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Efficiency and safety of nasal positive airway pressure systems during endoscopic procedures in high-risk patients: Endo-Breath study

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ABSTRACT

Background and study aims Sedation of high-risk patients is a relevant issue in interventional endoscopy. This is especially because standard oximetric monitors display only hypoxia and not the preceding hypercapnia. Therefore, the question arises whether use of a nasal positive airway pressure (nPAP) system can decrease the rate of sedation-associated events.

Patients and methods A randomized, prospective trial was conducted at University Hospital Ulm, including 98 consecutive patients, identified as high-risk (American Society of Anesthesiologists physical status ≥3) and scheduled for prolonged (>15 minutes) endoscopic procedures. Patients underwent 1:1 randomization to two groups: interventional (nPAP-Mask) and control (conventional oxygen supplementation). Levels of CO_2 were measured noninvasively by transcutaneous capnometry device. The primary outcome was incidence of hypoxia (SpO_2 <90% over 10 seconds) and incidence of severe hypoxia was incidence of SpO_2 <80% over 10 seconds. One of our secondary objectives was to determine if the nPAP-Mask could result in significant CO_2 retention among high-risk patients.

Results Data analysis showed lower incidence of hypoxia in the interventional group (10/47 vs. 31/251) P <0.05. Episodes of severe hypoxia (SpO_2 <80% over 10 seconds) were more frequent in the control group (8/51) compared with the intervention group (2/47) P <0.05. There was no significant difference in ΔCO_2 levels in the interventional vs. control group (–6.01±7.66 vs. –7.35±8.59 mm Hg).

Conclusions In high-risk patients use of a nasal positive airway pressure system could significantly lower risk of hypoxia, especially in prolonged procedures. The nPAP-Mask does not induce CO_2 retention when compared with conventional oxygen supplementation.

Introduction

Patient safety is imperative in all types of endoscopic procedures, particularly for those categorized as high risk due to underlying chronic diseases (classified as American Society of Anesthesiologists (ASA) III or ASA IV). Ensuring a safe intervention becomes even more challenging in such cases. Hypoxia, a potentially life-threatening complication, can arise during endoscopic procedures when patients are under deep sedation. Previous studies support the fact that episodes of hypoxia are more prevalent among patients with multiple comorbidities and elderly individuals. One of the leading causes of acute re-

spiratory failure during endoscopy is insufficient ventilation due to airway obstruction caused by soft palate and epiglottis falling back to the posterior pharynx.

Hypercarbia, resulting from insufficient clearance of CO_2 due to hypoventilation-associated ineffective gas exchange, can also have drastic consequences. However, unlike hypoxia, which manifests immediately, the accumulation of CO_2 takes time. Elevated levels of carbon dioxide can lead to altered mental status, respiratory acidosis, fasciculations, arrhythmias, and coma. Detecting hypercapnia in sedated patients is nearly impossible through standard monitoring. It requires specialized equipment for accurate measurement, which is not usually available in an endoscopy unit.

Endotracheal intubation remains the gold standard for optimal airway support due to its recognized safety. However, resource constraints might hamper the adoption of endotracheal intubation and continuous anesthesiologic support for routine endoscopy even in high-risk patients. Indeed, the invasive nature of general anesthesia has led to concerns regarding the efficiency of resource management within endoscopy units when considering performing endotracheal intubation on every high-risk patient scheduled for an endoscopic intervention.

In the pursuit of a safe and efficient alternative for airway management, previous studies have demonstrated promising results with significantly reducing the occurrence of hypoxia using noninvasive devices. One such device is the positive airway pressure system SuperNO2VA (Vyaire Medical Inc., United States), which has already demonstrated feasibility and safety in diagnostic endoscopic procedures for bariatric patients [1].

It remains unclear whether SuperNO2VA can decrease the incidence of hypoxia during prolonged endoscopic procedures in non-bariatric high-risk patients. Furthermore, the incidence and severity of hypercarbia using nasal positive airway pressure (nPAP) systems are poorly understood.

CO_2 levels are typically assessed by analyzing blood samples (venous, arterial, or capillary) or through detection of exhaled CO_2 using nasal capnography. In case of upper gastrointestinal endoscopy, the utility of nasal capnography appears limited, given the fact that many modern endoscopes use CO_2 for insufflation, which may lead to inconclusive data. Blood sampling for hypercarbia detection is invasive and does not provide real-time monitoring of CO_2 levels during interventions.

Novel noninvasive methods of CO_2 measurement, such as transcutaneous capnometry, have demonstrated high sensitivity and specificity when compared with capillary blood CO_2 levels. This method has already proven to be safe and effective in detection of hypercarbia during endoscopic procedures in the presence of high-flow nasal cannula oxygen [2].

This prospective study aimed to investigate whether nPAP systems can mitigate the risk of hypoxia and prevent hypercabia compared with conventional nasal oxygen cannulation in high-risk patients. Furthermore, we intended to analyze the relationship between various factors such as age, sex, procedure duration, type of procedure, sedation agent dosage and type, underlying chronic disease, and occurrence of hypercarbia during prolonged endoscopic procedures.

Patients and methods

Design

This single-center, randomized, controlled trial was performed at the University Hospital Ulm, Germany. The study protocol was approved by the local ethics committee. The study was conducted in accordance with the principles of the Declaration of Helsinki and established best clinical practice. The study was also registered on the Clinical Trials Database under the identifier NCT05972304.

Study protocol

A total of 98 consecutive patients with underlying chronic diseases were included in the study. These patients were stratified as high peri-procedure risk individuals based on the American Society of Anaesthesiologists physical status classification system (ASA III and ASA IV) [3]. They were scheduled for prolonged endoscopic procedures, including colonoscopy, gastroscopy, colonoscopy and gastroscopy, endosonographic ultrasound of the upper gastrointestinal tract, and endoscopic retrograde cholangiopancreatography (ERCP). A prolonged endoscopic procedure was defined as a diagnostic or interventional procedure with a duration longer than 15 minutes.

Study randomization was conducted using Study Randomizer (Version 2017, Phase Locked Software, Netherlands), a web-based randomization service. The participants were divided into two groups in a 1:1 ratio. The interventional group received nPAP with the SuperNO2VA system, which involved insufflation of 10 L of oxygen per minute. This flow rate was determined as the minimum insufflation required for the system to function properly, recommended by the manufacturer of the mask. In the control group, participants received conventional oxygen supplementation with a maximum flow rate of 6 L of oxygen per minute, as advised by the manufacturer to prevent potential damage to the nasal mucosa. None of the patients received preoxygenation therapy, except those who were already using supplemental oxygen. After the endoscopic procedure, the patients were transferred to the recovery room. Oxygen levels were maintained at the same level as at the end of the procedure. Observation was discontinued when patients reached full recovery, as indicated by achievement of a Richmond Agitation-Sedation Scale (RASS) Level of 0.

SuperNO2VA is a PAP device that consists of a tightly sealed nasal mask and 2-L reservoir bag. When completely inflated and firmly applied, it generates intermittent PAP, which enables pneumatic stenting of upper respiratory tract. This in itself leads to optimizing oxygen flow and reducing dead space [1]. However, it was not previously documented whether such a mechanism could lead to entrapment of CO_2 in the reservoir bag, thus increasing the risk of hypercarbia. It is also unknown whether such devices could reduce the risk of hypercarbia by lowering CO_2 levels through intermittent PAP, which could lead to increased ventilation of pulmonary dead space.

The procedures were performed by two experienced endoscopists, each with an extensive clinical experience of over 10 years. One endoscopist was responsible for conducting the intervention, while the other one was in charge of administering

sedation. The sedation protocol adhered to German national guidelines and represents standard practice for endoscopic procedures conducted in university hospitals. Procedure sedation and analgesia were administered by an experienced endoscopist certified in advanced life support, adhering to guidelines outlined by the European Society of Anaesthesiology and the European Board of Anaesthesiology for procedure sedation and analgesia in adults [4]. Sedation was administered using either the intermittent propofol bolus application method alone or in combination with midazolam bolus application [5].

All patients were monitored in accordance with a standardized protocol, which included monitoring blood pressure, oxygen saturation (SpO_2), and heart rate. In addition, a transcutaneous capnometry system (TCM 5 by Radiometer GmbH, Krefeld, Germany) was used for monitoring. Invasive capnometry was not used in this study. The transcutaneous CO_2 probe was attached to the forehead of each participant and the system was set to the minimum testing temperature of 42° C. Endoscopic procedure duration was calculated from initiation of sedation until the end of the endoscopic procedure and patient transfer to the recovery room. Continuous observation was carried out in the recovery room as well, to ensure the absence of any severe adverse events (AEs). However, data collected during this observation period were not intended for use in statistical analysis. Observation in the recovery room was discontinued once a patient achieved a RASS score of 0.

Participant recruitment

Recruitment of patients was performed regarding further inclusion and exclusion criteria. Inclusion criteria were: 1) estimated duration of endoscopic procedure ≥15 minutes; 2) patient age >18 years at time of recruitment; 3) underlying chronic disease, stratified as ASA III (poorly controlled diabetes mellitus or arterial hypertension, chronic obstructive pulmonary disease, morbid obesity (body mass index [BMI] ≥40), active hepatitis, advanced chronic liver disease, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, end-stage renal disease undergoing regularly scheduled dialysis, history (>3 months) of myocardial infarction, transient ischemic attack, or coronary atherosclerotic disease; 4) underlying chronic disease, stratified as ASA IV (recent (<3 months myocardial infarction, transient ischemic attack or coronary atherosclerotic disease, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, acute renal damage or end-stage renal diseases not undergoing regularly scheduled dialysis; 5) existence of active malignancy (Eastern Cooperative Oncology Group Performance Status ≥2); and 6) severe obesity (BMI ≥35 kg/m^2).

Patients were excluded if they had a tracheotomy, were pregnant, or had intubation-assisted endoscopy or a procedure without sedation.

Outcomes

Our primary outcome was incidence of hypoxia episodes (SpO_2 <90% >10 seconds) as well as occurrence of severe hypoxia (SpO_2 <80% >10 seconds) during the procedure. The determined SpO_2 cut-off values were in accordance with AWMF S3 German Guideline [6]. Our secondary outcomes were the difference in $tcpCO_2$ values from the beginning of the intervention to the mean $tpCO_2$ levels observed throughout the procedure, the number of manipulations/maneuvers needed to provide upper airway support, the rate of severe complications such as manual bag ventilation, intubation, reanimation or death. Furthermore, the correlation between procedure type and $tcpCO_2$ levels was assessed. Finally, we intended to investigate the impact multiple comorbidities on severity of CO_2 retention. Other factors such as procedure duration and amount and type of sedation were also analyzed in regard to their influence on hypercarbia.

Data collection

Data collection was performed with the assistance of the principal investigators' study assistants, who used "on-site" documentation of vital parameters while observing patients during endoscopy. The acquired data were then validated through a post-procedure analysis of CO_2 and SpO_2 measurements stored in the TOSCA TCM5 monitor capnometry device memory unit. After enrolling patients in the study and obtaining their previous medical history, they were assigned an identification number and kept blinded to the physicians conducting endoscopy. All patient data were pseudonymized, making them completely traceable only for the principal investigator and the principal investigator's study assistants.

Statistics

Descriptive statistics using absolute amounts and percentages of categorical variables, or mean and standard deviation of numeric variables, were performed to characterize the collective. To investigate the difference in hypoxia episodes between two groups, a Fisher Exact Test was performed. Analysis of CO_2 levels was conducted using the Student's *t*-test. For a correlation matrix to investigate the correlation and effect between type of procedure, comorbidities, procedure length, and type of sedative, the Spearmen correlation factor was applied. P <0.05 was considered to be statistically significant. Statistical analysis was performed using open-source statistical software RStudio (Version 4.2.2; Posit, PBC; Austria).

Results

This study was conducted at the Endoscopy Unit of University Hospital Ulm from April 2022 to November 2022. Of the initially enrolled 107 patients, nine were subsequently excluded from the study for the following reasons: In one case, a change in method of oxygen supplementation (from conventional to nPAP mask) was performed during the endoscopic procedure based on the endoscopist's decision. In four cases, the endoscopic procedure lasted l<15 minutes. In three cases, capnometry electrodes were disconnected for a prolonged period of time (>30 seconds). In one case, the stored data on the device became damaged, and therefore, were not suitable for analysis. Descriptive statistics as well as detailed data about the population of this study are shown in ▶ **Table 1**.

▶ **Table 1** Descriptive statistics and general study population.

	SuperNO2VA	Supplemental oxygen
Total number of patients (n = 98)	47	51
Gender (male/female) n = M/F (%)	27/20 (57%/43%)	24/27 (47%/53%)
Age (years) Mean ± (Standard deviation)	70.34±12.3 Max 90 Min 40 IQR (60.6–81.5)	73.7±10.8 Max 93 Min 40 IQR (66.9–80.7)
BMI (kg/m^2) Mean ± standard deviation	26.2±5.43 Max 44.4 Min 17.6 IQR (22.2–29.2)	26.09±5.04 Max 44.6 Min 18.8 IQR (24.4–28.7)
ASA Classification		
n (%)		
▪ **ASA III**	44 (94%)	43 (84%)
▪ **ASA IV**	3 (6%)	8 (15%)
Intervention duration (minutes) Mean ± standard deviation	33.8±25.2 Max 115 Min 15 IQR (16–38.5)	33.92±38.72 Max 270 Min 15 IQR (17.5–34.0)
Intervention types		
n (%)		
▪ **EGD**	7 (15%)	10 (19%)
▪ **EGD + endosonography**	2 (4%)	2 (4%)
▪ **EGD + colonoscopy**	15 (32%)	16 (31%)
▪ **Colonoscopy**	20 (42%)	15 (29%)
▪ **ERCP**	2 (4%)	7 (13%)
▪ **Endosonography + ERCP**	2(1%)	1 (2%)
Underling chronic conditions		
n (%)		
▪ **Heart disease**	27 (57%)	21 (41%)
▪ **Pulmonary disease**	10 (21%)	7 (14%)
▪ **Terminal renal disease**	1 (2%)	0 (0%)
▪ **Vascular disease**	21 (44%)	25 (50%)
▪ **Poorly controlled diabetes or hypertension**	22 (47%)	26 (51%)
▪ **Chronic liver disease**	10 (21%)	13 (25%)
Sedative agent		
Propofol (mg) Mean ± standard deviation	287.71±168.34 (Max 800, min 80) IQR (175–d355)	297.2±282.06 (max 1930, min 80) IQR (160–315)
Midazolam (mg)*	2 cases, 1 mg 5 cases, 2 mg 1 case, 4 mg	5 cases, 2 mg 3 cases, 3 mg 1 case, 4 mg

IQR, interquartile range; BMI, body mass index; ASA, American Society of Anesthesiologists; EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography.
*Midazolam was only applied in combination with propofol. The application was performed based on the decision of the endoscopist.

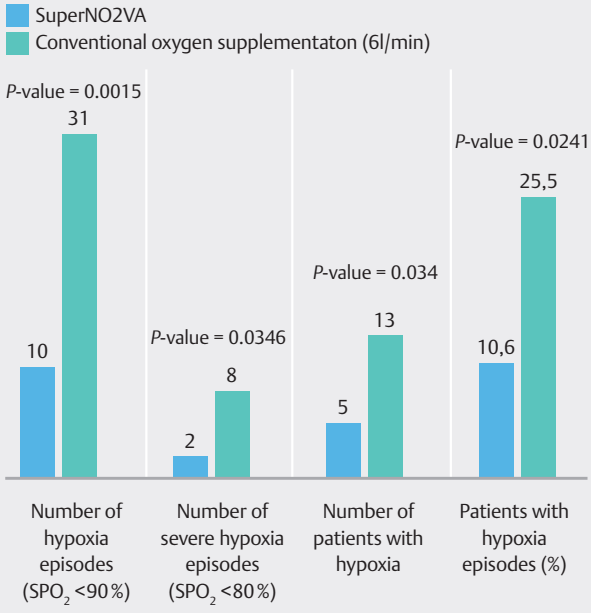
▶ **Table 2** Demonstration of data analysis performed to compare hypoxia events and hypoxia severity in interventional and control groups.

	SuperNO2VA	Supplemental oxygen	*P* value
Hypoxia episodes (SpO_2 <90% over 10 seconds) (n)	10	31	0.00015
Number of severe hypoxia episodes (SpO_2 <80% over 10 seconds) (n)	2	8	0.0346
Number of patients with hypoxia episodes (n)	5	13	0.034
Corelation between each patient and number of hypoxia episodes	1 patient (5 episodes) 1 patient (2 episodes) 3 patients (1 episode)	1 patient (6 episodes) 2 patients (4 episodes) 2 patients (3 episodes) 3 patients (2 episodes) 5 patients (1 episode)	–
Hypoxia duration (sec) Mean ± standard deviation*	174.6±154.4 Max 424 Min 16	390±696.9 Max 2544 Min 5†	0.0004
SpO_2 initial (%) Mean ± standard deviation	97.81±2.82	97.46±1.93	0.4693
SpO_2 max (%) Mean/± standard deviation	99.92±2.82	99.74±0.55	0.0766
SpO_2 min (%) Mean ± standard deviation	94.65±8.06	91.90±6.75	0.112

*IQR (interquartile range) could not be calculated due to small sample size.
†The shortest hypoxia episode, detected by the TOSCA Monitor system, lasted for only 5 seconds. There was only one instance of a hypoxia episode with SpO2 <90% that lasted less than 10 seconds. This particular episode was included in the statistical analysis.

Primary outcomes

We observed that 10.6% of patients (5/47) in the SuperNO2VA Group experienced hypoxia episodes, while 25.5% of patients (13/51) in the conventional oxygen supplementation group had episodes of hypoxia. The difference was statistically significant ($P = 0.034$; 95% confidence interval [CI] 0.105–1.079). The difference in the number of hypoxia episodes (SpO_2 <90% over 10 seconds) between the intervention group (10/47) and the control group (31/51) was also statistically significant (P <0.00015; 95% CI 1.737–∞). Episodes of severe hypoxia (SpO_2 <80% over 10 seconds) were more frequent in the control group (8/51) compared with the intervention group (2/47) (P= 0.0346; 95% CI 0.1805–2.7547). Not only the frequency of hypoxia episodes but also the duration of hypoxia was significantly longer in the control group ($P = 0.0004$). The data are presented in ▶ **Table 2** as well as in ▶ **Fig. 1**.



▶ **Fig. 1** Graphic demonstration of hypoxia and severe hypoxia event SuperNO2VA- and conventional oxygen supplementation (control) groups.

Secondary outcomes

There was no significant difference in initial levels of CO_2 between the two groups ($P = 0.615$; 95% CI –2.437–4.096), which could be interpreted as an optimal starting point for the analysis, indicating that patients in both groups started at the same level. However, no statistically significant difference was detected in mean transcutaneous CO_2 levels between the groups ($P = 0.734$; 95% CI –3.487–2.464). Results of the measured transcutaneous delta CO_2 levels (tcpΔ CO_2) did also not show any statistically significant difference ($P = 0.416$; 95% CI –4.594–1.914). The number of maneuvers aimed at upper respiratory tract support (head tilt, jaw thrust, repositioning of the nPAP mask) was comparable in both groups. Suction to remove mucus was used at almost the same rate in both groups. There was only one severe AE—manual bag ventilation—which

▶ **Table 3** Data analysis performed on rate of hypercarbia, number of episodes of upper respiratory tract support, and number of severe adverse events in the interventional and control groups.

	SuperNO2VA	Supplemental oxygen	*P* value
CO_2 initial (mm HG) Mean ± standard deviation	33.53±8.87 Max 65.3 Min 16.3 IQR 30.1–36.8	32.72±7.24 Max 67.9 Min 18.7 IQR 29.3–35.4	0.6151 95% CI –2.4373–4.0966
CO_2 mean (mm HG) Mean ± Standard deviation	39.6±7.62 Max 62.0 Min 23.7 IQR 35.1–43.0	40.08±7.18 Max 60.7 Min 23.2 IQR 35.1–46.1	0.7336 95% CI –3.4875–2.4642
Delta CO_2 (mm HG) **Initial CO_2, mean CO_2** Mean ± standard deviation	–6.01±7.66 Max 17.6 Min –27.7 IQR –8.15 to –2.51	–7.35±8.59 Max 26.0 Min –33.6 IQR –10.7 to –3.67	0.4159 95% CI –4.5946–1.9146
Number of episodes securing upper airway (n)	22	29	0.672
Number of patients who required upper airway securement (n)	15	18	0.641
Number of episodes using suction (n)	12	12	0.721
Number of patients who required suction (n)	6	8	0.678
Severe adverse events (n)	0	1	0.117

IQR, interquartile range.

occurred in the conventional oxygenation group in the recovery room. The data are presented in ▶ **Table 3**.

Analysis of CO_2 levels in relation to type of endoscopic procedure showed no significant differences in mean $tcpCO_2$ levels ($P=0.633$; 95% CI –4.539–7.339) or $\Delta tcpCO_2$ levels ($P=0.618$; 95% CI –4.981–8.241) during upper gastrointestinal endoscopy between the SuperNO2VA Group and the control group. No statistical significance was detected when analyzing data from patients who underwent only lower gastrointestinal colonoscopy (mean $tcpCO_2$ $P=0.754$; 95% CI –5.208–3.808) ($\Delta tcpCO_2$ $P=0.921$; 95% CI –7.019–6.357). Interestingly, we did observe a statistically significant result in favor of the intervention group when comparing $\Delta tcpCO_2$ levels between the groups during the combined endoscopic procedure ($P=0.019$; 95% CI –5.646–0.533). Detailed data are shown in ▶ **Table 4**.

We conducted a univariate analysis to investigate whether any of the variables exhibited statistically significant correlations with frequency of hypoxic episodes. After processing the data, we isolated those variables that demonstrated statistical significance or approached significance ($P<0.1$) in correlation (positive or negative) with the number of hypoxia episodes (SpO_2 <90 sec). These included: sex (male), height, colonoscopy, ASA status, and use of nPAP-mask. These variables were subjected to multivariate analysis, revealing that the most significant determinant leading to a higher frequency of hypoxia episodes was ASA status. Utilization of the nPAP mask displayed a negative correlation with hypoxia episodes; however, it did not reach statistical significance ($P=0.0831$). The results are shown in ▶ **Table 5** and ▶ **Table 6**.

Additional investigation into the comparison of different endoscopic procedures in relation to hypoxia events yielded interesting results. The incidence of events, including severe hypoxia episodes, was notably lower in the nPAP mask group compared with the conventional oxygen therapy group. This trend was particularly noticeable in the oral endoscopy group (comprising procedures such as esophagogastroduodenoscopy or endoscopic ultrasound [EUS], or a combination of both), as well as in the ERCP and ERCP + EUS subgroups, where results were statistically significant. However, due to the small sample sizes of the subgroups, we could not find any other statistically significant results in other types of endoscopic procedures. Further data are shown in ▶ **Table 7**.

To investigate factors contributing to development of hypercarbia, a correlation analysis was conducted using Spearman's correlation coefficient. The analysis revealed a weak correlation between mean transcutaneous carbon dioxide ($tcpCO_2$) levels and delta (Δ) $tcpCO_2$ levels observed during upper gastrointestinal endoscopy in patients. Furthermore, a weak correlation was observed between the amount of propofol administered during the procedure and both variables. Remarkably, a weak correlation was also identified in patients who underwent suction during the procedure. Conversely, no significant correlation was observed between the occurrence of hypoxia episodes and CO_2 levels. In addition, the duration of hypoxia episodes did not exhibit any correlation wither the mean transcutaneous carbon dioxide ($tcpCO_2$) level or delta (Δ) $tcpCO_2$. For a more comprehensive understanding of these findings, refer to ▶ **Table 8**, which presents detailed results.

▶ **Table 4** Comparison of rates hypercarbia independence for procedures performed in the interventional and control groups.

	SuperNO2VA	Supplemental oxygen	*P* value
Upper gastrointestinal endoscopy (EGD, EGD + endosonography, endosonography + ERCP, ERCP) n = 32			
Number of patients (n)	n = 12	n = 20	
CO_2 mean (mm HG) Mean ± standard deviation	42.01±10.0	43.41±6.50	0.6337 95% CI -4.5390–7.3390
Delta (Δ) CO_2 (mm HG) Mean ± standard deviation	–11.1±9.29	–9.47±8.61	0.6183 95% CI -4.9812–8.2412
Lower gastrointestinal endoscopy (colonoscopy) n = 35			
Number of patients (n)	n = 20	n = 15	
CO_2 mean (mm HG) Mean ± standard deviation	40.09±5.01	39.39 ± 8.07	0.7540 95% CI –5.2079–3.8079
Delta (Δ) CO_2 (mm HG) Mean ± standard deviation	–5.14±7.63	–5.47±11.8	0.9206 95% CI –7.0168–6.3568
Combined upper and lower gastrointestinal endoscopy (EGD and colonoscopy) n = 31			
Number of patients (n)	n = 15	n = 16	
CO_2 mean (mm HG) Mean ± standard deviation	36.79±3.60	36.58±3.35	0.8676 95% CI –2.7628 to –2.3428)
Delta (Δ) CO_2 (mm HG) Mean ± standard deviation	–3.07±3.61	–6.16±3.35	0.0195 95% CI –5.6465 to –0.5335)

EGD, esophagogastroduodenoscopy; ERCP, endoscopy retrograde cholangiopancreatography; CI, confidence interval.

Discussion

Hypoxia is a major AE that can occur during endoscopic procedures when using sedatives. In our literature research, we found that the reported incidence of hypoxia in endoscopy varies greatly. Rates of hypoxia (defined as oxygen saturation <90% for >10 seconds) in the general population undergoing endoscopy with sedation have been documented as low as 10% and as high as 50%. Furthermore, in patients with chronic comorbidities, hypoxia incidence tends to be even more frequent and is reported to be as high as 80% [7].

Invasive PAP systems, such as the SuperNO2VA, have been studied in a highly selective patient collective for their efficacy in preventing hypoxia during endoscopic procedures, and encouraging findings have been documented in prior research [1, 8]. However, application of SuperNO2VA masks in procedures involving a broader collective of non-bariatric patients with high periprocedure risk has not been previously explored.

In our study, we evaluated the efficacy of the SuperNO2VA Mask in comparison with conventional nasal oxygen supplementation for reducing risk of hypoxia (SpO_2 <90%) in high-risk patients undergoing endoscopic procedures. Use of the SuperNO2VA mask demonstrated superiority over conventional supplementation, with significantly fewer episodes of severe hypoxia (SpO_2 <80%) observed in the control group. Not only did the frequency of hypoxia episodes decrease, but the duration of insufficient oxygenation was also shorter when the nPAP system was applied. This effect is presumed to be achieved by generating sufficient positive intermittent airway pressure, which prevents collapse of small airways and facilitates additional ventilation surface in the lungs.

To evaluate the severity and incidence of hypercarbia in our patients, we assessed changes in transcutaneous carbon dioxide (Δ $tcpCO_2$) levels during the procedure, as well as mean $tcpCO_2$ levels throughout the entire procedure. This method proved to be more reliable for indicating susceptibility to CO_2 retention compared with simply counting the number of episodes during which CO_2 levels exceeded 60 mm Hg. Considering that some patients in our study already exhibited elevated baseline CO_2 levels due to underlying diseases, comparing absolute values of CO_2 seemed inadequate.

Statistical analysis revealed no significant differences in mean and Δ$tcpCO_2$ levels between the intervention and control groups. Furthermore, use of the nPAP mask did not result in clinically relevant CO_2 entrapment in the reservoir bag or emergence of hypercarbia. When considering the type of endoscopic procedure and $tcpCO_2$ levels, it was observed that patients undergoing lower gastrointestinal endoscopy tended to exhibit smaller mean and Δ $tcpCO_2$ levels compared with patients undergoing upper gastrointestinal endoscopy alone.

The number of standard manipulations performed to secure the upper airway, such as jaw thrust, head tilt, application of a nasopharyngeal tube, mask adjustment, and repositioning of the nasal oxygen cannula, was more frequent in the control group than in the intervention group. However, it is important to interpret these data cautiously because the specific type of airway support employed was not documented. In addition, due to the novelty of the nPAP mask in our endoscopy unit,

▶ **Table 5** Univariate analysis of variables and their impact on number of hypoxia episodes (SpO_2 <90%).

Variable	Coefficient	Standard Error	T value	*P* value
Age	0.02884	0.02657	1.085	0.278
Sex	−1.2131	0.5825	−2.082	0.0373
Size	−0.09238	0.03220	−2.869	0.00412
Weight	−0.02373	0.02002	−1.186	0.236
ASA grade	1.5180	0.7762	1.956	0.0505
Duration	0.007823	0.008292	0.943	0.3455
EGD	0.7940	0.7269	1.092	0.27471
EGD + EUS	−17.4729	0.7663	−0.006	0.99512
EGD + colonoscopy	0.3244	0.6276	0.517	0.60519
Colonoscopy	−1.6368	0.7024	−2.330	0.0198
ERCP	0.8743	0.9386	0.932	0.35158
EUS + ERCP	−16.4518	0.1469	−0.007	0.99465
Supernova	−1.0497	0.5932	−1.770	0.0768
Nasal cannula	1.0497	0.5932	1.770	0.076803
Initial CO_2	0.02065	0.03632	0.569	0.570
Midazolam	−17.8068	0.3122	−0.004	0.9968
Propofol	−0.001479	0.001754	−0.843	0.399
Suction	0.4833	0.3876	1.247	0.21249
Upper airway maneuver	0.3315	0.2845	1.165	0.24399
Cardiac disease	0.4463	0.5923	0.754	0.45112
Pulmonary disease	−0.9777	0.8837	−1.106	0.2685
Vascular disease	0.4674	0.5907	0.791	0.4287
Liver disease	0.5829	0.6788	0.859	0.39048
Diabetes mellitus or poorly controlled hypertension	0.8808	0.6008	1.466	0.142598
Oncologic disease ECOG 1	−0.70026	0.64472	−1.086	0.277
Oncologic disease ECOG 2	0.04594	0.88552	0.052	0.959
Oncologic disease ECOG 3	0.95266	1.52150	0.626	0.531

ASA, American Society of Anesthesiologists; EGD, esophagogastroduodenoscopy; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; ECOG, Eastern Cooperative Oncology Group.

there were frequent instances of mask dislocation during the initial stages of the study, likely attributable to a lack of experience with the device.

Only one severe AE, involving manual bag ventilation due to refractory hypoxia, occurred in the recovery room after the endoscopic procedure, and this event was observed in the control group. Following the procedure, patients in interventional group were kept on the SuperNO2VA mask in the recovery room, considering that the majority of peri-interventional hypoxia episodes occur during this period [9]. However, it is worth noting that this study did not specifically collect data during the recovery period, which could be an important area for investigation in future studies.

Analysis of the impact of different factors and their correlation with emergence of hypercarbia did not reveal any strong correlations. This is partially attributable to the small number of cohorts in this study. However, a weak correlation was observed between the dosage of propofol and Δ $tcpCO_2$. It can be suggested that the dosage of sedative is associated with decreased respiratory drive and, therefore, with the frequency and depth of respirations. It is important to note that procedure duration did not correlate with hypercarbia. Interestingly, the number of suction episodes also was weakly correlated with mean and Δ $tcpCO_2$ levels. However, the exact mechanism of this finding is unclear. It is also unclear whether the higher mean CO_2 levels led to hypersalivation or if hypersalivation and

▶ **Table 6** Representation of most significant multivariate analysis of variables and their impact on frequency of hypoxia episodes.

Variable	Coefficient	Standard error	T value	*P* value
Sex (male)	**–0.57961***	0.80840	–0.717	**0.4734**
Height	**–0.06027***	0.03923	–1.536	**0.1244**
ASA grade	**1.47484****	0.68511	2.153	**0.0313**
Colonoscopy	**–1.16990*****	0.72841	–1.606	**0.1083**
Supernova	**–1.03404*****	0.59673	–1.733	**0.0831**

***indicative of a moderate negative coefficient, while **signifies a moderate positive coefficient, *conversely, represents the absence of coefficient.
ASA, American Society of Anesthesiologists.

▶ **Table 7** Representation of hypoxia and severe hypoxia episodes in relation to type of endoscopic procedure.

	SuperNO2VA	Supplemental oxygen	*P* value
Upper gastrointestinal endoscopy (EGD, EGD + endosonography) n = 21			
Number of patients (n)	n = 9	n = 12	
Number of hypoxia episodes SpO_2 <90%	2	11	0.099
Number of severe hypoxia episodes SpO_2 <80%	1	0	0.717
Upper gastrointestinal endoscopy (endosonography + ERCP, ERCP) n = 11			
Number of patients (n)	n = 3	n = 8	
Number of hypoxia episodes SpO_2 <90%	0	8	**0.001**
Number of severe hypoxia episodes SpO_2 <80%	0	3	0.214
Lower gastrointestinal endoscopy (colonoscopy) n = 35			
Number of patients (n)	n = 20	n = 15	
Number of hypoxia episodes SpO_2 <90%	0	4	0.087
Number of severe hypoxia episodes SpO_2 <80%	0	1	0.981
Combined upper and lower gastrointestinal endoscopy (EGD + colonoscopy) n = 31			
Number of patients (n)	n = 15	n = 16	
Number of hypoxia episodes SpO_2 <90%	8	8	0.971
Number of severe hypoxia episodes SpO_2 <80%	1	3	0.064

EGD, esophagogastroduodenoscopy; ERCP, endoscopy retrograde cholangiopancreatography.

frequently applied suction led to obstruction of small airways, which then caused CO_2 retention, based on the gathered data.

Our study has several limitations. First, a significant number of patients were excluded due to practical issues, such as prolonged dislocation of the transcutaneous monitor sensor during the interventions, resulting in a loss of a considerable amount of data.

Second, oxygenation was only observed using pulse oximetry. Levels of true diluted oxygen in arterial or venous blood (paO_2 or pvO_2) remained unknown. It has been well-studied that oversaturation with oxygen could potentially be harmful to patients due to accumulation of reactive oxygen species [10]. Such species may be even more damaging for patients with multiple comorbidities.

Third, the initial setup process, which involved placement of the nPAP system, the $tpCO_2$ sensor, and calibration of transcutaneous monitoring devices, was performed by one of our trained study assistants. If the nPAP system became dislocated during a procedure, the endoscopy nurse was the first responder and attempted to reposition the mask for optimal respiratory support. During the initial stages of our study, this led to frequent incorrect placements of the device. It is evident that implementation of SuperNO2VA masks during endoscopy does require a certain level of initial experience to ensure provision of optimal support.

With this study we have intended to provide valuable insight about safety aspects in regard to incidence of hypoxia and hypercarbia during endoscopy in high-risk patients. The analyzed

▶ **Table 8** Examination of correlation between different factors and mean transcutaneous carbon dioxide ($tcpCO_2$) levels and delta (Δ) $tcpCO_2$.

Impact of variables on development of hypercarbia during endoscopy.			
	Mean tcCO2 (ρ(rho); df; P value)	**Delta (Δ) tcCO2* (ρ(rho); df; P value)**	**Chaddock scale Mean tcCO2 Delta (Δ) tcCO2**
Age	**0.129**; 96; 0.205	**–0.009**; 96; 0.929	Negligible correlation Absence of correlation
Sex (male/female)	**0.196**; 96; 0.096	**–0.049**; 96; 0.629	Negligible correlation Absence of correlation
BMI	**0.063**; 96; 0.001	**0.019**; 96; 0.852	Absence of correlation Absence of correlation
Hypoxia episodes	**0.058**; 96; 0.572	**–0.079**; 96; 0.438	Absence of correlation Absence of correlation
Hypoxia duration	**0.058**; 96; 0.559	**0.028**; 96; 0.784	Absence of correlation Absence of correlation
Upper gastrointestinal endoscopy	**0.299**; 96; 0.004	**–0.291**; 96; 0.004	*Weak correlation* *Weak correlation*
Lower gastrointestinal endoscopy	**–0.003**; 96; 0.975	**0.119**; 96; 0.244	Absence of correlation Negligible correlation
Combined upper and lower gastrointestinal endoscopy	**–0.289**; 96; 0.004	**0.172**; 96; 0.091	*Weak correlation* Negligible correlation
Suction	**0.292**; 96; 0.004	**–0.444**; 96; 0.001	*Weak correlation* *Weak correlation*
Maneuvers for upper airway support	**–0.051**; 96; 0.619	**0.156**; 96; 0.125	Absence of correlation Negligible correlation
Procedure duration	**0.162**; 96; 0.112	**–0.191**; 96; 0.061	Negligible correlation Negligible correlation
Multiple comorbidities	**–0.109**; 96; 0.284	**0.214**; 96; 0.035	Negligible correlation Negligible correlation
Sedation agent			
Propofol	**0.210**; 96; 0.038	**–0.424**; 96; 0.001	Negligible correlation *Weak correlation*
Midazolam in combination with propofol	**0.074**; 96; 0.572	**–0.175**; 96; 0.085	Absence of correlation Negligible correlation

It should be noted that the delta (Δ) tcpCO2 variable was calculated as a negative value, but the observed correlation indicated a negative relationship, contrary to the actual direct proportionality.
BMI, body mass index.

data show that hypoxia as well as severe hypoxia can still occur while using noninvasive airway support devices.

In a search for a noninvasive alternative, high-flow nasal cannulation therapy (HFNC) has been shown to be safe [11, 12, 13]. A significant number of studies have proven its efficacy in low- to moderate-risk patients, as well as in high-risk patients [14].

It is also known that HFNC therapy generates positive end-expiratory pressure [15], leading to passive ventilation of dead space volume and contributing to clearance of CO_2 from the lungs [16, 17]. Although technically easy to use, HFNC still requires qualified maintenance and cleaning by trained personnel. Therefore, its practicality, especially in centers with high patient turnover, would be questionable.

Head-to-head studies comparing SuperNO2VA masks and HFNC during endoscopic procedures and their influence on hypoxia and hypercarbia, as well as their cost efficiency, should be performed to generate new data about safety and feasibility of such devices in endoscopy units.

Conclusions

Use of SuperNO2VA masks during endoscopy has been shown to significantly reduce risk of hypoxia in high-risk patients when compared with conventional oxygen supplementation therapy.

Conflict of Interest

The authors declare that they have no conflict of interest.

Clinical trial

ClinicalTrials.gov (http://www.clinicaltrials.gov/)
Registration number (trial ID): NCT05972304
Type of Study: Prospective, Randomized, Single-Center

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