When Less Is More: Why Extubation With Less Than Routine 100% Oxygen May Be a Reasonable Strategy

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Glossary

- $Cao_2$ = arterial oxygen content; $DO_2$ = oxygen delivery; $FiO_2$ = inspiratory fraction of oxygen; $Hb$ = hemoglobin; $HFNOT$ = high-flow nasal oxygen therapy; $IOTA$ = Improving Oxygen Therapy in Acute Illness, systematic review and meta-analysis; $LAD$ = left anterior descending artery; $MBF$ = organ blood flow; $MVO_2$ = myocardial oxygen demand; $O_2$ = oxygen; $OS-CMR$ = oxygenation-sensitive cardiovascular magnetic resonance; $Pao_2$ = arterial pressure of oxygen; $PEEP$ = positive end-expiratory pressure; $PROXI$ trial = PeRioperative OXygen Fraction, effect on surgical site Infection and pulmonary complications after abdominal surgery multicenter trial; $Sao_2$ = arterial oxygen saturation; $SSI$ = surgical site infections

The high-pitched beep of the plethysmograph—announcing 100% oxygen ($O_2$) saturation—is well recognized by anesthesiologists. For this, however, a supraphysiological inspiratory fraction of oxygen ($FiO_2$) is frequently applied, exposing the patient to an excess of $O_2$. There is growing evidence that an exaggerated arterial partial pressure of oxygen ($Pao_2$), also called “hyperoxia,” may not be as benign as it was previously thought to be.

Clearly, in acute hypoxemia due to impaired gas exchange in the lungs, application of high $FiO_2$ may increase $Pao_2$. If the $Pao_2$ is increased excessively, however, it can lead to hyperoxia-mediated vasoconstriction in almost all vascular beds, particularly in the coronary arteries. Breathing an $FiO_2$ of 100% leads to a relative increase in coronary resistance of 40% compared to breathing air. In animal studies, Guensch et al. showed that hyperoxia resulted in a significant decrease of myocardial signal intensity in oxygenation-sensitive cardiovascular magnetic resonance (OS-CMR) imaging in the perfusion territory of a stenotic coronary artery. This was accompanied by a colocalized attenuation in peak circumferential strain. A decrease in left ventricular ejection fraction, cardiac output, and $O_2$ extraction ratio was also noted in stenosed animals under hyperoxia compared to healthy control animals.

Another side effect of $O_2$ is caused by gas absorption, which is a known mechanism of atelectasis formation. Calculations show that after tracheal intubation, alveolar collapse can be expected after 6 minutes of breathing pure $O_2$, compared to 30 minutes when breathing ambient air. It has been demonstrated that the amount of pulmonary atelectasis after induction of anesthesia is related to the level of $FiO_2$ used and the preoxygenation period. The amount of $O_2$ used during preoxygenation and induction is such a strong determinant of atelectasis formation that variations in inspiratory $O_2$ concentration during anesthesia do not seem to yield differences in the amount of atelectasis at the end of anesthesia; this is because most atelectases already occur during the first minutes of breathing 100% $O_2$.

Physiological considerations make it plausible that absorption atelectases can be reduced by positive end-expiratory pressure (PEEP). This principle was used, for example, in a landmark study of lower tidal volumes in acute respiratory distress patients with the use of $FiO_2$/PEEP tables. PEEP values as suggested by the table in Brower et al. (eg, 14 cm H$_2$O for an $FiO_2$ of 80%) may lead to negative hemodynamic consequences.

While using a high $FiO_2$ has been proposed to reduce surgical site infections (SSIs) in the past, a recent systematic review and meta-analysis did not show a convincing beneficial effect. Moreover, it questioned the strength of the related recommendation. The Danish PeRioperative OxYgen Fraction, effect on surgical site Infection and pulmonary complications after abdominal surgery multicenter trial (PROXI trial) compared an $FiO_2$ of 80% with 30% during emergency or elective laparotomy and found no difference in the rate of SSI or in mortality. A comparison between near-physiological $O_2$ targets ($Pao_2$ 130–150 mm Hg) and moderate hyperoxic $O_2$ targets ($Pao_2$ 200–300 mm Hg) in cardiac surgery with cardiopulmonary bypass showed no difference in myocardial injury, lactate levels, or hypoxic events.

There are situations in which the benefits of a high $FiO_2$ may outweigh the potential harm of hyperoxia. Intubation is the best example, as hyperoxia prolongs apnea tolerance, which results in invaluable extra time to manage the airway. This is also reflected by current guidelines for intubation,
in which preoxygenation with Fio2 of 100% is one of the
mainstays.9

Reducing the Fio2 after intubation often leads to safety
concerns among anesthesia caregivers. This might not be
reflected by physiological evidence. While the high O2
concentration in the functional residual capacity is a relevant
O2 reserve in case of airway problems (eg, 2.5–3 L of O2),
the amount of physically dissolved O2 in the blood is mini-
mal. Oxygen delivery (DO2) to the heart calculates from the
organ blood flow (MBF) multiplied by the arterial oxygen
content (CaO2): DO2 = MBF × CaO2. CaO2 can be derived
from the hemoglobin (Hb) concentration, arterial oxygen

saturation (Sao2) + (0.0031 × Pao2). Assuming a Pao2 of 100 mm Hg, a
consecutive Sao2 of 100%, and an Hb of 100 g/L, the result-
ing CaO2 is 134 mL O2/100 mL blood. Importantly, as Sao2
is already maximal, O2 can only be physically dissolved in
the plasma, represented by the second term of the equation.
At a Pao2 of 100 mm Hg, this physically dissolved portion
of CaO2 is 0.31 mL O2/100 mL plasma. Increasing the Pao2 to
300 mm Hg will increase this physically dissolved portion
to 0.93 mL O2/100 mL plasma, thus increasing CaO2 effec-

tively from 134.0 to 134.1 mL O2/100 mL blood. This is an
increase in DO2 by 0.075% given that Sao2 and Hb remained
unchanged. In the publication Guensch et al2 the authors
note a hyperoxia triggered decrease in left anterior descend-
ing artery (LAD) blood flow of −12.7% ± 2.3% in healthy
animals and −14.8% ± 2.0% in animals with a significant
LAD stenosis, respectively. Of note, drops in myocardial
blood flow of up to 30% have also been recorded in humans
during inhalation of O2.1 Thus, it is clear that the result-
ing decrease in blood flow (up to 30%) cannot be outweighed
by the 0.075% increase in CaO2, inadvertently leading to a
decrease in DO2. Increasing the Fio2 does only increase DO2
by an irrelevant amount, which may be even compromised
by a reduction in blood flow. This may lead to changes in the
myocardial oxygenation balance but does not lead to tissue
ischemia as long as myocardial oxygen demand (MVO2) is
matched by DO2. However, in scenarios where MVO2 is just
matched by DO2 with little reserve or with factors decreas-
ing CaO2 (eg, anemia) or MBF (eg, drop in blood pressure),
despite high Pao2, ischemia may be the consequence.

Thus, when speaking of safety attained through high
inspired O2 concentrations, this is true for loss of airway
descending hyperoxia that uses a reduced Fio2 before and after extuba-
tion for patients who are not at risk of a compromised air-
way, do not have impaired oxygenation, and have known
or suspected coronary artery disease. Because most of the
described unwanted O2 effects occur in a dose-dependent
manner, even a small reduction in Fio2 will benefit the
patient. We propose using an Fio2 of 60%–80%, based on the
individual risk assessment of the responsible clinician. After
extubation, O2 administration should be aimed at providing
normoxemia, with a target peripheral O2 saturation in the
range of 94% (or even 92%) to 98%.

Which oxygenation targets are optimal is the subject
of ongoing debate, but we believe that, given the potency
of the O2, we should use it with caution—like every other
drug—in a targeted, individualized manner. Signs of mis-
mash between O2 supply and demand should then trig-
ger an immediate search and appropriate treatment of the
underlying pathology (eg, hypoventilation, atelectases,
muscle weakness, obstructive sleep apnea syndrome) rather
than injudicious installation of a full-facemask with O2 and
dialing up O2 flow. To avoid atelectases, high O2 concentra-
tions should only be applied together with maneuvers that
prevent atelectases, such as continuous PEEP. While PEEP
and other noninvasive ventilation strategies may be diffi-
cult to apply in patients emerging from general anesthesia,
high-flow nasal oxygen therapy (HFNOT) has been shown
to provide PEEP in spontaneously breathing patients.18 Also
here, we would advocate using an O2/air blender to titrate
inspired O2 according to patient needs.

We believe that future research will further improve our
understanding of the effects of O2 and optimal O2 targets for
our patients. However, already today we can highlight the
principle of ensuring an adequate O2 supply. Because tissue
oxygenation is flow dependent, too much O2 will probably
hamper coronary supply via vasoconstriction, but severe
hypoxia will do this for sure via hypoxemia (in spite of the
vasodilatory effects of hypoxemia)! Stepping away from
established principles and guidelines, such as the Difficult
Airway Society Guidelines for the management of tracheal
extubation, has to be done deliberately and with careful
monitoring, whenever possible in research projects.
While further research is needed to better stratify risks
and benefits and to provide the basis for decision-making,
choosing the best Fio₂ is up to the treating clinician, who
should take into account the individual risk factors for each
extubation, thereby balancing the benefits and the harms of
O₂ therapy.

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