Protocol supporting the use of the SuperNO_2VA positive airway pressure device

Introduction

Sedation and anesthesia have long been associated with high rates of hypoxemia and hypoventilation, which can ultimately result in Respiratory Compromise.[1-3] This occurs due to a disproportionate decrease in genioglossus tone leading to upper airway obstruction and central respiratory depression.[4-5] In an attempt to prevent these complications the American Society of Anesthesiologists recommends the delivery of supplemental oxygen, monitoring of pulse oximetry, and continuous quantitative capnography monitoring "unless invalidated by the nature of the patient, procedure or equipment," during anesthesia.[6] Despite these recommendations inadequate oxygenation/ventilation remains the most common cause of morbidity and mortality.[7] These complications are multifactorial and the risk factors can be broken down into the following categories:

- Patient co-morbidities
- High risk procedures

Depending on the number of risk factors, the incidence of hypoxemia has been shown to be as high as 54% and the incidence of peri-operative Respiratory Compromise has been shown to be 9 – 44%.[8-10]

Risk factors for respiratory compromise: Patient co-morbidities

Respiratory Compromise is a result of either low blood oxygen levels and/or high carbon dioxide levels. Therefore, patients who start with low oxygen levels or high CO_2 levels *(ie: ASA III – V)* are at a higher risk.[11-12] Four significant patient co-morbidities for Respiratory Compromise include:

- Morbid Obesity
- Obstructive Sleep Apnea *(OSA)*
- Limited oxygen reserve *(Congestive Heart Failure and Chronic Obstructive Pulmonary Disease)*
- Difficult ventilation/intubation

Morbid obesity

There are three reasons why morbidly obese patients are at a higher risk for Respiratory Compromise. First, they have a significantly larger amount of pharyngeal soft tissue, which increases their risk for Upper Airway Obstruction under sedation.[13] Second, their larger amount of abdominal tissue compresses their lungs, resulting in decreased FRC, increased atelectasis, and a reduction in oxygen delivery.[14] Third, the oxygen consumption in obese patients is significantly increased.[14] Therefore, not only do they have less oxygen entering their blood, but their oxygen requirements are also much higher. Morbid obesity has been shown to significantly increase the risk of hypoxemia during endotracheal intubation as well as during procedural sedation.[15] The incidence of oxygen desaturation for morbidly obese patients has been shown to be up to 47%.[16]

Obstructive sleep apnea

The first reason for increased risk in this population is the tendency towards upper airway collapsibiity.[17] A patient who obstructs during normal sleep will certainly obstruct during anesthesia, which has been shown to lead to increased risk for hypoxemia and hypercarbia.[18] Second, over time chronic hypercarbia and hypoxemia leads to a reduced responsiveness of the normal respiratory centre in the brain.[19] This leads to chronically elevated pCO_2 levels at baseline, and a further reduced responsiveness under anesthesia.[19] Therefore, even small amounts of sedative medications can cause significant depression in respiratory drive.

Limited oxygen reserve

Congestive Heart Failure *(CHF)* and Chronic Obstructive Pulmonary Disease *(COPD)* are associated with decreased oxygen reserve, which has been shown to significantly increase the risk of Respiratory Compromise during the peri-operative setting.[20-21] Limited oxygen reserve with CHF is due to the heart's inability to pump sufficiently to maintain blood flow to meet the body's demands *(ie: oxygen delivery < oxygen demand)*. This causes blood to back up into the alveoli, resulting in pulmonary edema.[20] As fluid fills the alveoli, there is no opportunity for air or oxygen to enter, and therefore no opportunity for gas exchange in those lung segments.[20] Limited oxygen reserve with COPD is from breakdown of lung tissue, which prevents a significant amount of oxygen from being able to diffuse from the alveoli into the blood and due to inflammation of the small airways, which blocks the small airways and prevents the patient from exhaling CO_2.[21] Since a significant amount of CO_2 remains in the lungs, it prevents oxygen from entering. Therefore, patients with COPD have significantly less oxygen in their lungs because they have less alveoli and CO_2 taking its place.[21] These patients are at very a high risk for oxygen desaturation once sedation is induced because they have significantly less oxygen stored in their alveoli.

Difficult ventilation/intubation

The most dangerous situation in all of airway management is "can't intubate, can't ventilate," where the clinician attempts both mask ventilation and endotracheal intubation, and fails at both. Since the patient is not receiving oxygen or eliminating CO_2, they are at risk of desaturation resulting in cardiac arrest and eventually death. To avoid this life-threatening situation, clinicians examine patient's airways for specific risk factors that are associated with difficult mask ventilation as well as difficult intubation.[22-23] Difficult ventilation has been defined as the inability of a trained anesthetist to maintain the oxygen saturation > 90% using a facemask for ventilation and 100% inspired oxygen.[22] Below is a list of risk factors associated with difficult ventilation.

- Body Mass Index (BMI) > 26
- Age > 55 years
- Edentulous (no teeth)
- Beards
- History of Snoring

Difficult intubation has been defined by the need for more than three intubation attempts or attempts at intubation that last > 10 min.[23] Below is a list of some of the risk factors associated with difficult intubation:

- History of difficult intubation
- Small mouth opening
- Increased Mallampatti classification

If a patient is at risk for either difficult mask ventilation or difficult intubation, it is recommended by the Difficult Airway Society *(DAS)* to provide the patient with a continuous source of high flow oxygen *(apneic oxygenation)* to help to maintain their oxygen saturation levels and prevent life-threatening Respiratory Compromise.[24] High flow oxygenation during intubation has been shown to significantly prolong the time to oxygen desaturation.[25]

Risk factors for respiratory compromise: High-risk procedures

The incidence of hypoxemia, hypoventilation, and Respiratory Compromise have been shown to be significantly higher during non-operating room anesthesia *(NORA)* sedation procedures as well as post-operatively after major head and neck surgery, thoracic surgery, and major abdominal surgery.

Specifically, NORA has grown significantly over the last decade but has also presented unique challenges to anesthesia providers such as new minimally invasive procedures being performed without advanced airways, managing older and more medically complex patients, and having to recover patients more quickly has not only led to more cases being performed under deep sedation but also a significantly higher mortality.[8,26-28]

With regards to major head and neck surgery, the incidence of postoperative pulmonary complications *(PPCs)* is between 9% - 44% and is associated with longer ICU stays, hospitals stays, and an increase in mortality.[9,29-31]

Finally, thoracic surgery and major abdominal surgery are associated with significantly post-operative pulmonary complications. Incidences have been shown to be up to 55% and associated with poorer quality of life and decreased survival.[32-33]

The objectives required to address respiratory compromise

In today's practice, there is an increasing frequency of deeper levels of sedation without the use of an advanced airway and more medically complex patients resulting in Respiratory Compromise secondary to upper airway obstruction and hypoventilation. Deep sedation has become a preferred method because it renders the patient amnestic, allows for physical relaxation during highly stimulating procedures, and improves turn-round time. Also, there has been an increase in the number of procedures that require access to the patient's mouth, such as upper endoscopy, transoesophageal echocardiography, and laryngoscopy, which significantly increases the risk of Respiratory Compromise due to the inability to apply positive pressure ventilation as the current devices cover both the nose and mouth.

"...NORA has grown significantly over the last decade but has also presented unique challenges to anesthesia providers..."

To address Respiratory Compromise, the following objectives need to be addressed.

- Effectively pre-oxygenate
- Provide apneic oxygenation
- Relieve upper airway obstruction
- Maintain effective ventilation in unconscious patients
- Provide access to the oral cavity during intra-oral procedures

Delivering 100% FiO_2 effectively pre-oxygenates by denitrogenating the alveoli, which allows the entire lung volume and FRC to be exchanged with 100% oxygen to maximize the stores of oxygen. This maximum storage of oxygen has been shown to prolong the time to oxygen desaturation and thus reduce Respiratory Compromise.[34] All patients who receive anesthesia incur the risk of apnea, and current recommendations are to maximize oxygen stores during anesthesia to best prepare for apnea even if it is not expected.[34] In current practice, pre-oxygenation during NORA procedures and intra-oral procedures is nearly impossible and therefore not performed.

Providing continuous oxygenation during Endotracheal Intubation *(ETI)* has been shown to reduce the incidence of hypoxemia and Respiratory Compromise by prolonging the time to oxygen desaturation.[35] Devices that have shown to be effective at providing apenic oxygenation consists of nasal cannula and high flow nasal cannula. That said, neither have been shown to be effective at prolonging the time to desaturation in morbidly obese patients or patients with obstruction because they fail to deliver high enough positive end-expiratory pressures to prevent upper airway obstruction and/or compression atelectasis.[35]

Patients who receive anesthesia develop upper airway obstruction, due to relaxation of the muscles of the airway and decreased central *(brain)* control of ventilation.[1-3] Current methods employed during sedation, such as apnoeic oxygenation and passive supplemental oxygenation, are not capable of generating positive pressure and thus are not equipped to relieve UAO, thereby rendering them effectively useless in these situations.[35] Nasal continuous positive airway pressure *(CPAP)* has been shown to be an effective means of relieving upper airway obstruction in patients receiving deep sedation as well as significantly lowering the $PaCO_2$ compared to the current standard.[36-37] That said, the use of intra-operative nasal CPAP is rarely performed.[38]

As apnea is common and at times unpredictable during anesthesia, maintaining effective ventilation in unconscious patients is essential in order to prevent the complications associated with Respiratory Compromise. In current practice several procedures, such as upper endoscopy, TEE, and laryngoscopy, require the surgeon/proceduralist to have access to the patient's mouth. This makes full facemask ventilation impossible. Recently, nasal mask ventilation has been shown to be an effective alternative and actually superior to full facemask ventilation by providing similar tidal volumes with lower peak airway pressures.[39] The current challenge with nasal mask ventilation, which has prevented widespread adoption is the cost and workflow requirement for the additional capital equipment that's needed.

The optimal solution: The SuperNO_2VA™ device

The SuperNO_2VA™ device is a nasal anesthesia mask designed to maintain upper airway patency and support ventilation in patients who are undergoing general anesthesia, procedural sedation, or recovering in the post anesthesia recovery unit *(PACU)*. It was designed to address all of the objectives required to minimize the impact of respiratory compromise.

Summary statistics of vital signs for the 29 successfully ventilated patients.

	Systolic Blood Pressure (mmHg)	Diastolic Blood Pressure (mmHg)	Heart Rate (Beats/min.)	SpO_2 (%)	Respiratory Rate (Breaths/min.)	$EtCO_2$ (mmHg)
Pre-oxygenation	141.2 ± 12.5	83.9 ± 13.0	75.1 ± 11.0	99 (96, 100)	11.2 ± 1.7	36.2 ± 8.3
Pre-induction	138.5 ± 16.2	81.3 ± 12.1	72 (65, 83)	100 (99, 100)	10.6 ± 4.0	30.7 ± 9.8
Pre-ETT Insertion	125.9 ± 21.2	74.6 ± 13.4	75.5 ± 13.9	100 (100, 100)	12.9 ± 3.9	31.2 ± 8.5
During Laryngoscopy	110.2 ± 22.0	68.0 ± 15.8	76.8 ± 15.0	100 (99, 100)	10.0 ± 3.7	33.7 ± 6.4
Post-ETT Insertion	113.8 ± 24.7	73.4 ± 20.3	88.3 ± 18.2	100 (100, 100)	13 (11, 14)	36.8 ± 6.7
Postoperative (PACU)	135.1 ± 19.4	76.7 ± 9.5	76.3 ± 14.3	98 (97, 99)	17.1 ± 4.3	[a]

Data were represented as Mean ± Standard Deviation for variables with normal distribution or median (1st quartile, 2nd quartile) for variables with non-normal distribution.
[a] No measurement or numerical value was obtained containing $EtCO_2$, as no patient remained intubated during their recovery (in PACU) and study period.

Effective pre-oxygenation

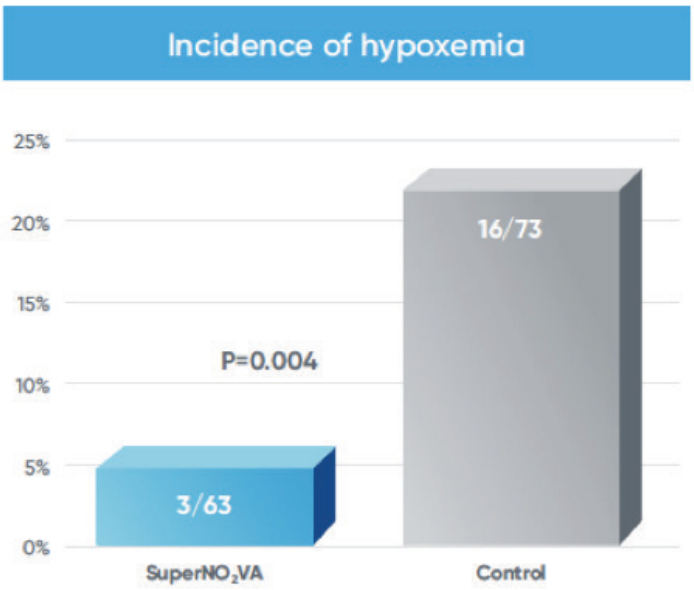
The SuperNO$_2$VA™ device creates an airtight seal around the nose, which allows for 100% oxygen delivery. In addition, the airtight seal prevents air leak and allows positive end-expiratory pressure *(PEEP)* to be generated during pre-oxygenation. Delivering 100% FiO_2 in combination with > 5cmH_2O PEEP has been shown to be the most effective method for maximizing PaO_2.[40] Dr. Ghebremichael demonstrated that the SuperNO$_2$VA™ device could be used to both effectively pre-oxygenated obese patients and nasal mask rescue ventilate patients after being induced with general anesthesia and paralyzed.[41]

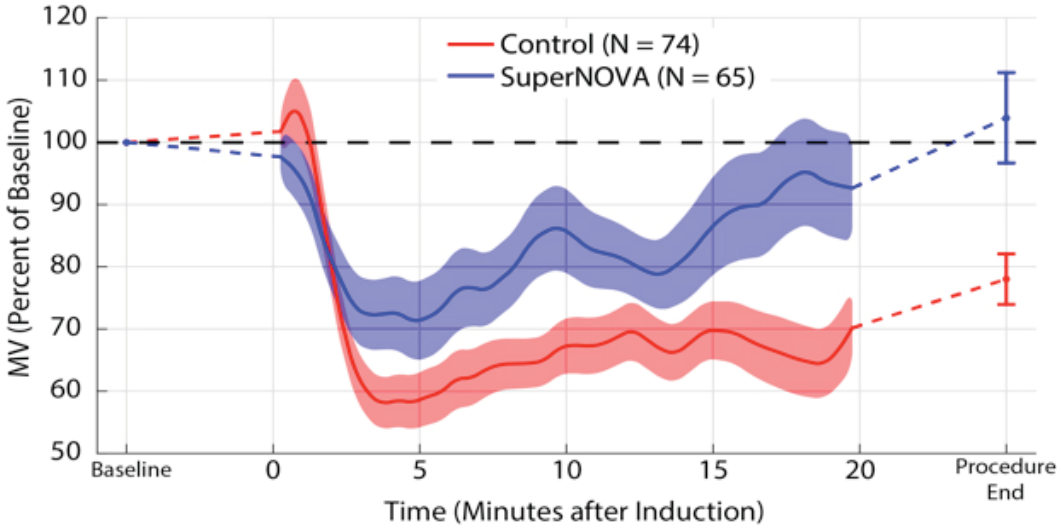
Provide apneic oxygenation

Dr. Ghebremichael and Lester demonstrated that the SuperNO$_2$VA™ device could be used to successfully deliver up to 30 liters per minute *(LPM)* of oxygen allowing for effective apneic oxygenation and PEEP during endotracheal intubation in obese and OSA patients. None of the patients suffered an oxygen desaturation event during the intubation attempts.[41-42] In addition, Dr. Bastien showed that the SuperNO$_2$VA™ device could be used during endotracheal intubation to successfully rescue patient's suffering from acute respiratory failure secondary to angioedema by providing a continuous source of oxygen and positive pressure, which results in stenting open of the upper and lower airways.[43]

Relieve upper airway obstruction

Dr. Jiang proved that the SuperNO$_2$VA™ device was the first completely disposable nasal positive airway pressure *(PAP)* device that effectively relieves anesthesia and sedation related upper airway obstruction in obese patients.[45] He also showed that the SuperNO$_2$VA™ device significantly reduced the incidence of oxygen desaturation compared to their standard of care *(4.7% vs 22% respectively)*.[44]





Maintain effective ventilation in unconscious patients

Dr. Jiang also demonstrated that the SuperNO$_2$VA™ group maintained effective ventilation in unconscious patients. Specifically he showed that the SuperNO$_2$VA™ device maintained a statistically significant higher minute ventilation immediately after a bolus of Propofol, while recovering from the Propofol bolus, and until the Propofol infusion was stopped.[44]

Provide access to the oral cavity during intra-oral procedures:

Dr. Dimou prospectively and comparatively observed the incidence of oxygen desaturation in morbidly obese patient and OSA patients undergoing upper endoscopy with Propofol sedation. He too found that the SuperNO$_2$VA™ device significantly reduced the incidence of oxygen desaturation compared to their standard of care *(11% vs 47% respectively)*.[16] In addition, several case reports have been published where the SuperNO$_2$VA™ device has been used for intra-oral procedures and none of the patients suffered from respiratory compromise.[45]

Surgical Endoscopy

Table 2 Outcomes of patients who underwent pre-bariatric surgery EGD with oxygenation via SuperNO$_2$VA™ mask or traditional nasal cannula

	All	SuperNO$_2$VA™	Control	*P* value
Baseline SpO2 [mean ± SD]	98.7 ± 1.9	98.8 ± 1.5	98.6 ± 2.2	0.74
Patient desaturations				
0	39 (69.6%)	23 (88.5%)	16 (53.3%)	0.06
1	5 (8.9%)	0 (0%)	5 (16.7%)	
2	7 (12.5%)	2 (7.7%)	5 (16.7%)	
> 2	5 (8.9%)	1 (3.9%)	4 (13.3%)	
Desaturations (yes/no)	17|39	3|23	14|16	**0.004**
Desaturations (> 2/none)	5|34	1|25	4|26	0.21
Median lowest O2 [IQR]	95 [85–100]	100 [95–100]	90.5 [79–95]	<

Summary of the SuperNO$_2$VA™ device's benefits

The SuperNO$_2$VA™ device has the following clinical benefits:

- Delivers 100% oxygen via the mask and can be used for pre-oxygenation with PEEP
- Creates a pneumatic stent in the posterior pharynx, used to maintain upper airway patency.
- Provides access to the oral cavity and allows for rescue ventilation in apneic patients.
- Delivers >30 L/min fresh gas flow during open airway procedures.
- Connects to standard anesthesia equipment readily available in procedural areas.
- Is a nasal anesthesia mask designed to maintain upper airway patency and support ventilation in patients who are sedated with anesthetic medications.
- It was designed to utilize all the benefits of nasal ventilation both inside and outside the OR.

Recommendations for use:

Anticipated difficult ventilation/intubation

The current recommendations for the Difficult Airway Society and the Journal of Anesthesiology is to provide >15 LPM of oxygen during tracheal intubation in patients with known risk factors for difficult ventilation or intubation in order to prevent severe oxygen desaturation.[24,46] Therefore, we recommend the SuperNO$_2$VA™ device to be used on patients with >1 risk factor listed below for pre-oxygenation during the induction of general anesthesia and apneic oxygenation while attempting to ventilate and/or intubate:

- Body Mass Index (BMI) > 26
- Age > 55 years
- Edentulous *(no teeth)*
- Beards
- History of Snoring
- History of difficult intubation
- Small mouth opening
- Increased Mallampatti classification

High-risk patient undergoing deep sedation

The European Society for Anesthesia as well as the American Society for Anesthesiology consider the following patients to be at significant risk for hypoxemia and hypoventilation.[47]

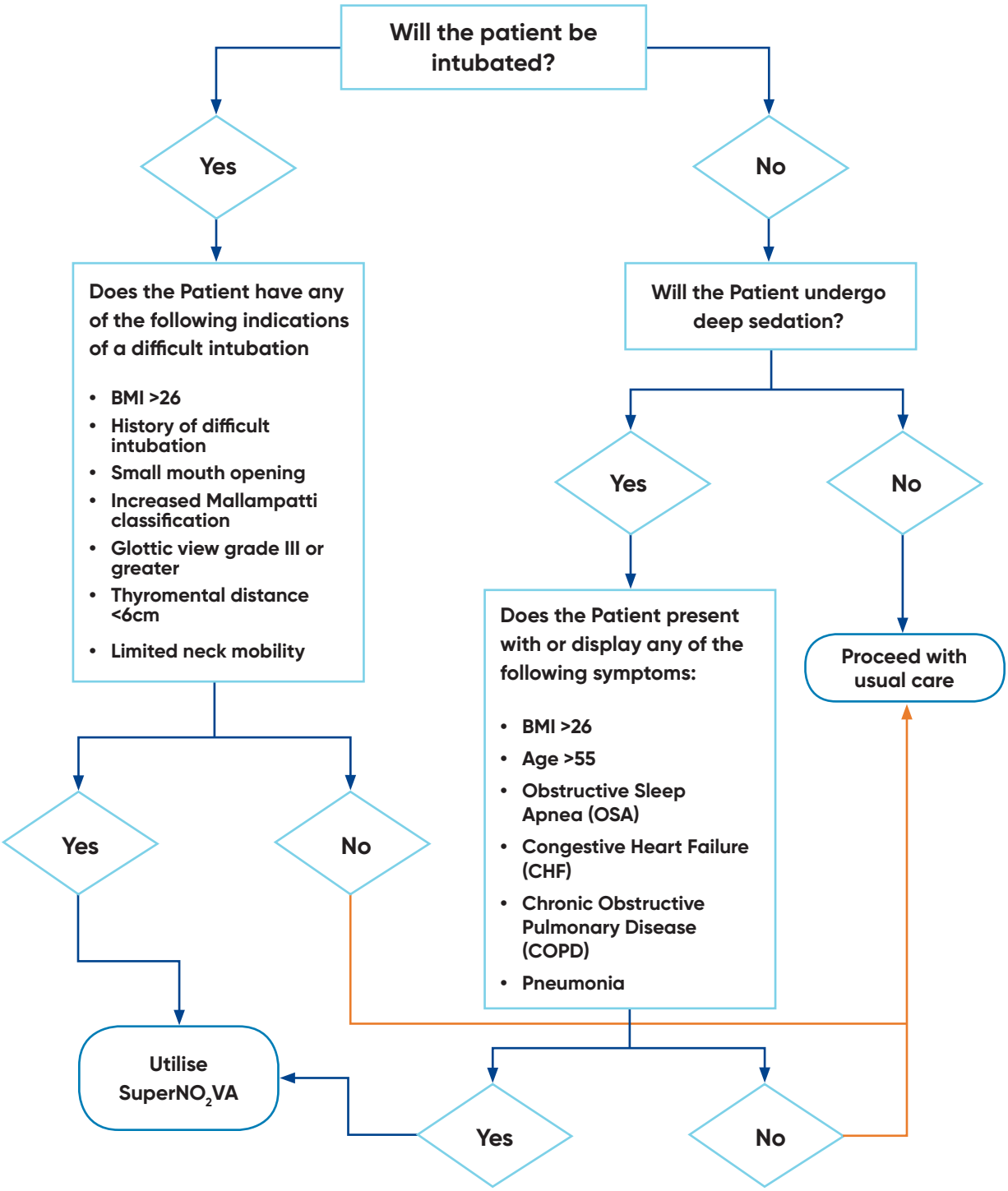
- Severe cardiovascular disease
- Severe chronic respiratory disease
- Morbidly obese
- Obstructive sleep apnea

Therefore, we recommend the SuperNO$_2$VA™ device be used during deep procedural sedation in these patients in order to maximize oxygen reserves prior to the induction of anesthesia and prevent upper airway obstruction as well as assist ventilation throughout the procedure.

High-risk patients postoperatively

The Society for Sleep Medicine recommends all patients either at risk for or has a history of sleep disordered breathing be placed on positive airway pressure while recovering from general anesthesia.[39] There we recommend the SuperNO$_2$VA™ device to be used on patients postoperatively who are at risk for upper airway obstruction.

Decision tree to support use of SuperNO$_2$VA



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