Recruit}_{\mathrm{PEEP}}$) and overdistended ($\mathrm{Overdistend}_{\mathrm{PEEP}}$) volumes caused by PEEP increase are calculated as follows:

$$\Delta V_{\mathrm{PEEP},i} = \Delta \mathrm{EELI}_i - \left(C_{\mathrm{EIT},i,\mathrm{lowP}} \times \Delta \mathrm{PEEP}\right) \tag{2}$$

$$\mathrm{Recruit}_{\mathrm{PEEP},r} = \Delta V_{\mathrm{PEEP},r};\ \text{if for pixel } r,\ \Delta V_{\mathrm{PEEP},r} > 0 \tag{3}$$

$$\mathrm{Overdistend}_{\mathrm{PEEP},o} = \Delta V_{\mathrm{PEEP},o};\ \text{if for pixel } o,\ \Delta V_{\mathrm{PEEP},o} < 0, \tag{4}$$

where $C_{\mathrm{EIT,i,lowP}}$ represents the regional compliance of pixel i at low PEEP.

If the calculated volume $\mathrm{Overdistend}_{\mathrm{PEEP,o}}$ is negligible, which cannot explain the decrease of C_{EIT}, Step 3 can be conducted to confirm that V_T results in overdistension.

Step 3. Confirm the overdistension is caused by tidal breathing

$$\Delta V_{\mathrm{PEEP+TV},i} = \Delta \mathrm{EELI}_i + \mathrm{TV}_{i,\mathrm{highP}} - \left(C_{\mathrm{EIT},i,\mathrm{lowP}} \times \left(\Delta \mathrm{PEEP} + \Delta P_{\mathrm{highP}}\right)\right) \tag{5}$$

$$\mathrm{Recruit}_{\mathrm{TV},r} = \Delta V_{\mathrm{PEEP+TV},r};\ \text{if for pixel } r, \Delta V_{\mathrm{PEEP+TV},r} > 0 \tag{6}$$

$$\mathrm{Overdistend}_{\mathrm{TV},o} = \Delta V_{\mathrm{PEEP+TV},o};\ \text{if for pixel } o, \Delta V_{\mathrm{PEEP+TV},o} < 0, \tag{7}$$

where $\mathrm{TV}_{\mathrm{i,highP}}$ is V_T of pixel i at high PEEP and $\Delta P_{\mathrm{highP}}$ is the driving pressure at high PEEP. To briefly summarise, Step 1 compared two V_T distributions at two PEEP levels; Step 2 compared the volume changes introduced by PEEP increase with the expected changes calculated from low PEEP; and Step 3 compared the actual volume changes introduced by PEEP plus V_T with the expected ones. Figure 1 illustrates the process with data from patients with acute respiratory distress syndrome (ARDS).

To demonstrate three possible scenarios determined by the proposed method, EIT data from three patients with ARDS are presented (data from an ongoing study approved by our ethics committee, with patient consent for publication). EIT analysis of Patient A showed that the PEEP increase was adequate (Fig. 1, Step 2; large recruitment without signs of overdistension). However, overdistension introduced by tidal breathing at high PEEP was observed, although the pre-set V_T (6 ml kg^{-1}) should have been lung protective (Fig. 1, Step 3; $-\Delta V=-226$ ml). Patient B showed adequate recruitment through the PEEP increase and negligible overdistension of V_T (Fig. 1, Patient B). Overdistension was observed through PEEP increase in Patient C (Fig. 1, Patient C; $-\Delta V=-47$ ml).

Previous studies compared tidal ventilation distributions after PEEP change to evaluate ventilation gain or loss.[5] However, such comparisons could not distinguish the cause of redistribution (PEEP or V_T). Other studies proposed calculation of recruited volume with EIT without using the regional information.[3,4] Only the volume increase was taken into account, without considering the negative values. Regional ventilation decrease could be caused by overdistension or ventilation redistribution, therefore interpretation of the findings should be cautious. We took one step forward to use the full spatial EIT image resolution to calculate recruited and overdistended volumes separately. The pixel C_{EIT} was used instead of global C_{rs} from the ventilator to obtain regional volume changes. To our knowledge, this is the first attempt to explore whether V_T is too large in the context of lung-protective ventilation at the bedside using EIT.

Declarations of interest

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References

1. He H, Chi Y, Long Y, et al. Influence of overdistension/recruitment induced by high positive end-expiratory

pressure on ventilation—perfusion matching assessed by electrical impedance tomography with saline bolus. *Crit Care* 2020; **24**: 586
2. Zhao Z, Chang MY, Gow CH, et al. Positive end-expiratory pressure titration with electrical impedance tomography and pressure-volume curve in severe acute respiratory distress syndrome. *Ann Intensive Care* 2019; **9**: 7
3. Mauri T, Spinelli E, Scotti E, et al. Potential for lung recruitment and ventilation—perfusion mismatch in patients with the acute respiratory distress syndrome from coronavirus disease 2019. *Crit Care Med* 2020; **48**: 1129—34
4. Lowhagen K, Lindgren S, Odenstedt H, Stenqvist O, Lundin S. A new non-radiological method to assess potential lung recruitability: a pilot study in ALI patients. *Acta Anaesthesiol Scand* 2011; **55**: 165—74
5. Luepschen H, Meier T, Grossherr M, et al. Protective ventilation using electrical impedance tomography. *Physiol Meas* 2007; **28**: S247—60

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Calculating positive and negative predictive values. Comment on *Br J Anaesth* 2021; 126: 564-7

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Editor—We read the editorial by Hadjipavlou and colleagues[1] entitled 'What is the true worth of a p-value? Time for a change' with great interest. We share the concern of the authors regarding the use of statistics in biomedical science. In their paper, the authors show the worth of a study's conclusion by calculating positive and negative predictive values (PPV and NPV, respectively) using equations given in their Table 1. Such calculations were reported earlier by others including Ioannidis,[2] who refers to earlier work in his paper. The calculations are founded on contingency tables and Bayesian inference.

When comparing the papers from Hadjipavlou and colleagues[1] and Ioannidis,[2] we encountered several discrepancies. In short, when recalculating PPV and NPV using a power of 0.8, $\alpha=0.05$, and prior probability of 50%, we obtained values of 94% and 83%, respectively, whereas the editorial reports the reverse values, that is 83% and 94%. To gain understanding of the entries in Table 1 of Hadjipavlou and colleagues,[1] the following definitions and derivations may be helpful.

The $\mathrm{PPV}=P(E|+)$ is the probability that there is an effect (E) given a positive outcome of an experiment (+); the $\mathrm{NPV}=P(\neg E|-)$ is the probability that there is no effect ($\neg E$) given a negative outcome of an experiment (−). The type I error rate $\alpha=P(+|\neg E)$ is the probability of a positive outcome when there is no effect, and $P(-|\neg E)=1-\alpha$; the type II error rate $\beta=P(-|E)$ is the probability of a negative outcome when there is an effect, with $\mathrm{power}=1-\beta=P(+|E)$. Here, the null hypothesis is that there is no effect. Furthermore,

$$P(+)=P(+|E)\cdot P(E)+P(+|\neg E)\cdot P(\neg E) \text{ and } P(-)=P(-|E)\cdot P(E)+P(-|\neg E)\cdot P(\neg E)$$

where $P(E)$ is the *a priori* probability of effect, and $P(\neg E)=1-P(E)$.

Using Bayes' theorem, the PPV and NPV can be calculated as

$$\mathrm{PPV}=P(E|+)=P(+|E)\cdot P(E)/P(+)=\mathrm{power}\cdot P(E)/(\mathrm{power}\cdot P(E)+\alpha\cdot(1-\mathrm{P(E)}))$$

$$\mathrm{NPV}=P(\neg E|-)=P(-|\neg E)\cdot P(\neg E)/P(-)=(1-\alpha)\cdot(1-\mathrm{P(E)})/((1-\alpha)\cdot(1-\mathrm{P(E)})+\beta\cdot \mathrm{P(E)})$$

from which it may be inferred that for example A in the authors' Table 1 would be $A=\mathrm{power}\cdot P(E)$. When the prior $P(E)=0.5$, the equations simplify to (see also Heston and King[3])

$$\mathrm{PPV}=\mathrm{power}/(\mathrm{power}+\alpha) \text{ and } \mathrm{NPV}=(1-\alpha)/(1+\beta-\alpha)$$

We hope that this analysis sheds some light on the calculation of PPV and NPV. As the authors discuss, the PPV and NPV do not only depend on the P value, but also on the power of a study, and the prior probability. Assessing their interdependencies may indeed be valuable when designing a study. Finally, it is important to keep in mind that powering a study on desired PPV and NPV and possibly biased prior belief may suggest a possibly downward biased sample size.

Declarations of interest

The authors declare that they have no conflicts of interest.

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