Perioperative oxygen administration: finding the sweet spot

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Oxygen administration over the years can be summarised as a “Goldilocks phenomenon.” The risk of inadequate patient oxygenation was recognised in the earliest days of anaesthesia, leading to the routine administration of supplemental oxygen during surgery, often far exceeding that required to avoid hypoxaemia. In the 1980s, continuous pulse oximetry made the practice of down-titration of oxygen administration possible while maintaining a level of oxyhaemoglobin thought to be safe. Clinical textbooks on anaesthesia at the time spoke of oxygen toxicity only in terms of atelectasis and subjective chest discomfort, meaning that intraoperative hyperoxegenation persisted. By the early 2000s, clinical trials reported potentially important benefits from high levels of perioperative oxygen administration for important outcomes such as postoperative nausea, vomiting, and surgical site infection. At the same time, however, laboratory studies increasingly reported harmful cellular effects of excess oxygen exposure, and earlier clinical trial results favouring high levels of perioperative oxygen administration could not be reliably replicated. With newfound equipoise, multiple clinical trials of hyperoxia avoidance were initiated in critically ill cohorts. The operating room, however, has remained relatively unexplored by research testing the effects of hyperoxia avoidance strategies.

In this rapidly evolving landscape, our research group started considering the building blocks required to conduct a definitive comparative effectiveness trial of an intraoperative hyperoxia avoidance strategy versus usual oxygen administration practice on clinically important outcomes. More than 300 million major surgeries are estimated to be performed globally each year. Clearly, for clinically important outcomes, even a small effect size may represent a large global burden of potentially iatrogenic and avoidable injury. But, of course, powering a trial to reliably detect, or refute, such an effect to inform global practice requires an enormous sample size, with extensive resourcing, collaboration, and goodwill. There must be a compelling rationale to justify the resource investment into such an ambitious trial.

The Multicenter Perioperative Outcomes Group (MPOG) was formed in 2009, collecting highly granular perioperative data on patients from more than 60 institutions within and beyond the United States (https://mpog.org/about/). These data include 43 billion physiological observations from 20 million surgical cases, including minute-by-minute intraoperative data on inspired concentration of oxygen and non-invasively monitored oxyhaemoglobin saturation, baseline characteristics, and outcome data. We approached the outcomes group with our research question, built a data query, and came up with a statistical analysis plan. Then we accessed a well curated dataset of over 500 000 cases meeting our inclusion criteria that provided a sufficient cohort size to build the complex models capable of detecting small but potentially important effects of excess oxygen on clinical outcomes.

Despite the benefit of a large, well maintained, and validated database, it was quickly apparent that this was no low-hanging fruit. Managing data density varying across diverse medical centres and anaesthesia providers, planning sensitivity analyses to reduce bias, and keeping momentum among the necessarily large team were major challenges.

The result of this team effort is the demonstration of a small but potentially important effect of excess oxygen administration during surgery on adverse clinical outcomes. It offers objective outcome data that emphasise the compelling need for a definitive clinical trial and considers usual practice to inform trial design. Like the old adage says: “In the absence of data, all opinions are equal.”


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