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EDITORIAL

High-flow nasal cannula in the postoperative period: is positive pressure the phantom of the OPERA trial?

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"Erik is not truly dead. He lives on within the souls of those who choose to listen to the music of the night."

Gaston Leroux, *The Phantom of the Opera*.

Patients undergoing major abdominal surgery are at risk for the development of postoperative pulmonary complications (PPCs), playing a major role in postoperative morbidity and mortality [1, 2]. Several measures have been proposed to reduce the incidence of PPCs, thus improving the outcome in surgical patients, including protective intraoperative mechanical ventilation [3], chest physiotherapy [4], and postoperative prophylactic or therapeutic non-invasive continuous positive airway pressure (nCPAP) [5] or positive pressure ventilation (NPPV) [6].

High-flow conditioned oxygen therapy, delivered through dedicated high-flow nasal cannulas (HFNCs), has been recently introduced in adults. Randomized controlled trials have tried to clarify the role of HFNCs in the prevention and treatment of respiratory failure in critically ill patients [7] as well as in the postoperative period [8–10]. The exact mode of action of HFNCs is matter of debate, and several mechanisms have been proposed and investigated: positive effects on comfort and tolerance compared to conventional oxygen, stable fraction of inspired oxygen delivery due to a reduction of room air entrainment, dead space wash-out and positive end-expiratory pressure (PEEP) effect [11]. All these aspects could be of value during the postoperative period; however, few studies investigated the efficacy of HFNCs in this specific setting.

In an article recently published in *Intensive Care Medicine*, Futier and co-authors [12] report a randomized controlled trial (OPERA) in which the clinical value of HFNCs in preventing post-extubation hypoxaemia in non-obese patients undergoing major abdominal surgery was investigated. The primary endpoint was the absolute risk reduction for the occurrence of hypoxaemia at 1 h after extubation, compared to standard oxygen therapy. The authors did not observe any advantage of HFNCs for this endpoint nor concerning the incidence of PPCs. This negative result is in line with previously published small randomized trials that assessed preventive HFNC in the postoperative period in thoracic surgery [8], cardiac surgery [9] and obese cardiac surgery patients [10, 13]. The trial was sized assuming a 50% absolute risk reduction with the use of HFNCs, and incidence of postoperative hypoxaemia of 40%, while the observed incidence was around 20%. This might be in part due to the recent improvements in intraoperative ventilation that reduced the occurrence of postoperative respiratory dysfunction [3]. Sensu stricto, as frequently seen in such studies [14], the huge estimated effect size and high estimated incidence of the primary outcome resulted in an underpowered study. With a pragmatic approach, the authors thoroughly discussed how their cohort of patients was large enough to reject HFNC as a preventive strategy in postoperative patients but not able to detect small differences between the two groups. In fact, in order to achieve statistical significance with the observed incidence, thousands of patients should have been enrolled. Nonetheless, even if a statistically significant difference was found in this setting, its ability to be translated into clinical practice would have been questionable, also because of the

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non-negligible economic burden associated with the routine use of disposable HFNCs. We agree with the authors' interpretation of the trial's results, concluding that the use of postoperative HFNC after major abdominal surgery should not be considered a standard measure to improve clinical outcome.

When HFNCs were tested in the post-extubation period in critically ill patients, results were more encouraging [7, 15]. Interpreting this discrepancy between the findings in postoperative and critically ill patients can be challenging. The application of nCPAP or NPPV is the only known measure able to re-expand collapsed lung tissue and revert atelectasis, even though only poor degree of evidence is available to support that this translates into an improved outcome [5, 6]. As illustrated in Fig. 1, the evidence arising from trials seems to support the hypothesis that HFNCs are able to provide an intermediate solution between conventional oxygen and positive pressure ventilation, whose clinical usefulness depends on the presence of an underlying reversible lung impairment: in this context, HFNCs represent a well-tolerated bridge solution to avoid more uncomfortable or invasive procedures, while the lung condition is improving. This is not the

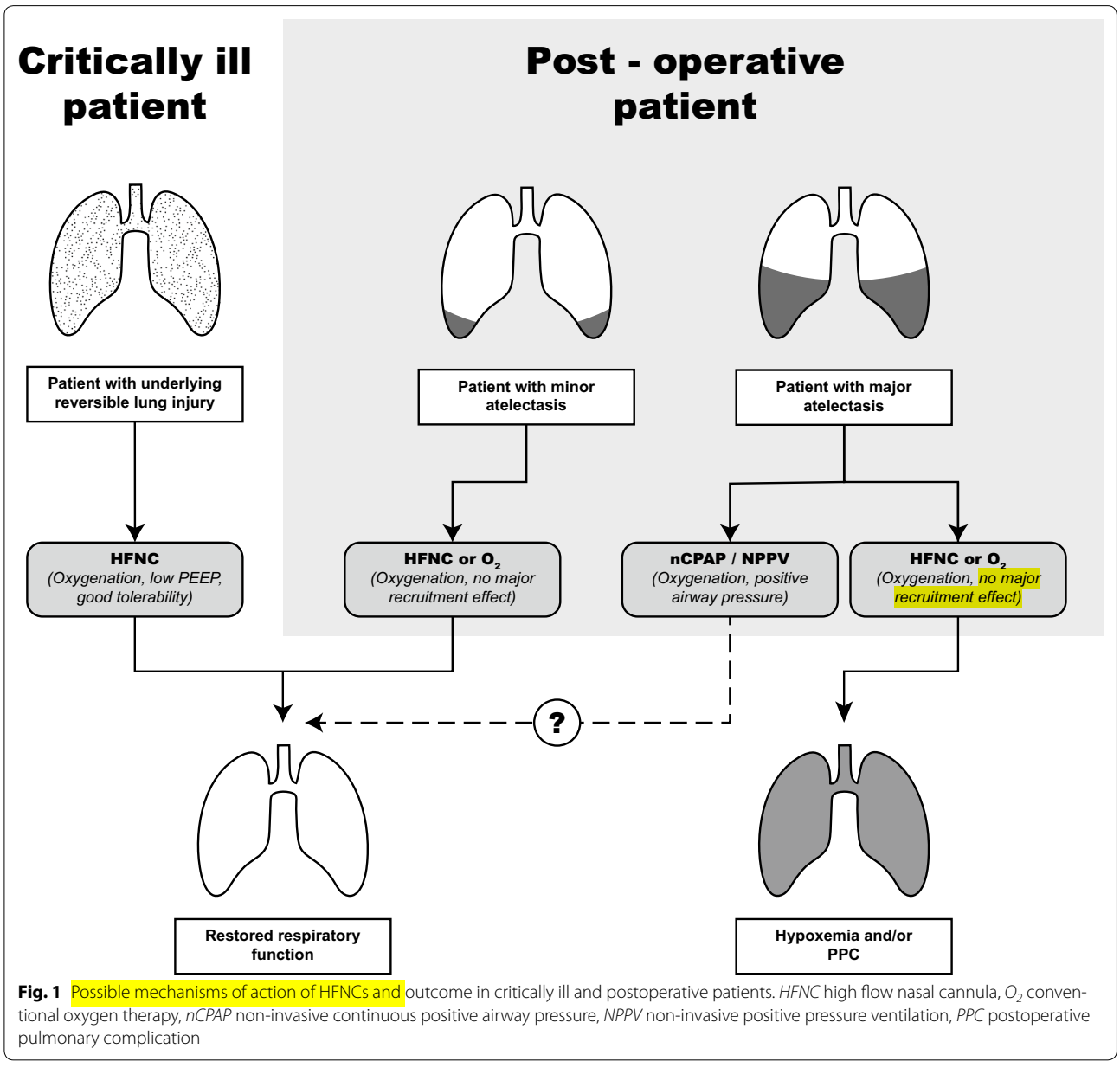

Fig. 1 Possible mechanisms of action of HFNCs and outcome in critically ill and postoperative patients. *HFNC* high flow nasal cannula, O_2 conventional oxygen therapy, *nCPAP* non-invasive continuous positive airway pressure, *NPPV* non-invasive positive pressure ventilation, *PPC* postoperative pulmonary complication

case for most surgical patients, as in the postoperative period the patient is in a specific condition not often seen in the intensive care unit: the lungs are essentially healthy, and an important role in respiratory function impairment is played by atelectasis, which is also believed to trigger pro-inflammatory mechanisms leading to the development of other PPCs [2]. This might explain the paradoxical result that HFNCs seem beneficial in critically ill patients, while not after elective surgery. In fact, the positive-pressure effect attributable to HFNCs operating at 60 L/min is estimated around 6 cmH_2O, but drops to 3 cmH_2O when the patient opens the mouth [11]. These values are unlikely to be sufficient to re-expand collapsed areas of the lung. Moreover, one of the advantages of HFNCs, namely the higher achieved fraction of inspired oxygen, might be unwanted in patients whose primary lung dysfunction is atelectasis, for the increased risk of gas resorption. In the postoperative period, probably the increasing use of low tidal volume intraoperative ventilation brought us to a plateau in patient safety, and further improvements are difficult to achieve. Exploring the field of post-extubation respiratory assistance seems an interesting field of research, but an integrated approach combining different interventions might be needed to further improve the safety of our patients [2].

In the era of large randomized trials, there is the need for building evidence combining data from physiological studies, small trials and pilot studies. However, the pathophysiological rationale, the mechanism of action of the intervention, the effect size estimation and the expected incidence of the primary endpoint should be carefully taken into account.

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Compliance with ethical standards

Conflicts of interest
The authors have no conflict of interest to disclose.

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