Study protocol

# The effect of nasal continuous positive airway pressure on oxygenation in high-risk patients having gastrointestinal endoscopy under deep sedation

Responsible:

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## 1. Backround

Deep sedation during gastrointestinal endoscopy in patients with cardiopulmonary risk factors such as respective co-morbidities or also morbid obesity is challenging. Those high-risk patients are at risk of upper airway obstruction and hypoxemia. Nasal continuous positive airway pressure may help to decrease the incidence of peri-interventional hypoxemia. However, data on nasal continuous positive airway pressure in high-risk patients having gastrointestinal endoscopy are scarce; only one randomized trial on gastroscopy in obese patients is available (Kang et al. J Anesth 2021). In a very high-risk group, namely patients assessed for heart or lung transplantation in our hospital, the risk was especially high (unpublished data)

## 2. Objective

We aim to investigate the effect of nasal continuous positive airway pressure – compared to nasal oxygen insufflation – on the incidence of hypoxemia in high-risk patients having gastrointestinal endoscopy in deep sedation.

## 3. Hypothesis

We hypothesize that nasal continuous positive airway pressure – compared to nasal oxygen insufflation – reduces the incidence of hypoxemia in high-risk patients having gastrointestinal endoscopy in deep sedation.

## 4. Setting

Single-centre prospective randomised trial in the Department of Interdisciplinary Endoscopy and the Department of Anesthesiology of a German university medical center.

## 5. Patients

Inclusion criteria

• Adult and obese high-risk patients (ASA class ≥3 and/or BMI ≥30 kg/m², in accordance with the current WHO definition of obesity) scheduled for elective gastrointestinal endoscopy with deep sedation.

Exclusion criteria

- Age < 18 years
- Pregnancy
- Cognitive impairment, that makes consent to study impossible
- Known but untreated heart disease (e.g. PFO, recent congestive heart failure), complicating comparability within groups

Outcome

*Primary outcome*:

- The incidence of hypoxemia defined as a peripheral oxygen saturation of ≤90% registered with the monitoring system of our working station (Phillips IntelliVue and Massimo Rad-97) after inducing deep sedation while unter endoscopy intervention.

*Secondary outcomes*:

- Duration of intervention (absolute)
- Duration of hypoxemia/Time until recovery (>90%) (absolute)
- Hypoxemic events per intervention
- Ratio of hypoxemia duration compared to procedure duration (relatively)
- Incidence of need for airway intervention (mask ventilation, intubation, interruption)
- Comparison between subgroups BMI 30+; 35+; 40+ kg/m²

- Sedation score (Modified Observer Assessment of Alertness/Sedation)
- Continuous measurement of endtidal CO2 via the mask

## 6. Protocol

Patients will be randomized to nasal continuous positive airway pressure or nasal oxygen insufflation.

Patients randomized to nasal continuous positive airway pressure will receive a positive pressure between 3 and 10cm H2O depending on the type of endoscopy, and an oxygen flow rate of 6l/min. Patients randomized to nasal oxygen insufflation nasal oxygen will be started with a flow of 6L/min.

Deep sedation will be performed under surveillance of an anaesthesia-team (physician and nurse) using a propofol bolus of 1 mg/kg adjusted body weight, followed by a continuous propofol infusion of 4mg/kg/h (adjusted to lean body weight) (MacDonald JJ, Moore J, Davey V, Pickering S, Dunne T. The weight debate. J Intensive Care Soc. 2015 Aug;16(3):234-238. doi: 10.1177/1751143714565059), until a MOAA/S Score of 1-2 is reached (Kowalski R, Mahon P, Boylan G, et al. Validity of the modified observer's assessment of alertness/sedation scale (MOAA/S) during low dose propofol sedation: 3AP6-3. Eur J Anaesthesiol. 2007;24:26–27, DOI:10.1097/00003643-200706001-00097). If necessary, additional boluses of 20mg Propofol will be administered until the desired sedation depth is achieved. SpO2 and heart rate will be monitored continuously. Blood pressure will be monitored using upper-arm cuff oscillometry (3-minute intervals). Additional data collected from the medical record will include baseline SpO2, post-interventional SpO2, procedure length, and length of stay in the post anesthetic care unit (PACU).

## 7. Statistics

Descriptive analysis will be performed to describe patient characteristics and clinical data. The primary and secondary outcomes will be analysed according to the intention-to-treat principle. The primary outcome and dichotomous secondary outcomes of treatment arms will be compared by means of Chi-squared tests and odds ratios with 95% confidence intervals. Secondary outcomes measured on interval scales will be compared by means of t-tests, Welch-tests or Mann-Whitney test as appropriate, depending on whether test assumptions (particularly normal distribution and variance homogeneity) are met. Data will be checked for normal distribution and variance homogeneity prior to these analyses. Secondary outcomes measured on ordinal scales will be compared by means of Mann-Whitney U-tests. Reporting will be consistent with CONSORT guidelines. Statistical analyses will be performed with standard statistical software such as SPSS (IBM Corp., Armonk, NY), SAS (SAS Institute Inc., Cary NC) or R (R Core Team, 2017).

Sample size:

The sample size calculation is based on the primary outcome of the incidence of hypoxemia defined as a peripheral oxygen saturation of ≤90% after inducing deep sedation while performing endoscopy.

The incidence of the primary outcome was assumed to be 30% in nasal oxygen insufflation group and 10% in the nasal continuous positive airway pressure group. A total sample size of 158, i.e., 79 patients per group, is required to achieve 90% power in the detection of a difference of 20% between the group incidences at a significance level of 0.05 using a two-sided test of proportions. It is assumed that all patients stay within their treatment group within the observational period.

The randomization and division in subgroup “nasal continuous positive airway pressure” and “nasal oxygen insufflation” will occur prior to study entry. The entire

collective will be divided into 2 populations and the allocation sealed in envelopes. The envelope will only be opened directly before the study so that investigator bias can be minimized.

## 8. Abbreviations

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| ASA | American Society of Anaesthesiology |
| BMI | Body Mass Index |
| WHO | World Health Organisation |
| MOAA/S | Modified Observer Assessment of Alertness/Sedation |
| PBW | Predicted Body Weight<br>males (kg) = 50 + [0.91 ×(Height in cm − 152.4)]<br>females (kg) = 45.5 + [0.91 ×(Height in cm − 152.4)] |
| IBW | Ideal Body Weight<br>Male (kg): 50,0 kg+2,3kg*(cm-60)<br>Female (kg): 45,5 kg+2,3kg*(cm-60) |
| ABW | Adjusted Body Weight<br>IBW+0,4*(actual body weight-IBW) |
| LBW | Lean Body Weight<br>males (kg) = (9270 × TBW)/ [6680 + (216 × BMI)]<br>females (kg) = (9270 × TBW)/ [8780 + (244 × BMI)] |