General anesthesia using low fresh gas flows has been widely discussed with respect to the saving potential for anesthetic gases and oxygen, enticing us with significant economic and ecologic benefits. Taking a broader perspective reveals that low- and minimal-flow anesthesia is also capable of offering clinically relevant benefits in a way that has been out of focus in the recent discussions on intraoperative protective ventilation.
Clinical Benefits of low- and minimal-flow anesthesia

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There has been a lot of research and discussion around intraoperative protective ventilation (PV) in the past years – for a good reason. Various studies demonstrated that protective ventilation approaches allow the reduction in incidence of postoperative pulmonary complications (PPC). With an incidence of approx. 5 %, PPC are common complications in a broad, heterogeneous patient group. One out of five patients who develops a PPC dies within the first 30 days postoperatively. Being in line with other research, these results of a population-based cohort study suggest a substantial impact on morbidity and mortality. Independent risk factors for PPC include low preoperative SpO2, recent acute respiratory infections, high age (> 75 years), anemia, pre-existing pulmonary disease and obesity (BMI > 30 kg/m²).

However, the above mentioned discussion on intraoperative protective ventilation has very much focused on parameters of mechanical ventilation, such as tidal volume, ventilation pressures, PEEP and recruitment maneuvers. Other potentially influencing factors seem to be neglected in this discussion although they are known to be important from the intensive care unit (ICU) environment. One of these factors is the humidification and warming of respiratory gas. In the ICU it is undisputed that respiratory gas conditioning is important to protect the lungs and is a universal standard of care. But this aspect does not play a role in the discussion on intraoperative protective ventilation although low- and minimal-flow techniques offer an effective and easy way to humidify respiratory gas.

In this paper, we will explore the potentially harmful effects of ventilation with unconditioned (cold and dry) gas. Furthermore we will elaborate on the capabilities of low- and minimal-flow anesthesia in humidifying and warming ventilation gas mitigating the potentially negative effects of ventilation with cold and dry gas.

Temperature and humidity of the inspired gas – forgotten components of protective ventilation?

For optimal gas exchange, the lungs require the inspired gas to be at a temperature of 37 °C and approx. 44 mg H₂O/l of absolute humidity (100 % relative humidity). Under normal conditions the respiratory tract warms the air during passage and the conditions described above are already met 5 cm below the carina. The upper respiratory tract has a greater effect on humidification and temperature compared to the lower respiratory tract as the respiratory epithelium changes towards the terminal bronchioles successively decreasing the capability to humidify and warm the inspired gas. During anesthesia, however, the upper respiratory tract is bypassed by endotracheal intubation or the placement of a laryngeal mask, leaving the lower respiratory tract potentially overcharged with the task of adequately acclimatizing the cold and dry gas applied during high flow anesthesia. Mechanical ventilation with cold and dry gas can thus lead to damage of respiratory epithelium and the lung parenchyma and influence the pulmonary function.

Mucociliary clearance, body core temperature and potential tissue damage

It is known that the ciliary activity (mucociliary clearance) - one of the important defence mechanisms of the lung - can be impaired by anesthesia. Direct damage of the respiratory epithelium and reduced mucous transport can ultimately lead to complications such as infections and atelectasis (due to mucous retention). Studies suggest that structural and functional damages of the respiratory...
epithelium can occur when ventilating patients with cold and dry gas – even in a fairly short period of perioperative ventilation. In one study, 39% of damaged ciliated cells have been observed after 3 hours of ventilation with cold and dry gas. It has been stated that this adverse effect can be reduced by adequately conditioned respiratory gas.\(^{12-14}\)

Another aspect to look at is the homeostasis of body core temperature and fluid balance. The respiratory tract acts like a huge heat and moisture exchanger as cold and dry gas entering the respiratory tract will absorb this heat and moisture. It is concluded that heat and fluid loss could be substantial and conditioned gas (warm and moist) would be more efficient in maintaining the body temperature and limiting the loss of humidity.\(^{7,11}\) This may be even more important in children as they have a larger ratio of minute volume to body surface area. A study demonstrated a loss of 0.75 °C of body core temperature in children after 90 minutes from induction of anesthesia using non-acclimatized gas.\(^{13}\)

In addition to the direct effect on mucociliary clearance and body core temperature, cold and dry respiratory gas is also considered responsible for the increased release of inflammation mediators\(^{15}\). It has been shown in animal models that the use of pre-warmed and humidified breathing gas reduced the release of inflammatory mediators TNF-α, IL-6 and IL-8, suggesting a reduction of the harming effects of inflammation.\(^{11, 16-18}\) Although studies on the clinical relevance for the human being are still pending, this factor may become relevant when discussing the theory of a “second hit” impact on patients with unfavorable conditions.\(^{19}\)

**Respiratory air conditioning and low-flow anesthesia**

An absolute humidity of 30 - 35 mg H\(_2\)O/l is described as a target value for prolonged mechanical ventilation and a minimum of 15 - 20 mg H\(_2\)O/l to mitigate the risk of the negative effects that perioperative ventilation with unconditioned gas has on the airways.\(^{6, 7, 11, 12, 14}\) In clinical studies on low- and minimal-flow techniques, values from 20 mg H\(_2\)O/l up to 30 mg H\(_2\)O/l and 32° C could be well achieved.\(^{7, 9, 11, 12, 21}\) A recent trial by De Oliveira et al. demonstrated that the aforementioned minimum conditions were achieved running a fresh gas flow of 1 L/min without any additional means of warming or humidification.\(^{9}\) In their booklet on low- and minimal-flow anesthesia, Hönemann and Mierke state similarly positive findings from their measurements.\(^{21}\)

For optimal use of conditioned gases in shorter procedures, adequate temperature and humidity must be reached as early as possible. Research has demonstrated that 10 minutes after tracheal intubation the humidity profile of the low-flow technique starts to differ positively from the values associated with high-flow anesthesia. After one hour the difference potentiates in favor of low-flow. Some authors therefore recommend the use of low- and minimal-flow technique even for interventions of 15 - 30 minutes and suggest to switch to low or minimal fresh gas flows right from the start.\(^{21}\)

**Breathing gas temperature in °C measured at the Y-piece in the inspiratory arm of the Dräger Primus / Apollo anesthesia machine over the course of anesthesia**

**Absolute humidity in g/m³ measured at the Y-piece in the inspiratory arm of the Dräger Primus / Apollo anesthesia machine over the course of anesthesia**
Practical use of low- and minimal-flow

The use of low-flow (FGF 1 L/min) and minimal-flow techniques (FGF 0.5 L/min) creates both clinical and financial opportunities. But it also places demands on the technology deployed. Among the technical requirements are:

- Leak tightness of the breathing system: The less components and connections, the better the system is suitable for low flow
- Returning the exhaust sample gas from gas measurement back into the breathing system (rebreathing system)
- Robustness and precision of O₂, CO₂ and anesthesia gas measurement in a humid environment
- Performance of the anesthetic vaporizers

A complete list of technical requirements for the effective application of low- and minimal-flow technology can be found in our paper “Technology Insights” (Link).

There is an additional aspect for the anesthetist to consider: Anesthetic systems running at low or minimal fresh gas flows react more slowly to changes in oxygen or anesthetic gas concentration. This is not difficult to handle, but needs to be understood and anticipated for effective operation. The booklet “Low-flow, minimal-flow and metabolic-flow anesthesia. Clinical techniques for use with rebreathing systems” by C. Hönemann and B. Mierke provides background information and best-practice examples on the use of the low- and minimal-flow technique (Link). In addition to that, modern anesthetic machines can provide additional software tools to help make low- and minimal-flow anesthesia a consistent practice (see our Technology Insights paper (Link)).

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DEFINITION OF LOW-LOW AND MINIMAL-FLOW

Low-flow anesthesia is considered to be achieved at a fresh gas flow of 1 L/min, any higher fresh gas flow settings are considered high-flow. A general anesthetic with fresh gas flows of approx. 0.5 L/min is called minimal-flow anesthesia. The lower the fresh gas flow, the lower is the quantity of cold and dry gas from the central gas supply or gas cylinders streaming into the system, therefore more of the gas circulates in the breathing system and less is exhausted through the gas scavenging system. This keeps the warmth and the humidity from the patient’s lungs and the chemical reaction of the soda lime with the expired CO₂ within the system. For effective operation of anesthesia with low fresh gas flows, adequate equipment is required that allows for robust and precise control of flows, gas concentration and minimal leakage, as well as precise continuous anesthetic gas monitoring.

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