Review

Can the OSA patient be managed within an ERAS protocol? A narrative review

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Abstract

Obstructive sleep apnea (OSA) is the most common sleep-related breathing disorder among surgical patients and is associated with an increased risk of perioperative cardiopulmonary complications leading to increased health expenses. Therefore, preoperative OSA screening should be instituted to inform patients of their increased perioperative risk and measures can be taken in to decrease this risk. Meanwhile ERAS (Enhanced recovery after surgery) guidelines are becoming standard of care and being widely implemented. The purpose of these recovery programs is to standardize medical care, enhance outcomes and decrease health care expenses using evidence-based protocols. According to the current evidence it is unclear if OSA patients could benefit from these protocols. The first part of this narrative review states the current evidence on OSA definition, classification, pathophysiology and risk factors, postoperative complications, endotypes and their relevance for the anesthesiologist. The second part investigated the feasibility of ERAS measures within the OSA-population. Preoperatively there are many parallels to be drawn between the ERAS measures and Society of Anesthesia and Sleep Medicine (SASM) guidelines on OSA management: Risk stratification by OSA-screening, information counselling on the increased perioperative risk and optimization of preoperative health conditions by initiation of CPAP-therapy. Perioperatively the use short acting anesthetics allows for both early mobilization and avoid postoperative respiratory compromise by sustained drug effect. ERAS measures to maintain the patient in the zone of normovolaemia are advantageous for OSA patients as excessive fluid administration can worsen OSA. The use of multimodal analgesia sparing opioids might be the most important element beneficial for OSA patients they are more prone to develop opioid induced respiratory depression (OIRD). As OSA patients are at risk for venous thromboembolism appropriate thromboprophylaxis should be applied. Postoperatively OSA patients should be closely monitored in the prevention of OIRD. In conclusion many ERAS measures seem to be applicable or of benefit for OSA patients. However, large prospective randomized controlled trials are needed to evaluate if these patients can be managed within an ERAS protocol.

Keywords: **Obstructive sleep apnea, ERAS, Perioperative management.**

Introduction

OSA (obstructive sleep apnea) is the most common sleep-related breathing disorder[1]. In patients presenting for elective surgery the prevalence is estimated to be 25%[2]. Patients with OSA presenting for surgery have a higher risk of cardiopulmonary complications leading to increased health care expenses[3]. Unfortunately, around 80% of the patients aren't diagnosed by the time of surgery[2,4]. The Society of Anesthesia and Sleep Medicine (SASM) guidelines recommend screening for OSA as patients and caregivers could be notified the of heightened perioperative risk. Identification of patients high at risk for OSA provide opportunities for possible risk reduction by application of perioperative interventions. The goal is to identify high risk patients and implement strategies mitigating the risk without creating a disproportionate economic burden. The SASM developed guidelines for screening and intraoperative management, but most recommendations are expert opinions due to a paucity of high-level evidence[5–7].

Meanwhile Enhanced recovery after surgery (ERAS) guidelines are regarded as standard of care and being widely implemented. The purpose of these recovery programs is to standardize medical care, enhance outcomes and decrease health care expenses using evidence-based protocols8. It is unclear whether ERAS can be safely implemented in specific vulnerable patient populations like OSA[9].

The first objective of this manuscript is to review the epidemiology, pathophysiology, and perioperative outcome of OSA.

The second part covers the latest evidence on perioperative management of patients with known or suspected OSA and determine whether general ERAS principles can be safely applied. The review will also provide an overview of the preferred methods of anesthesia and analgesia when OSA patients are listed for ERAS protocols in specific surgical domains.

Methods

Search strategy

Literature citations are retrieved from PubMed. Scientific evidence is based on articles from peer-reviewed journals. The literature search included reports from 01-01-1990 up to 02-28-2023. The Medical Subject Heading (MeSH) terms were used for the search in PubMed. The following MeSH terms were used: "Sleep Apnea, Obstructive" AND "Care, perioperative"; "Sleep Apnea, Obstructive" AND "Prevalence"; "Sleep apnea, Obstructive sleep" AND "Enhanced recovery after surgery"; "Sleep Apnea, obstructive" AND "Postoperative Complications"; "Sleep Apnea, Obstructive" AND "Pathophysiology". We looked in PubMed for the OSA guidelines of the American Society of Anesthesiologists (ASA) and the guidelines of the Society of Anesthesia and Sleep Medicine (SASM), ERAS protocols and Prospect guidelines. References cited in the retrieved articles were searched to identify additional manuscripts of value for this paper that were not found by the initial search. By implementing this search strategy, we found 10012 articles. We excluded articles by screening of the title and abstract when they were found irrelevant to the subject and by the following criteria: 1/ comments, editorials, or letter to the editors; 2/ language other than English, French, German; 3/ abstract or poster only, with no full text available. Based on these criteria 287 articles were considered valid and were completely reviewed. 101 were included in the final manuscript.

Epidemiology and pathophysiology of OSA(S)

Definition of OSA and OSA(S) and classification of OSA severity

Obstructive sleep apnea (OSA) is a pathophysiological process characterized by obstruction of the upper airway during sleep, resulting in repeated cessation of breathing with concomitant drop in oxygen saturation and arousal from sleep. Measuring the apnea-hypopnea index (AHI) by polysomnography (PSG) is regarded as the "gold standard" for OSA diagnosis.

OSA is defined as an AHI of >5 events per h of sleep. When this results in daytime sleepiness, leads to impaired cognition, or increased cardiovascular morbidity it is called the obstructive sleep apnea/hypopnea syndrome (OSAS). These terms are often used interchangeable in the medical literature which leads to conflicting results[10,11].

The International Classification of Sleep Disorders (ICSD-3) gives a very broad definition of OSAS (a synonym for OSA) worsening the already existing confusion. They're defining it as: '1) clinical symptoms and complaints of diurnal sleepiness, or witnessed apneas by a partner, or cardiometabolic abnormalities and AHI of >5 events per h of sleep; or 2) 15 or more predominantly obstructive breathing events per h of sleep (with no attendant symptoms or comorbidities specifically listed)[12].'

OSA severity can be defined as mild (5–15 events per hour of sleep), moderate (15–30 events per hour of sleep) or severe (>30 events per hour of sleep).

However, the number of AHI is a poor measure of clinical disease as it has no correlation with sleepiness or comorbidities. Therefore, its role as an indicator of severe or clinically relevant OSA is questionable[13]. It might also not be the most suited marker in predicting postoperative outcomes. Alternatives like cumulated duration of oxygen desaturation <90%, oxygen desaturation index, the lowest oxygen saturation and mean oxygen saturation may show a better correlation with postoperative outcomes[14].

Prevalence

OSA is common and often undiagnosed before surgery. The prevalence in the general population is predicted to be 1 in 4 men versus in 1 in 10 women but increases with age and body mass index[2,15]. As the population ages and obesity rates rise, the prevalence of OSA is likely to follow16. The prevalence of OSA in patients presenting for elective surgery is estimated to be around 25% but depends on the type of surgery and can be as high as 70 % in some populations (bariatric surgery). Table I shows the prevalence of OSA in the different

Table I.

Type of surgery	OSA prevalence in this specific population
Lumbar spinal fusion	7,7%[19]
Cardiac surgery	50%[20]
Pregnancy	15-20%[21]
Total joint artroplasty	8,7%[22]
Bariatric surgery	70%[17,18]

surgical populations[2,17–22]. Unfortunately, around 80 % of the patients don't have a diagnosis by the time of surgery[2,4].

Pathophysiology and risk factors

Characteristic of OSA are the repeated episodes of complete (apnea) and partial obstruction (hypopnea) of the airway. They are terminated by brief cortical arousals from sleep to resume airflow. This results in cyclic pattern of breathing as the patient shifts between wakefulness and sleep leading to daytime sleepiness and neurocognitive impairment. The apneas and hypopneas lead to hypoxemia and hypercapnia. These intermittent oxygen desaturations lead to oxidative stress, endothelial dysfunction, low grade inflammation and increased catecholamine levels explaining the risk for cardiovascular complications[23,24].

OSA is heterogeneous disease with both anatomical and non-anatomical traits. Traditionally OSA was considered a consequence of a narrow-gauged upper airway anatomy that is prone to collapse. During wakefulness this is prevented by a reflex-mediated increase in upper airway dilatator muscle activity but after sleep onset when muscle activity is reduced the airway collapses. Apart from this anatomic trait that probably plays a role in most patients by varying extent there are several other non-anatomic traits contributing to the pathophysiology of OSA. These non-anatomical traits include: (1) a poor capacity of upper airway muscles to counter pharyngeal collapse when asleep, (2) a low tendency to be aroused from sleep because of a respiratory disturbance (arousal threshold), (3) instability of respiratory control (loop gain)[23,24].

Although most risk factors are fixed like male sex, age, macroglossia, increased neck circumference, craniofacial abnormalities, adenoidal and tonsillar hypertrophy some others are modifiable like obesity, smoking, alcohol consumption and fluid retention. These risk factors predispose to OSA by different and often more than one pathophysiologic mechanism[23,24].

Endotypes

Dividing a disease in specific endotypes is a way to classify this disease based on mechanism. This is different from phenotypes where only the expression of the disease is taken into consideration resulting from specific genetic and environmental interactions. Based on these different pathophysiologic mechanisms OSA can be classified into different endotypes. Each endotype has their own risk profile with specific postoperative complications[25].

Anatomic traits

Obesity and craniofacial shape are the key anatomic traits that lead to a narrow collapsible upper airway. Treatment of obesity, the most common risk factor, by diet or bariatric surgery is associated with improved OSA severity[26,27]. Airway collapsibility is also influenced by body and head position[28–30]. The supine position narrows the airway by the rostral fluid shift especially after fluid loading and states of fluid retention[31]. Collapsibility worsens with neck flexion and improves with extension which is the rationale for the chin lift maneuver[30].

Non-anatomic traits

The capacity of the pharyngeal muscles to increase muscle tone in reaction to a respiratory stimulus is a characteristic feature in the pathophysiology of OSA. The genioglossus muscle is activated by an increased chemical drive (hypercarbia and hypoxia) via the brainstem and increased negative intra-pharyngeal pressure acting by reflex via upper airway mechanoreceptors or it's combination[32,33]. There is some evidence in animal studies that opioids might reduce genioglossus activity[34]. After the use of NMBA genioglossus muscle can be reduced even in the absence of respiratory symptoms[35].

Respiratory arousal threshold is defined as the propensity to wake up during sleep. It is characterized by the degree of respiratory effort measured by epiglottic pressure before cortical arousal (three seconds of high frequency activity on the EEG) ensues. People with a high pre-existing arousal threshold may be especially prone to respiratory events when opiates and hypnotics are used. Both opioids and hypnotics increase the arousal threshold so profound hypoxia and hypercapnia were to develop before arousal ensues.

Conversely patients with low thresholds could benefit from hypnotics or sedative medication as they become less arousable[25,34,36].

The development cyclic breathing where the patient shifts between obstructed breathing during sleep and arousal is key determinant of OSA. Loop gain is best understood as the magnitude of a ventilatory response to a certain rise or fall in arterial CO_2 tension. When the ventilatory response overcompensates the rise in CO_2 tension we speak of high loop gain. This creates an unstable breathing pattern where the patients fluctuate between hyperventilation and apnea. A system with low loop gain that creates little, or no fluctuations is said to be stable[25,34]. Oxygen might be effective in the postoperative setting for patients with a high loop gain as this increases the stability of breathing pattern by reducing the peripheral chemoreceptor responsiveness[37].

Postoperative complications

Multiple studies have investigated the impact of OSA on postoperative outcomes. These can mainly be categorized in pulmonary and cardiac complications, and clinical outcomes.

Two large meta-analyses that used pulmonary complications (postoperative desaturation, acute respiratory failure, reintubation, prolonged mechanical ventilation), cardiac complications (myocardial infarction, hypotension, cardiac arrest, arrythmia) and ICU transfer as primary outcomes showed that patients screened positive for OSA or confirmed by polysomnography carried a fourfold increased risk of cardiopulmonary complications. Table II shows potential outcomes that can be used in evaluating the risk of postoperative complications[38]. Although it is unknown if AHI is the best metric to predict postoperative outcomes studies have shown that there is a positive correlation between OSA severity measured by AHI and the risk of postoperative cardiac and pulmonary complications[39,40].

Depending on the type of surgery OSA leads to an increased use of health care resources as they use more critical care, stepdown and telemetry services and have increased duration of hospitalization[41].

The risk of postoperative complications also depends on the type of surgery. Not all types of surgery have been specifically invested. The rate of complications is higher in abdominal surgery, orthopedic surgery (lumbar spinal fusion and total joint arthroplasty) and cardiac surgery[20,42–44]. This was not the case for bariatric surgery in morbidly obese patients, however this might be explained by the universal use of postoperative non-invasive ventilation is this population[45].

In cardiac surgery a meta-analysis revealed that OSA-patients had a 33% increased risk of developing major cardiac events (MACEs). The risk of new onset postoperative atrial fibrillation was increased with 18%[20].

OSA undergoing lumbar spinal fusion had an increased rate of postoperative complications like renal and respiratory failure, and venous thromboembolism[19,43].

Perioperative management

Currently, perioperative management has evolved into specific structures of ERAS. This means that a bundle of specific measures is proposed to improve the outcome quality and consequently these ERAS

Table II.

Outcome category	Relevant outcomes
Pulmonary complications	Acute respiratory failure
	Reintubation
	Pneumonia
	Pulmonary embolism
	Prolonged mechanical ventilation
Cardiac complications	Arrythmias
	Heart failure
	Cardiac arrest
	Myocardial infarction
Clinical outcomes	Mortality
	Hospital lenght of stay
	ICU admission
	ICU length of stay
	Health care costs
	Health care utilization

protocols often lead to a reduction in hospitals stay. ERAS is best adjusted according to the specific procedure and several organizations have published procedure specific protocols. In this section, we will evaluate a generic bundle of ERAS measures and assess if this bundle is applicable and relevant for the OSA patient. Indeed, ERAS protocols differ depending on the type of surgery, but the following paragraphs on preoperative and intraoperative (Table III) management are a review of general ERAS recommendations that are relevant and recur in every type of surgery. This also accounts for the paragraph on postoperative management except for the part on pain management where we chose for a tailored approach for different types of surgery. Figure 1 shows a schematic representation of ERAS measures where the interventions could be beneficial for OSA patients[46].

Preoperative elements

Preadmission risk stratification

The SASM guidelines strongly recommend preoperative screening for OSA. According to the SASM guidelines adults at increased risk of OSA should be recognized before surgery. Screening allows for risk stratification and opportunities to implement perioperative interventions that might decrease the risk of postoperative complications. Of all available screening tools, the STOP-Bang is the most validated in surgical patients[5].

Patients with STOP-bang scores between 0 and 2 are classified low risk for OSA and those with a score between 3-8 should be classified as high risk for OSA. Patients considered to be high risk for OSA had a higher risk of postoperative adverse events and a longer hospital stay. This assumes that the STOP-Bang is effective in risk stratification[47].

A score of 3 or greater is 84% sensitive and 56 % specific for the presence of OSA. Because of the high sensitivity patients with scores of 0 up to 2 can be safely ruled out. But because of the modest specificity many of the patients categorized as 'high risk' will not have the disease which may result in unnecessary utilization of recourses[48].

With increasing STOP-bang scores the probability of having moderate-to-severe and severe OSA increases proportionally[49]. This might be useful given the fact that patients with severe OSA are at increased risk of perioperative complications[40]. For patients whose STOP-Bang scores fall between 3 and 4, additional criteria can be employed to identify patients as high risk for OSA, thereby improving specificity. These additional criteria include a combination of a STOP score of at least 2 plus one of the following: a BMI more than 35 kg/m^2, male gender and a neck circumference more than 40[48].

Optimization of pre-existing health conditions

Preoperative optimization of the OSA patient

The SASM guidelines has made specific recommendations for three different patient groups: Known OSA adherent to CPAP, known OSA not adherent to CPAP and patients with a high probability of having OSA detected by screening. All patients with known OSA and patients screened high at risk of having OSA should be informed of their heightened perioperative risk. In all patients with a diagnosis or a high probability of OSA, the known perioperative risk reducing strategies regarding anesthetic protocol, postoperative analgesia and monitoring should be implemented.

Table III.

	ERAS general	OSA
Airway management	No recommendations	Risk factor for difficult airway
Choice of technique: TIVA inhalational anesthesia	No clear recommendations favoring one over another	Desflurane or sevoflurane, evidence from obese population
Choice of technique: General Vs locoregional	Depends on type of surgery	Locoregional whenever possible
Anesthesia monitoring BIS or end tidal	To minimize side effects and facilitate rapid awakening	Vulnerable for sustained drug effect
NMBA		
Monitoring	+	+
Reversal agents	No recommendation	Suggamadex
Fluid management		
GDFT	In high risk patients	Considered to be high risk?
Fluid choice	Balanced kristalloids	Balanced kristalloids
Prevention hypothermia	+	+ High prevalence of PHT
Intraoperative glycemic control	Should be kept close to normal	CPAP use is considered beneficial

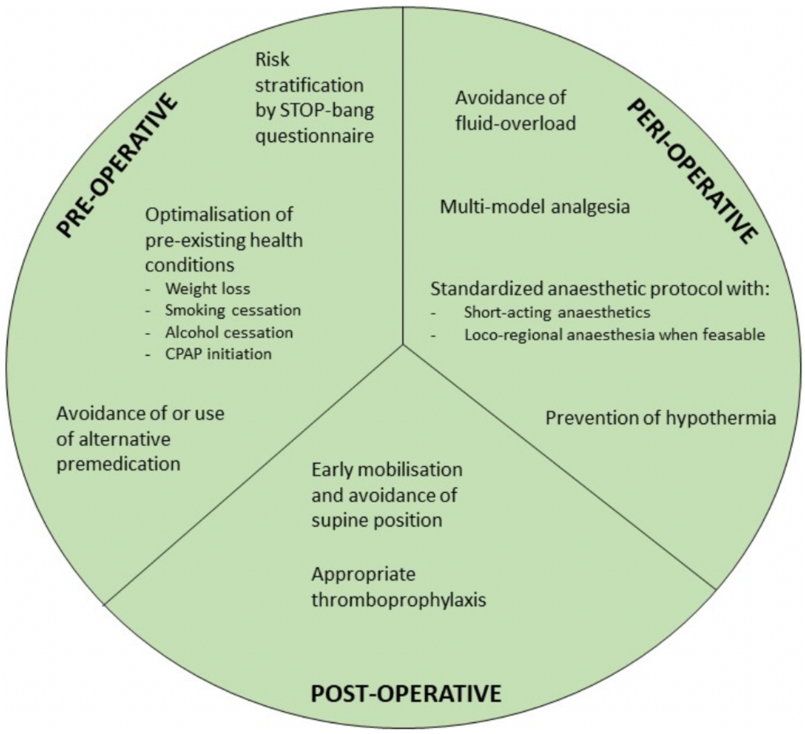

Fig. 1 — Schematic representation of ERAS measures where interventions could be beneficial for OSA patients.

In known OSA patients non adherent to CPAP and patients screened high at risk for having OSA with a suspicion of uncontrolled cardiopulmonary disease accompanying OSA (pulmonary hypertension, resting hypoxemia) the SASM recommends considering further preoperative evaluation and optimalisation of the patient's cardiopulmonary status. In absence of uncontrolled systemic disease or after optimization of the patient's cardiopulmonary status, all patients can proceed to surgery in the same way as patients with confirmed and treated OSA on the condition that perioperative risk reducing strategies are implemented. Currently there is insufficient evidence to postpone surgery and wait for a formal diagnosis and initiation of PAP therapy in patients screened high at risk for OSA. However, this should be reviewed case by case depending on the urgency and type of surgery and the patient's comorbidities[5].

There is some evidence that patients diagnosed OSA, and prescribed CPAP have less cardiovascular and pulmonary complications compared to patients undiagnosed and as result denied of CPAP[40,50]. Perioperative CPAP use also resulted in a reduction in the number of AHI and higher oxygen saturation levels[51]. A meta-analysis conducted in 2015 however failed to demonstrate a reduction in postoperative adverse events in OSA patients on CPAP compared the control group not on CPAP. There was however a reduction in the length of stay and significantly reduced postoperative AHI in the CPAP group[52].

Given the above-mentioned evidence the SASM guidelines recommend using CPAP pre and postoperative during their stay in the hospital for all patients diagnosed with OSA. Those non adherent should be encouraged. The same settings should be used as prescribed previously, although sometimes adjustments need to be made postoperatively. The use of CPAP in those suspected to have OSA by screening should be considered case by case. In patients with known OSA results of the sleep study should be reviewed to assess the severity of OSA[5].

Preoperative weight loss

Obesity is a key anatomic trait that leads to a narrow, crowded, or collapsible upper airway. Treatment of obesity, the most common risk factor, by diet or bariatric surgery is associated with an improvement of OSA severity[26,53]. According to the ASA guidelines preoperative weight loss should be considered when feasible[7].

Alcohol cessation

Cessation of alcohol consumption is advantageous for OSA patients as alcohol consumption increases the risk of sleep apnea and sleep apnea with hypoxia. Cessation of alcohol for a month reduced the increased risk of OSA[54,55].

Smoking cessation

Smoking is a known risk factor for OSA. It is thought to worsen OSA by affecting sleep architecture, upper airway neuromuscular function, arousal mechanisms, and inflammation of the upper airway.

Currently there is little evidence that cessation of smoking improves OSA[56].

However, both OSA and smoking increase the risk of poor wound healing, postoperative pulmonary complications (PPC's) and thrombo-embolic events. As the reduction of smoking of at least four weeks has shown to increase wound healing and reduce PPC's this ERAS recommendation should be encouraged in OSA patients[46].

Premedication

Pharmacological sedation to reduce anxiety should be avoided in ERAS protocols to prevent reduced mobilization and recovery[57]. As benzodiazepines decrease the activity upper airway muscles and increase the arousal threshold thereby increasing the respiratory event duration leading to possible hypoxemia some authors warned they should be avoided in patients with OSA[58]. However, recent data on OSA endotypes has shifted this paradigm and stated that they can be of benefit for patients with a low arousal treshold[59]. While premedication must not be standard of care, their use should not be withheld in anxious patients who are comfortable with the use of CPAP. Whenever premedication is used, monitoring oxygen saturation and intravenous access should be available to antagonize drugs if needed[60]. Oral clonidine has been suggested as a more suitable alternative for the OSA population as ventilation is only minimally impaired[61].

Intraoperative elements

General/locoregional

Although most ERAS protocols state clear recommendations in choosing general versus regional anesthesia depending on the type of surgery, physicians are left the choice in some types of surgery like joint arthroplasty or peripheral vascular surgery[62]. As a result of OSA patients' increased vulnerability to the effects of general anesthetics on the upper airway general perioperative guidelines recommend that whenever possible, regional anesthesia techniques should be preferred over general anesthesia. For superficial procedures the use of local anesthesia or peripheral nerve block should be considered, while spinal or epidural anesthesia should be considered for peripheral procedures[6,7]. Specifically for joint arthroplasty this was confirmed as OSA patients receiving neuraxial anesthesia had reduced odds for major complication complications, mechanical ventilation, use of critical care services, extended hospitalization, and increased costs compared to general anesthesia[63]. Reduced complication rates were also observed when peripheral nerve blocks and neuraxial anesthesia were used in addition to general anesthesia in patients undergoing total joint artroplasty[63]. A possible explanation may be the reduced need for anesthetic consumption. Another consideration favoring the use locoregional anesthesia is the avoidance of airway manipulation as OSA patients are at increased risk for difficult airway management[6]. Both the ERAS and OSA guidelines recommend that whenever general anesthesia is performed medication regimens with short acting agents and lowest possible drug doses should be used to reduce residual effects as they could delay recovery or result in adverse respiratory events in case of ERAS and OSA respectively[6,7,64].

Inhalational/Intravenous

With regard of the choice between intravenous versus inhalational agent there is a considerable variability in ERAS protocols depending on the type of surgery. Some protocols have a clear preference while others don't. Currently there is insufficient evidence which maintenance agent is best fitted for OSA patients. They assume the application of evidence gathered from the obese population might also be of benefit for OSA patients as they are closely associated regarding prevalence, shared difficulties in anesthesia management and postoperative complications. They recommend using inhalational anesthesia (desflurane and sevoflurane) over propofol as result of their rapid and consistent awakening profile, implying improved oxygenation[5]. In facilitating rapid awakening ERAS protocols recommend anesthetic depth monitoring. This alongside determining the appropriate regimen, including the drug dose, action time and metabolism should help minimizing the OSA patient's vulnerability to sustained drug effect. It is assumed that in OSA BIS is suitable to titrate doses of hypnotics and prevent overdosage of anesthetics leading to an improved anesthetic recovery with the possibility of less respiratory compromise in sevoflurane anesthesia[65].

Neuromuscular blocking agents

According to the latest ASA guidelines, Sugammadex is recommended for reversing deep, moderate, and shallow levels of neuromuscular blockade that are induced by rocuronium or vecuronium. For minimal blockade (train-of-four ratio ranging from 0.4 to less than 0.9), neostigmine is a viable alternative[66]. Compared to non-OSA patients, OSA patients may be at higher risk for postoperative hypoxemia, respiratory failure, and residual neuromuscular blockade when neuromuscular blocking drugs (NMBD) are used. There is some evidence suggesting that using Sugammadex instead of neostigmine for NMBD reversal in OSA patients may be beneficial[67].

Perioperative fluid management

During operations the supine or Trendelenburg position causes fluid that has built up in the legs to move rostrally to the thorax, neck and head because of gravity and its effect on starling forces[68]. In the supine position the reduced hydrostatic pressure opposing colloid osmotic pressure causes fluid in the legs to move intravascularly. This fluid can accumulate in the neck because of the process of rostral fluid shift and can cause narrowing of the upper airway increasing its collapsibility contributing to OSA[31]. As fluid retention states with oedema are associated with an increased volume of fluid mobilization from the legs excessive fluid administration and fluids with high salt content should be avoided in the OSA population particularly in the perioperative period as the stress response from surgery already results in increased fluid and salt accumulation[68–70]. In this setting ERAS protocols seem to come in handy as they aim to keep the patient normovolemic and the intravascular volume optimized reducing fluid shifts. Given the evidence OSA patients might be labeled as high risk and there should be a low threshold to use a goal directed fluid therapy, monitoring the cardiac output non-invasively and avoid excess fluid administration[64].

Preventing intraoperative hypothermia

Prevention of intraoperative hypothermia is a key component of the ERAS recommendations as it is associated several complications impeding recovery[64]. In the OSA population intraoperative hypothermia should especially be avoided as it might be a trigger for pulmonary hypertension, complicating 5-20% of the OSA population[21,71].

Intraoperative glycemic control

The ERAS guidelines recommend that we should aim for close to normal glucose concentrations by using perioperative treatments that decrease insulin resistance without increasing the risk hypoglycemia[64]. CPAP treatment increased medium term insulin sensitivity in non-diabetic and type 2 diabetic-patients with OSA favoring their glucose control[72,73]. One study even showed an improvement after two days of CPAP treatment in non-diabetic patients[74].

Postoperative elements

Pain management

Adequate postoperative pain management is essential in ERAS. The aim of pain management is to facilitate early postoperative ambulation and physical therapy reducing the length of hospital stay. This is achieved by applying multimodal analgesia. The benefit of a multimodal regimen for pain management is based on the concept that using a combination of multiple mechanisms for pain reduction will result in better pain control and avoidance the side effects of each drug. A reduction of opioids is the main target because of their unfavorable side effects[75]. In addition, we also

Table IV.

Total hip replacement	OSA[63]	ERAS[62]	Prospect[81]
General/Neuraxial	Neuraxial	Both	Neuraxial
Aceteminophen	+	+	+
NSAIDS	+	+	+
Gabapentinoids	-	-	-
Spinal opioids	-	-	+
Epidural	+	-	-
Fascia iliaca	+	-	+ or
Local infiltration analgesia	+	-	+ or

Table V.

Total knee replacement	OSA[63]	ERAS[62]	Prospect[82]
General/Neuraxial	Neuraxial	Both	/
Aceteminophen	+	+	+
NSAIDS	+	+	+
Gabapentinoids	-	-	-
Spinal opioids	-	-	+
Epidural	+	-	-
Adductor canal block	+	-	+
Local infiltration analgesia	+	+	+

Table VI.

C-section	OSA	ERAS[83]	Prospect[84]
Aceteminophen	+	+	+
NSAID's	+	+	+
Dexamethasone	+	No recommendation	+
Spinal morphine	In pregnant woman receiving intrathecal morphine for cesarean delivery, OSA diagnosis by Berlin questionnaire and obesity is associated with increased odds for a SpO_2 <90%. [85].	+	+
Epidural morphine	-	No recommendation	+
Regional anesthesia (TAP-block, fascial plane block, quadratus lumborum)	+	If intrathecal morphine is not used	If intrathecal morphine is not used

Table VII.

Bariatric surgery	OSA	ERAS[86]	Prospect[87]
Aceteminophen	+	+	+
NSAID'S	+	+	+
Dexmedetomidine	+	+	-
Ketamine	+	+	-
Pregabalin	-	-	If contra-indication for standard regimen
Dexmedetomidine	+	Not standard	-
Epidural	+ Without opioids	For laparotomy	
TAP-block	+	+	-

Table VIII.

Cardiac surgery	OSA	ERAS[88]
Aceteminophen	+	+
NSAID's	+	-
Pregabalin	-	+
Ketamine	+	No recommendation
Dexmedetomidine	+	+

shortly evaluated the applicability of the Prospect guidelines for patients with OSA.

Multimodal analgesia

One retrospective cohort study on OSA patients undergoing total joint arthroplasty of the lower extremity demonstrated the benefit of multimodal analgesia in this population. The study evaluated the effectiveness of multimodal analgesia, which involved combining opioid use with one, two, or more analgesic modalities such as nonsteroidal anti-inflammatory drugs, cyclooxygenase-2 inhibitors, acetaminophen, peripheral nerve blocks, glucocorticoids, gabapentin, pregabalin, or ketamine. The findings indicated that the use of multimodal analgesia resulted in a gradual decrease in opioid consumption and a reduction in complications, including critical respiratory failure and the need for critical care admissions[6,76].

Regarding safety in using ketamine in the OSA population evidence is scarce. Theoretically OSA patients could benefit from its use as it known to activate upper airway respiratory muscles during general anesthesia[77]. The use of gabapentinoid drugs as part of multimodal analgesia for surgical pain management remains controversial as they have been associated with sedation, respiratory depression when combined with opioids in non-OSA patients. They should therefore be avoided or used at reduced doses in known OSA-patients[78,79]. Clonidine and dexmedetomidine are both centrally acting α-2 agonists causing sedation, analgesia, and sympatholysis causing only minimal respiratory depression. This safe respiratory profile makes them an attractive choice as opioid-sparing analgetic in a population that is at increased risk for PPC's. However, current literature on the use of α-2 agonists in patients with OSA is scarce and provides mixed results[6]. Despite obese OSA patients are more likely to suffer from diabetes or resistance to insulin the use dexamethasone should not the withheld if close glycemic control can be obtained80.

In Table IV, V, VI, VII and VIII we give a schematic representation of the medications that can be used for multimodal analgesia for OSA patients in different types of surgery[62,63,81–88].

Opioids and OSA

Patients with OSA seem to at increased risk for postoperative opioid-induced respiratory depression (OIRD)[89,90]. Apart from the diminished respiratory drive to hypoxia and hypercarbia OSA patients are considered more vulnerable to opioids because of their ability to reduce pharyngeal muscle activity leading to collapse. Because of the intermittent hypoxia in OSA patients leading to an altered pain perception and potentiated opioid analgesic effects drug OIRD can occur without obvious drug overdosing. Opioid requirements could be substantially lower in patients who exhibit preoperative nocturnal hypoxia rendering oxygen saturation as a more accurate predictor for perioperative complications than preoperative AHI[36,90]. A closed claim analysis revealed that most respiratory events happened within the first 24 hours after surgery. Contributing factors may be concomitant sedative use and the use of opioids in more than one modality[91]. This coincides with the fact that OSA patients experience the greatest disturbance of sleep architecture with a significant decrease in sleep efficiency, rapid eye movement sleep, and slow-wave sleep on the first night postoperatively compared with the preoperative baseline. However, unexpectedly the highest prevalence of AHI with an increase in oxygen desaturation was on N3 and not N1 postoperatively. The increased AHI can be a result of the recovery of REM-sleep on night 3 in which the AHI's were higher during other phases of sleep. Another possible explanation could be the high oxygen utilization the first night postoperatively that could have attenuated the oxygen desaturation episodes[92]. The postoperative worsening of OSA measured by AHI is associated with opioids in a dose dependent manner[93]. Endo-typing might play a role as only those with a high arousal threshold and decreased ventilatory response at increased risk of developing opioid induced ventilatory comprise as they might develop deep hypoxemia before arousal develops[36].

Regarding the use of neuraxial opioids in patients with OSA evidence is limited. The SASM suggests there is a possible augmented risk for neuraxial opioid-induced respiratory depression in OSA patients. Therefore, OSA patients receiving neuraxial opioids should be under constant monitoring evaluating the adequacy of ventilation and oxygenation[7].

Thrombo-embolism prophylaxis

The perioperative period remains an important risk factor for venous thrombo-embolism (VTE). ERAS protocols aim at preventing this complication by pharmacological prophylaxis, compression devices and early mobilisation[94]. Patients with OSA are at an increased risk of developing venous thrombo-embolic events during the perioperative period. Therefore, patients should be encouraged to mobilize as quick as possible, and antithrombotic prophylaxis should be considered when indicated. When compression devices are used in the supine position it should be noted that they may exacerbate the rostral fluid shift possibly worsening OSA[68]. Smoking cessation should especially be encouraged in this population as both share pathophysiological pathways in the generation of thrombotic events: endothelial dysfunction and blood hypercoagulability. Currently there is no evidence to believe that CPAP can reduce the risk of postoperative VTE. Although from a pathophysiological point of view it would make sense as both the endothelial dysfunction and blood hypercoagulability are induced by intermittent hypoxia which can be treated with CPAP[95].

Postoperative respiratory support and follow-up

Supplemental oxygen - The ASA recommends postoperative patients should be on oxygen until they are able to maintain their preoperative saturation while breathing room air[7]. Postoperative oxygen improves oxygenation and decreases the number of AHI without increasing the length of apnea-hypopnea events in patients with OSA. However, patients developed hypercapnia while receiving supplemental oxygen. This might occur as supplemental oxygen abolishes hypoxemia increasing the length of apnea causing hypercapnia. This can be dangerous as this might go undetected by pulse oximetry[96]. Therefore, detection of respiratory rate and capnography should be used. As oxygen stabilizes breathing by reducing peripheral chemoreceptor responsiveness to hypoxia and hypercapnia oxygen administration may help to control breathing instability in OSA patients with a high loop gain. However, in patients with a low loop gain and high arousal thresholds it could prolong the apnea duration.

CPAP-therapy - Patients preoperatively adherent to PAP should continue its utilization pre-and postoperatively. If airway obstruction or hypoxemia is observed postoperatively in patients suspected to have OSA or diagnosed with OSA this should be treated with CPAP[5,7].

Early mobilization is an integral component of postoperative care in ERAS protocols. Delayed ambulation leads to respiratory (pneumonia, atelectasis) and thromboembolic complications, insulin resistance and delirium[97]. As OSA patients are prone for developing these complications early mobilization may be of particular benefit. Interventions like incentive spirometry, ambulation and head-of-bed elevation showed a 4-fold decrease in the incidence of postoperative pneumonia[98].

Upright positioning - In the postoperative period patients the number of AHI is significantly increased when supine compared to the non-supine position[93]. According to the SASM guidelines the supine position should be avoided as it increases the number of obstructive apneas compared to the upright, semi-upright, 0° reverse Trendelenburg or lateral position[7]. Perioperatively the rostral fluid shift could also worsen oedema further worsening airway obstruction.

Postoperative monitoring - Extra vigilance is necessary during anesthesia emergency because of potential residual effects of sedatives and opioids. Patients should always be monitored postoperatively as lack of it is a risk factor for respiratory depression[99]. Currently evidence is lacking to determine the proper length of stay before patients can be discharged to an unmonitored setting. Patients should not be discharged before the can achieve adequate saturations on room air and airway obstruction does not occur while left undisturbed. The ASA recommends continuous oximetry monitoring after discharge from the recovery for patients at increased risk of respiratory compromise. This can be done on the intensive care, stepdown units or on routine wards[7]. In addition to the routine use of pulse oximetry there increasing evidence supporting the use of capnography as it is a more sensitive indicator to detect adverse respiratory events[100]. Patient monitoring can also be used to detect patients at risk of deterioration after PACU discharge. This is demonstrated by Gali et who demonstrated that patients screened high at risk of OSA with recurrent PACU events (bradypnea, apnea, oxygen desaturation) were at higher risk for perioperative respiratory desaturations and complications[101]. As the increased need for postoperative monitoring carries an increased burden on postoperative care providers (PACU, intensive care, routine wards) it should be remembered that ERAS is a multidisciplinary approach that can only succeed after participation of all team members.

Discussion

OSA is a common and multimodal disease with specific treats for the perioperative setting.

We have critically assessed and compared the ERAS bundle with OSAS and highlighted the specific elements that should be considered when anesthesiologists manage these patients. Currently there are no prospective studies investing the safety, feasibility, and benefits of managing OSA patients in an ERAS protocol. Preoperative ERAS measures for risk stratification by screening, informing patients on their increased perioperative risk and optimization of pre-existing health conditions are all perfectly tailored for OSA patients. As OSA is such a prevalent condition associated with a considerable increased perioperative risk the wide application of the structured preoperative ERAS approach on risk stratification and optimization of pre-existing health conditions could be an opportunity to increase vigilance on OSA, aiming to reduce the perioperative risk for this large vulnerable group of patients. We therefore recommend the screening for OSA should be specifically mentioned in the ERAS protocols, especially for the types of surgery where OSA is prevalent. When proceeding to surgery the general, the intraoperative care bundle from the ERAS protocols to achieve goals like early ambulation and recovery by minimizing sustained drug effect and avoidance of opioid induced side effects by implementation of multimodal analgesia are all of benefit for the specific risk profile of the OSA patient reducing their complications. However, it remains unclear if undiagnosed OSA patients could benefit from a standard ERAS protocol as there will unavoidably to variable extent be exposure to measures placing this population at increased risk. If OSA is diagnosed or suspected, this offers an opportunity to adjust ERAS protocols to the specific vulnerabilities of this population. Therefore, ERAS protocols should not be denied but rather be tailored the OSA patient. Figure 2 shows a schematic conclusion on the different perioperative management scenarios of the OSA patient in relation to the ERAS protocols. Large prospective randomized controlled trials are needed to evaluate if OSA patients can be safely managed within an ERAS protocol. Vice versa there is some evidence supporting that properly treated OSA with CPAP can help achieving ERAS goals like reducing cardiopulmonary complications

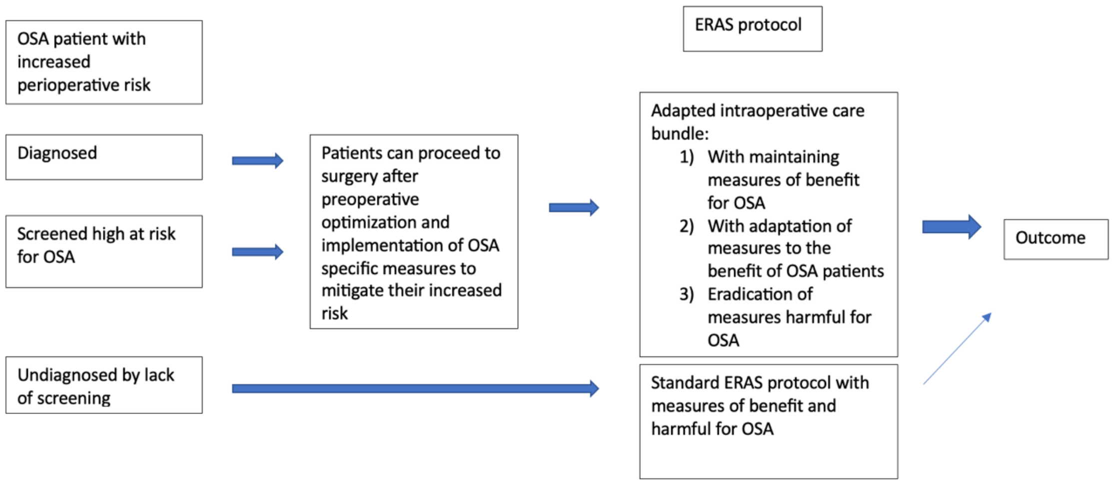

Fig. 2 — Schematic representation of the OSA patient's perioperative management in relation to the ERAS protocols.

and minimizing health care expenses. For future investigations it would also be interesting to stratify in future studies the impact of diagnosed versus undiagnosed and treated versus untreated OSAS in relation to enhanced recovery. In conclusion the goal of ERAS protocols, to improve perioperative outcome, should not only be procedure specific, but also be further developed in a patient-tailored personalized approach.

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