## Is non-invasive ventilation really non-invasive?

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With interest we read the article: Observational study of changes in utilization and outcomes in mechanical ventilation in COVID-19.

In Plos-One https://doi.org/10.1371/j....

The authors report that, in a series of German hospitals, non-invasive respiratory support was used more often during the second wave of the Covid-19 pandemic than in the first period, but that this didn't result in a reduction of mortality. In this comment we will argue that this disappointing result might relate to the fact that positive pressure is applied in both Invasive Mechanical Ventilation (IMV) as well as in Non-Invasive Ventilation (NIV).

Most doctors feel that it is the intubation and the associated sedation and muscle relaxation, that represents the difference in invasiveness between IMV and NIV. We would like to draw the attention to the invasiveness of positive airway pressure per se, as compared to natural negative pressure respiration, and that this aspect of "invasiveness" is much the same, whether it is delivered via IMV or NIV.

Why is positive pressure in the lung invasive? This is most easily understood looking at the effects of positive airway pressure on the pressure in the pleural space (pleural pressure) and its consequence: peripheral airway closure.

The pleural pressure is under normal circumstances always negative relative to atmospheric pressure, since lung tissue tends to contract, due to the surface tension of the water film in the alveoli and elastic tissue within the lung, whereas the chest wall tends to expand. However, when positive pressure is applied to the airways, the pressure in the lung rises, therefore the pulling inward of the lung decreases, and the pressure in the pleural space will rise.

Dollfuss<sup>1</sup> showed that airways close when the pleural pressure rises above a certain point, for instance during exhalation below FRC, thus trapping air into the lung distal to this closure. In this way, peripheral airway closure prevents the complete collapse of posterior alveoli. Indeed Leannec already observed in 1820 that trapped air remained in an excised lung<sup>2</sup> (Milic-Emili, 2007). Such closure of airways takes first place in the dependent parts of the lung due to the gradient in pleural pressure as a result of gravity.

Hedenstierna<sup>3</sup> showed that many surgical patients showed peripheral airway closure at a volume well above FRC. He blamed anaesthesia and mechanical ventilation, without specific emphasis on the positive pressure. However, raised pleural pressure is the driver of closure, and since positive airway pressure raises pleural pressure, it follows that the positive airway pressure is the driver of lung closure in these anaesthetised surgical patients.

When fully exhaled under the level of FRC, the resulting volume is named the Closing Capacity (CC). CC is known to increase with age and obesity. This higher CC in obese and elderly patients helps to explain the increased risk for these groups during the Covid-19 pandemic.

Recently total airway closure has been reported in intubated patients by several authors <sup>4,5,6</sup>. An Airway Opening Pressure (AOP) can be defined below which no air flows into the lung. Talmor et al. <sup>7</sup> measured pleural pressure in ARDS patients. From their data it can be concluded that the high end-expiratory pleural pressure (>17 cm water) implies an even higher AOP and therefore total lung closure as well as hyperinflation. Apparently low compliance and high airway resistance induces a vicious circle of raising inspiratory pressure and PEEP until expired volume is equal to the inspired volume, at the cost of hyperinflation and very high pleural pressures. This process is much the same for IMV and NIV, since they both use positive pressure. Therefore, we hypothesise that the use of positive airway pressure might be an explanation for the failure to reduce mortality by

choosing NIV instead of IMV.

A potential solution to this serious problem could well be the re-introduction of Negative Pressure Ventilation (NPV)<sup>8,9,10</sup>. During/after the polio pandemic the switch was made from NPV (using so called "iron lungs") to Positive Pressure Ventilation (PPV) without any randomized trial to prove that PPV is safe and/or better than NPV. This switch was made largely because of availability, cost and practical issues<sup>11</sup>. The problems that soon appeared, such as atelectasis, were accepted as a normal complication that could be attacked by PEEP and recruitment procedures. However, it seems that few people realised that before the polio pandemic, atelectasis was treated or prevented in the iron lung. However, given the fact that in all anaesthesia manuals it is recommended to let the mechanically ventilated patient take a few deep sighs directly after awakening, shows that the risk of atelectasis when using positive pressure is well known and also that the knowledge that negative pleural pressure (deep sigh) is an effective remedy.

The practical objections against the original iron lungs do not apply to the modern NPV devices. These devices are light-weight and enclose the torso only <sup>8,9,10</sup>. In addition to advantages of NPV over PPV for the lungs<sup>12</sup>, we would like to point out the benefits for the brain: no narcosis or muscle relaxation required, patients can eat and drink normally and can also communicate with both staff and the loved ones<sup>13,14</sup>.

We therefore advocate that the reintroduction of NPV may prove to be a worthy addition to the current range of respiratory support strategies.

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