High flow nasal oxygen during procedural sedation for cardiac implantable electronic devices: A randomized controlled trial

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**Running head:** High flow nasal oxygen during sedation

### Abstract

**Background**

High flow nasal oxygen may better support the vulnerable breathing state of patients during procedural sedation.

**Objective**

The objective of this study was to investigate the effects of high flow nasal oxygen in comparison to facemask oxygen on ventilation during cardiac implantable electronic device procedures performed with procedural sedation.

**Design**

Randomized controlled trial.

**Setting**

The study was conducted at one academic teaching hospital in Canada.

**Participants**

Adults undergoing elective cardiac implantable electronic device procedures with sedation administered by an Anesthesia Assistant (supervised by an Anesthesiologist) from August 2019 to March 2020.

**Interventions**

Participants were 1:1 randomized to facemask (≥ 8L/min) or high flow nasal oxygen (50L/min and 50:50 oxygen to air ratio).

**Main outcome measures**

The primary outcome was peak transcutaneous carbon dioxide. Outcomes were analysed using Bayesian statistics.

**Results**

The 129 participants who were randomized and received sedation were included. The difference in peak transcutaneous carbon dioxide was 0.0mmHg (95% CI = -1.3 to 1.37). Minor adverse sedation events were 6.4 times more likely to occur in the high flow nasal oxygen group. This estimate is imprecise (95% CI = 1.34 to 42.99). The odds ratio for oxygen desaturation for the high flow nasal oxygen group compared with the facemask group was 1.2 (95% CI = 0.37 to 3.75). The difference in satisfaction with sedation scores between groups was 0.0 (95% CI = -0.33 to 0.23).

**Conclusions**

Ventilation, as measured by TcCO2, is highly unlikely to differ by a clinically important amount between high flow nasal oxygen at 50L/min or facemask oxygen at 8L/min. Further research with a larger sample size would be required to determine the optimal oxygen:air ratio when using high flow nasal oxygen during cardiac implantable electronic device procedures performed with sedation.

**Trial registration number:** NCT03858257

## Introduction

Cardiac implantable electronic device (CIED) procedures are commonly performed with procedural sedation.1 Oxygen supplementation is administered to reduce hypoxemia from sedation-induced hypoventilation.2,3 High flow nasal oxygen (HFNO) is a promising device for oxygen supplementation.4 HFNO allows for heated, humidified gas with a titratable oxygen:air ratio to be administered via nasal prongs at up to 70L/min. Delivering oxygen supplementation at such high flow-rates has physiological effects that may support the vulnerable breathing state of patients during procedural sedation. In particular, one of the proposed physiological effects of HFNO is that it facilitates active gas exchange during times of apnea due to turbulent supraglottic flow vortices.5 The effects of the potential disadvantages of using HFNO during sedation should also be evaluated. It is possible that the potential gains arising from the HFNO device may be offset by the reduced ability to monitor ventilation from capnography waveforms when it is being used, as exhaled carbon dioxide concentrations are “washed out” by the high gas flow. Guidelines from the American Society of Anesthesiology have stated that there is insufficient evidence regarding which supplemental oxygen device (e.g., nasal cannula, face mask, or specialized devices such as HFNO) is most effective.6 The objective of this study was to investigate the effects of HFNO in comparison to facemask oxygen on ventilation during CIED procedures performed with procedural sedation.

## Methods

### Design

A randomized controlled trial design was used with participants 1:1 randomized to:

* Facemask oxygen; or
* High flow nasal oxygen.

Informed consent was obtained. The study protocol conforms to the 1975 Declaration of Helsinki. Ethical approval for this study (Ethical Committee Number: 18-6343) was provided by the University Health Network Research Ethics Board, Toronto, Canada (Co-chair Morris Sherman) on June 21 2019. The trial was prospectively registered (NCT03858257).

### Participants

Adults undergoing an elective CIED procedure with sedation administered by an Anesthesia Assistant at one large academic teaching hospital in Canada were included.

*Exclusion criteria*

* <16 years.
* Underlying condition requiring chronic oxygen supplementation.
* Diagnosed respiratory condition with current hypercapnia defined as PaCO2 during admission over 45mmHg.
* Pre-existing untreated pneumothorax.
* Planned transesophageal echocardiography.
* Active nasal-bleeding.
* Complete nasal obstruction.
* Recent upper-airway surgery or base of skull fracture.
* Previous participation.

### Sedation

The model of sedation at the site where this trial was conducted follows recommendations from the Canadian Anesthesiologists' Society.7 Sedation was provided by a team that included a sedation supervisor (Anesthesiologist) and an approved and credentialed sedation assistant (Anesthesia Assistant) who is delegated tasks of providing sedation and monitoring the patient. The Anesthesia Assistant remains in constant attendance with the patient, providing continuous monitoring and immediately informing the sedation supervisor of any concerns. The sedation supervisor (Anesthesiologist in this case) retains responsibility for the patient. It is standard practice at this site for a combination of midazolam, fentanyl and propofol administered as bolus doses to be used. There were no additional restrictions on the type or dose of sedation used by Anesthesia Assistants imposed for participants enrolled in the trial. The actual doses of sedation used for participants in the trial were recorded.

### Interventions

**Facemask oxygen supplementation**

Supplemental oxygen was delivered using a standard facemask with an integrated exhaled CO2 sampling line. The flow-rate chosen by the Anaesthesia Assistant as per their standard practice, which was mostly ≥8L/min.

**High flow nasal oxygen**

The Optiflow device (Fisher and Paykel Healthcare, Auckland, New Zealand), heated breathing tube and chamber, and nasal cannula was used. This system is a humidifier with an integrated flow generator, able to humidify respiratory gases and deliver them down a heated breathing tube and through the nasal cannula interface. The gas temperature was set to the 'High' setting (ranges 30-32º Celsius). The gas flow-rate was commenced at 30L/min prior to sedation administration and titrated up to 50L/min as tolerated by the patient after sedative medication was administered. The fraction of oxygen in the gas was commenced at 50% but could be titrated according to patient requirements. A Research Assistant who was trained in the use of the HFNO device was present during all procedures to assist Anesthesia Assistants with set-up, application and trouble-shooting if required.

**Concomitant care**

There were no restrictions on concomitant care. Anesthesia Assistants were permitted to use standard physioligcal monitoring devices, as dictated by the Canadian Anesthesiologists’ Society (CAS), and to titrate sedation according to their usual practice.7 Concomitant care most relevant to this trial was the use of capnography. Anesthesia Assistants elected to use capnography regardless of whether supplemental oxygen was delivered via HFNO or facemask, as this is a requirement from the Canadian Anesthesiologist Society anytime procedural sedation is being administered.7 The facemask had an integrated CO2 sampling line. For participants randomized to HFNO, Anesthesia Assistants used the CO2 sampling adapter integrated with the latest model of the HFNO nasal cannula for the majority of participants (all those recruited after September 2019 - recruitment started in August 2019). Prior to this model becoming available, Anesthesia Assistants placed a facemask with an integrated CO2 sampling line over the HFNO nasal cannula. Oxygen supplementation was delivered through the HFNO nasal cannula and CO2 was sampled from the sampling line integrated into the facemask.

### Outcomes

Outcome selection was informed by recommendations from the Sedation Consortium on Endpoints and Procedures for Treatment, Education and Research (SCEPTER).8 The primary outcome was peak transcutaneous carbon dioxide (TcCO2) concentration. Secondary outcomes were:

* Mean TcCO2.
* Trajectory of TcCO2 as a function of time.
* Area under the curve of oxygen desaturation (AUCDESAT). This is the difference between the threshold (90%) and actual oxygen saturation (SpO2) summed every minute during which oxygen saturation was below the threshold.
* Adverse sedation events, measured using the Tracking and reporting outcomes of procedural sedation (TROOPS) tool.
* Patient satisfaction with sedation.
* Comfort of the oxygen delivery device.
* Anesthesia Assistant rating of difficulty maintaining oxygenation status.
* Anesthesia Assistant rating of difficulty using oxygen delivery device.

### Data collection

#### Instruments

TcCO2 was measured continuously using the Sentec Digital Monitoring system with VSign 2 sensor. TcCO2 monitoring provides continuous, accurate and precise estimates of PaCO2.9 TcCO2 monitoring may provide even more precise estimates of changes in PaCO2 (mean bias 0.03 mmHg, 95% limits of agreement -0.44 to 0.38 mmHg).10 The Sentec VSign 2 sensor was attached to the forehead. Once the TcCO2 stabilized, the monitor was covered with a drape so that it was not visible to research staff or clinicians. The monitor was not used by the clinicians to guide treatment. TcCO2 was sampled at a frequency of one measurement per second. The recorded SpO2 was extracted from the Drug Reconciliation and Electronic Monitoring System at a frequency of one measurement per minute. Adverse sedation events were measured using the tracking and reporting outcomes of procedural sedation (TROOPS) tool.11 Satisfaction with sedation was measured using the Iowa Satisfaction with Anesthesia Scale (ISAS).12 Participants were asked to rate comfort with the oxygen delivery device and Anesthesia Assistants were asked to rate their: 1) perceived level of difficulty in maintaining oxygenation; and 2) perceived level of difficulty in using the oxygen delivery device, using a 6-level rating scale.

### Sample size calculation

We estimated based on our prior work2 that the peak TcCO2 level in the control group would be 47 mmHg and standard deviation would be 7 mmHg. Assuming a type I error rate of 5%, a sample of 130 participants would achieve 90% power to detect a reduction in mean TcCO2 levels of 4 mmHg in the intervention period. A difference in TcCO2 levels of 4 mmHg was selected for this sample size calculation because it was deemed of potential clinical relevance and was used to power previous trials.13 Differences in CO2 level of a similar magnitude have been detected in previous trials evaluating the efficacy of interventions to improve sedation safety.14,15

### Random sequence generation and concealment

A stratified (by diagnosis of obstructive sleep apnea and type of procedure – cardiac resynchronization therapy device implant), block randomized sequence was generated and concealed using the web-based randomization feature in REDCapTM. The RA retrieved the allocation for each consecutive participant in REDCapTM prior to the procedure.

### Statistical analyses

Bayesian statistical models were used. Data and code are available [here](https://hfnosedrct.netlify.app/flexdashboard) and is archived [here](https://doi.org/10.5281/zenodo.3908492). A detailed summary of the statistical models is presented in the [Appendix](https://hfnosedrct.netlify.app/appendix). Prior distributions were chosen to be weakly informative, which is appropriate in the absence of information concerning the likely values of model parameters.16 Covariate adjustments were made for the stratification variables obstructive sleep apnea (OSA) status and whether or not the procedure was a cardiac resynchronization therapy (CRT) device implant as well as for baseline TcCO2 concentration, which was modelled using splines.17 Continuous outcomes were analyzed using robust regression models. A functional analysis of variance (ANOVA) model was used to investigate how mean TcCO2 concentration levels differ between groups as a function of procedure time18. Logistic regression was used for dichotomous outcomes. Proportional-odds models were used for ordinal outcomes. Analysis was performed only on those participants whose SPO2 was observed to fall below the 90% threshold for the AUCDESAT outcome.

Posterior inference for all models except the functional ANOVA model was performed using Hamiltonian Monte Carlo through the brms package19, version 2.12.0. For this set of models, 2000 posterior samples were obtained from 4 independent chains of 2000 samples, where the first 1000 warm-up samples were discarded. Posterior inference for the functional ANOVA model was performed using the Integrated Nested Laplacian Approximation20 through the INLA package, version 20.5.12. The marginal posterior distribution of parameters was summarized by their mean and a 95% credible interval defined by the interval spanning the 2.5% and 97.5% percentiles of their distributions. The clinical significance of treatment effects relating to TcCO2 concentration were evaluated by computing the posterior probability that an effect exceeds 4 mmHg in either direction. When the proportion of missing data was large and the missing completely at random (MCAR) assumption was unlikely to be satisfied, a sensitivity analysis was performed to investigate the robustness of the conclusions of the complete-case analysis.

## Results

### Participants

From August 2019 to March 2020, we screened 270 patients undergoing CIED procedures (Figure 1). A total of 130 participants were randomized. One participant was excluded because the procedure was cancelled. The procedure for one participant, who was randomized to the HFNO group, was rescheduled to a time that the Research Assistant was not available. As such, this participant received oxygen via standard face mask and TcCO2 data were not collected. For two participants, the TcCO2 sensor failed to calibrate prior to commencement of the procedure. Most (n=29; 45%) Anesthesia Assistants reported having used HFNO between 2-5 times.

Participant characteristics are presented in Table 1. The sample was mostly elder and male. Anesthesia Assistants’ rated the ASA Physical Classification Status as either III or IV. Obstructive sleep apnea was common. About 20% of procedures were for cardiac resynchronisation therapy. Table 2 presents a comparison of the total doses of sedation. The difference in doses was not statistically different for midazolam, fentanyl or propofol.

### Comparisons between groups

#### Primary outcome

Results are presented in Table 3. The effect of HFNO on the peak TcCO2 was estimated to be 0.0mmHg (95% CI = -1.3 to 1.37). The probability that it exceeds the 4mmHg clinical significance threshold of 4mmHg in either direction is 0.

#### Secondary outcomes

The effect of HFNO on the mean TcCO2 concentration was estimated to be -0.1 mmHg (-1.31, 1.14). The probability that it exceeds the 4mmHg clinical significance threshold is 0 in either direction. TcCO2 concentrations for all patients throughout procedures are displayed in Figure 2, with the longest procedure highlighted as a reference. The estimated effect did not exceed the 4mmHg clinical significance threshold in either direction with probability greater than 0.95. There is no discernable trend observed in how the effect varies with procedure time. Precision decreases as time increases, reflecting the shrinking number of participants.

The effect of HFNO on ISAS score was estimated to be 0.0 (95% CI = -0.33 to 0.23). The probability that patients are more likely to rate comfort with the oxygen supplementation device higher with HFNO compared to the facemask is 70%.

The odds ratio for Anesthesia Assistant ratings of difficulty maintaining oxygenation status and difficulty using the oxygen delivery device as estimated using a complete-case analysis are 0.1 (95% CI = 0.05 to 0.31) and 0.3 (95% CI = 0.14 to 0.83), where a value less than 1 indicates a greater level of difficulty for respondents in the HFNO group. It should be noted, however, that the Anesthesia Assistants’ ratings of difficulty using the oxygen device and difficulty maintaining oxygenation were missing 45 and 46 responses, respectively, likely due to the survey being voluntary. It is unlikely that missingness among these ratings occurred completely at random, so a best- and worst-case imputation approach was used to investigate the impact that the missing data could have on the results in extreme cases. The best- and worst-case sensitivity analysis gave estimates ranging between 0.0 (95% CI = 0.01 to 0.08) and 3.3 (95% CI = 1.72 to 6.62) for difficulty maintaining oxygenation status and from 0.1 (95% CI = 0.04 to 0.18) and 5.0 (95% CI = 2.49 to 9.79) for difficulty using the oxygen delivery device.

The odds ratio for a minor adverse sedation event related to airway or breathing for the HFNO group compared with the facemask group was 6.4. This effect estimate is very imprecise due to the small number of events (95% CI 1.3 to 43). A similar number of participants in the HFNO group (n=8; 12%) experienced an oxygen desaturation event in comparison with the facemask oxygen group (n=7; 11%) (1.2; 95% CI = 0.37 to 3.75). The effect estimate for the absolute difference in the AUCDESAT was imprecise, spanning from 5 minutes.% higher in the face mask group to 24 minutes.% higher in the HFNO group. The probability that AUCDESAT is higher with HFNO is 0.83. A visualization of the SpO2 trajectories for patients whose SpO2 was below 90% is available [here](https://hfnosedrct.netlify.app/flexdashboard).

#### Oxygen flow-rates

Most participants randomized to the HFNO group had the flow-rate set at 50L/min (Figure 3). Most participants randomized to the facemask group received oxygen at ≥8L/min. Two participants who were randomized to HFNO did not receive this intervention at all and four participants who were randomized to HFNO stopped receiving this intervention at a certain timepoint during procedures at the discretion of the Anesthesia Assistant, with the rationale that the quality of the capnography waveform was not sufficient while the HFNO device was in use.

## Discussion

We found that HFNO at 50L/min for patients undergoing elective CIED procedures with sedation is highly unlikely to *decrease* or *increase* peak TcCO2 concentration by a clinically important amount in comparison with standard facemask oxygen at ≥8L/min. A prior physiological modeling study of apneic oxygenation identified a mechanism by which HFNO promotes carbon dioxide clearance.5 We did not observe a significant reduction in peak TcCO2 concentration. This result is consistent with prior clinical research in the non-sedation context. The difference in PaCO2 observed between HFNO (5.81 kPa; sd=1.1) and facemask oxygen (5.6 kPa; sd=1.0) from a randomized trial of 20 patients who were receiving pre-oxygenation for induction of anesthesia prior to emergency surgery was not significant (p=0.631).21 Likewise, in a larger trial of pre-oxygenation with 80 patients, the end-tidal CO2 in the first breath after intubation was not significantly different between HFNO (5.0 kPa; sd=0.8) and standard facemask (5.3 kPa sd=1.0) oxygen supplementation (p=0.18).22 Importantly, in contrast to these trials where ventilation status was assessed at one specific point in time with either PaCO2 or ETCO2 samples, we used continuous TcCO2 monitoring so that we could estimate differences in ventilation between groups over the whole duration of procedures. There was no discernible trend observed in how the effect varied over time.

Another commonly proposed physiological effect of HFNO, which has been observed in a study of healthy volunteers, is increased pressure in the upper airways.23 However, more recent data from a clinical population of apneic patients undergoing general anesthesia for elective surgery found that airway pressure increases were negligible during HFNO with an open mouth and remained below 10 cmH2O with closed mouths and flow rates up to 80L/min.24 We neither directly measured airway pressure or imposed strict restrictions in regard to maintaining a closed mouth during HFNO administration. Therefore, it is unknown whether mouth positioning (closed or open) influenced our results.

The probability that minor adverse sedation events related to airway and breathing are more likely to occur with HFNO is 0.99. The suspected etiology noted for these events by the Anesthesia Assistants in the TROOPS tool was oxygen desaturation. There are two plausible mechanisms that may explain this result. It is possible that the oxygen:air blend (50:50) used in the HFNO group was simply not equivalent to the amount of oxygen supplementation received in the facemask group. Most participants in the facemask group received ≥8L/min of 100% O2. Further research with a larger sample size would be useful to determine the optimal oxygen:air ratio for HFNO during sedation for CIED procedures, with a focus on adverse sedation events or hypoxemia as the primary outcome.

Another plausible mechanism is that the ability to monitor capnography waveforms was diminished with HFNO. Capnography is widely considered to be an essential aspect of physiological monitoring during sedation.25–27 The concern about reduced ability to monitor capnography waveforms when HFNO is used potentially increasing the risk of more prolonged, undetected episodes of hypoventilation during sedation has been raised previously in the literaure.28 However, it should be noted that if undetected episodes of hypoventilation were considerably more frequent and prolonged when HFNO was used in our study, presumably, we would have observed higher TcCO2 concentrations in this group. We did not observe higher TcCO2 concentrations in the HFNO group for the peak measurement or at any particular time-point during procedures.

In our study, a new HFNO cannula with an integrated CO2 sampling line was used for the majority of patients. According to manufacturer instructions, the CO2 sampling line in these cannulas was positioned at the entrance of a nostril or the mouth. There have been no studies published reporting on a comparison in the quality of the capnography waveform produced from this new cannula and alternative ways to monitor capnography during HFNO therapy. Capnography monitoring for the subset of patients enrolled in the first two months of our trial who were randomized to HFNO was achieved by placing a facemask with an integrated CO2 sampling line (the same mask used for the control group) over the HFNO cannula. Although we did not perform a formal comparison, anecdotally, the quality of the capnography waveform produced using this method was not worse or better than that achieved with the new HFNO cannula. This is likely due to the fact that both methods involve CO2 sampling from an unsealed airway in the presence of very high flows of gas from the HFNO device. Novel airway management devices that provide a sealed airway with separate channels for ventilation, oxygenation and EtCO2 sampling may be a potential solution.29 A potential consequence of using a (unsealed) facemask superimposed over the HFNO cannula is that it could mimic the airway conditions achieved with a closed mouth even when it is opened. Due to the small number of patients who received capnography monitoring in this fashion, it is unlikely to have impacted our results to a significant degree.

The evidence base for the effects of HFNO therapy for procedural sedation in other clinical contexts is limited. One large30 and three small randomized controlled trials were published in 2019, with several more on-going trials registered.31 The primary outcomes for all the trials to date have focused on investigating the impact of HFNO on oxygenation with inconsistent results. One of the small trials randomized 60 participants undergoing bronchoscopy to receive HFNO at 50L/min with 100% oxygen or oxygen at 10-15L/min through a facemask.32 There was no difference observed between the treatment groups for the primary outcome, which was the proportion of patients who experienced oxygen desaturation (defined as SpO2 90%). Another trial randomized 59 morbidly obese patients undergoing endoscopy to receive a fraction of inspired oxygen concentration of 0.36 either via HFNO at a flow-rate of 60L/min or via nasal cannula at 4L/min.33 Again, there was no difference in the primary outcome of oxygen desaturation (SpO2 < 90%). The third study randomized 30 participants undergoing dental sedation into three groups to receive a fraction of inspired oxygen concentration of 0.4 either via HFNO at a flow-rate of 50L/min, via HFNO at a flow-rate of 30L/min or via nasal cannula at 5L/min.34 Participants randomized to the HFNO groups had higher nadir blood oxygen levels recorded than the low flow oxygen group. In contrast, a large trial of 1994 participants undergoing gastroscopy with propofol sedation reported a large reduction in risk of hypoxemia (8.4% in the control group and 0% in the HFNO group).30 This result is likely explained by the large difference in FiO2 that was delivered between the two groups. In the HFNO group participants received 60L/min of 100% oxygen and in the control group participants received just 2L/min of oxygen.

Satisfaction with sedation is very likely to be similar between HFNO and facemask oxygen. The probability that patients are more likely to rate comfort with the oxygen supplementation device higher with HFNO was 0.70. In contrast, we identified that the HFNO device was rated as more difficult for Anesthesia Assistants to use compared with the standard facemask. None of the Anesthesia Assistants rated the HFNO device as *difficult* to use and most had very limited experience using the device. Also, most Anesthesia Assistant participants reported they had used HFNO between 2 and 5 times. Experience with HFNO is likely to influence clinicians’ perceptions about the difficulty using the device.

### Limitations

The primary outcome was peak TcCO2 and we accounted for the correlation between baseline and peak measurements by including the baseline measurements as a covariate in the model. However, a potential limitation is that results may be sensitive to how the baseline and peak measurements were chosen. We did not blind participants or clinicians to group assignment. The small dropout and cross-over rate are unlikely to have exerted a major impact on the effect estimates. Participants received propofol, midazolam and fentanyl, which is a common and recommended approach for CIED procedures.35 Severe oxygen desaturation is not a common event when oxygen supplementation is delivered at flow-rates between 6-10L/min through a face mask during procedures performed with sedation.1,3 Results from our trial cannot be directly generalized to other clinical settings where desaturation is more severe and occurs more often. Considering Anaesthesia Assistants had limited prior use of HFNO for sedation, results may not reflect the use of this device by more experienced users. We did not use a validated sedation scale to measure level of sedation. Although doses of the medications used for sedation were similar between groups, dosage does not necessarily reflect sedation depth. As such, it is possible that differences in sedation depth between groups could have influenced the results. The direction or magnitude of this potential effect is unknown. It should also be noted that, when planning the trial, we anticipated that an initial setting for the oxygen to air ratio of 50% for the HFNO would achieve and FiO2 approximately similar to what was achieved with standard practice in the facemask group (typically ~8L/min). Results for the secondary outcomes related to oxygenation and minor adverse sedation events suggest this may not have been the case. We chose the settings for the oxygen to air ratio because we were primarily interested in the effect of HFNO on ventilation, not the effect of increasing FiO2 on oxygenation. Further research with a larger sample size would be required to determine the optimal oxygen:air ratio.

### Conclusion

We compared HFNO with the flow-rate set to L/min and a 50:50 oxygen to air ratio for the majority of time during sedation compared with facemask oxygen at ≥ 8 liters per minute. The main finding from our primary outcome is that ventilation, as measured by TcCO2, is highly unlikely to differ by a clinically important amount. Results from secondary outcomes yielded some important additional insights. The probability that minor adverse sedation events were more likely to occur in the HFNO group was high and the severity of oxygen desaturations is probably worse with HFNO at 50 liters per minute and a 50:50 oxygen to air ratio compared with facemask oxygen at ≥ 8 liters per minute. Further research is required for confirmation, however, this result suggests that an oxygen to air ratio setting higher than 50% may be required for HFNO to achieve oxygenation status similar or superior to standard practice with facemask oxygen ≥ 8 liters per minute in the population we studied. Finally, there is a higher probability that patients will be more comfortable during procedures with HFNO in comparison to the facemask, but overall patient satisfaction with sedation is likely to be similar.

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# Figure legend

Fig. 1 CONSORT Flow Diagram

Fig. 2 Transcutaneous carbon dioxide measurements throughout procedures

Fig. 3 Oxygen flow-rates

## Table 1. Participant characteristics

| Characteristic | High Flow nasal oxygen, N = 641 | Face mask oxygen, N = 651 |
| --- | --- | --- |
| *Age (years)* | 67 (14) | 70 (13) |
| *Gender* |  |  |
| Female | 19 (30%) | 17 (26%) |
| Male | 45 (70%) | 47 (72%) |
| Prefer not to say | 0 (0%) | 1 (1.5%) |
| *Smoking history* |  |  |
| Never | 23 (36%) | 25 (38%) |
| Current | 7 (11%) | 7 (11%) |
| Past | 34 (53%) | 33 (51%) |
| *Obstructive sleep apnea* | 17 (27%) | 18 (28%) |
| *Uses Continuous Positive Airway Pressure therapy for sleep apnea* | 9 (14%) | 12 (18%) |
| *Admission source* |  |  |
| Day surgery | 45 (70%) | 44 (68%) |
| Ward | 17 (27%) | 18 (28%) |
| Cardiovascular Intensive Care Unit | 2 (3.1%) | 3 (4.6%) |
| *American Society of Anesthesiology classification status* |  |  |
| I | 0 (0%) | 0 (0%) |
| II | 0 (0%) | 0 (0%) |
| III | 21 (33%) | 16 (25%) |
| IV | 43 (67%) | 49 (75%) |
| *Body mass index* | 28.5 (5.1) | 28.8 (6.7) |
| *Procedure* |  |  |
| Implantable cardioverter defibrillator | 19 (30%) | 13 (20%) |
| Permanent pacemaker insertion | 11 (17%) | 17 (26%) |
| Implantable cardioverter defibrillator generator change | 10 (16%) | 13 (20%) |
| Cardiac resynchronisation therapy with defibrillator | 11 (17%) | 11 (17%) |
| Permanent pacemaker generator change | 6 (9.4%) | 7 (11%) |
| Cardiac resynchronisation therapy with pacing | 2 (3.1%) | 2 (3.1%) |
| Other | 3 (4.7%) | 1 (1.5%) |
| Implantable cardioverter defibrillator lead revision | 2 (3.1%) | 0 (0%) |
| Permanent pacemaker lead revision | 0 (0%) | 1 (1.5%) |
| *Charlson Comorbidity Index* | 4.46 (2.14) | 5.15 (2.51) |
| 1Statistics presented: mean (SD); n (%) | | |

## Table 2. Participant characteristics

| Characteristic | High Flow nasal oxygen, N = 641 | Face mask oxygen, N = 651 | p-value2 |
| --- | --- | --- | --- |
| Total dose of midazolam (mg) | 1.58 (0.84) | 1.45 (0.71) | 0.3 |
| Total dose of propofol (mg) | 100 (126) | 88 (104) | 0.6 |
| Total dose of fentanyl (mcg) | 71 (28) | 76 (56) | 0.5 |
| 1Statistics presented: mean (SD) | | | |
| 2Statistical tests performed: t-test | | | |

## Table 3. Results

|  | | Randomization | |  | |
| --- | --- | --- | --- | --- | --- |
| Outcome | Summary value | High flow nasal oxygen | Face mask oxygen | Effect type | Estimated treatment effect (95% CI)\* |
| Peak TcCO2 | N | 61 | 65 |  |  |
|  | Mean (sd) | 47.8 mmHg (9.7) | 49.0 mmHg (6.9) | Absolute difference | 0.0 mmHg (-1.3, 1.37) |
| Mean TcCO2 | N | 61 | 65 |  |  |
|  | Mean (sd) | 42.7 mmHg (7.2) | 44.3 mmHg (5.9) | Absolute difference | -0.1 mmHg (-1.31, 1.14) |
| SpO2 | N | 64 | 65 |  |  |
|  | SpO2 <90% event | 8 (12%) | 7 (11%) | Odds ratio | 1.2 (0.37, 3.75) |
|  | Median (IQR) Area under SpO2 desaturation curve | 9.5 (5.75, 25.25) | 8 (3.5, 9.5) | Absolute difference | 5.6 % minute (-5.39, 24.24) |
| ISAS score | N | 63 | 63 |  |  |
|  | Mean (sd) | 2.0 (1.0) | 2.1 (0.9) | Absolute difference | 0.0 (-0.33, 0.23) |
| Patient comfort | N | 63 | 65 |  |  |
|  | Maximal comfort | 9 | 17 | Odds ratio | 1.2 (0.64, 2.17) |
|  | Very comfortable | 26 | 13 |  |  |
|  | Comfortable | 22 | 22 |  |  |
|  | Uncomfortable | 3 | 10 |  |  |
|  | Very uncomfortable | 2 | 2 |  |  |
|  | Maximal discomfort | 1 | 1 |  |  |
| Difficulty maintaining oxygenation status | N | 52 | 31 |  |  |
|  | Extremely easy | 9 | 17 | Odds ratio | 0.1 (0.05, 0.31) |
|  | Very easy | 14 | 10 |  |  |
|  | Easy | 17 | 4 |  |  |
|  | Difficult | 6 |  |  |  |
|  | Very difficult | 4 |  |  |  |
|  | Extremely difficult | 2 |  |  |  |
| Difficulty using oxygen delivery device | N | 52 | 32 |  |  |
|  | Extremely easy | 15 | 17 | Odds ratio | 0.3 (0.14, 0.83) |
|  | Very easy | 17 | 9 |  |  |
|  | Easy | 20 | 6 |  |  |
| Minor airway or breathing event | N | 64 | 65 |  |  |
|  | Yes | 9 | 2 | Odds ratio | 6.4 (1.34, 42.99) |
|  | No | 55 | 63 |  |  |
| \*Adjusted for covariates | | | | | |
| Odds ratios are interpreted as the odds of the event occuring in the HFNO group compared with the odds of the event occuring in the facemask group | | | | | |
| TcCO2 = Transcutaneous carbon dioxide concentration | | | | | |
| SpO2 = Percentage of hemoglobin saturate with oxygen | | | | | |
| ISAS = Iowa Satisfaction with Anesthesia Scale | | | | | |
| 95% CI = 95% credible intervals | | | | | |