Universitat de Girona
Facultat de Medicina

Can the use of postoperative CPAP in patients at high risk of OSA reduce desaturation episodes after surgery?

A CONTROLLED, RANDOMIZED, CLINICAL TRIAL

2017
FINAL DEGREE PROJECT

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I would like to express my gratitude to all the professionals that step by step helped me to improve and carry out this work, especially to my mentor Dra. Parramon for her patience and dedication.

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1. LIST OF ABREVIATIONS

AHI: Apnea-Hypopnea Index

ARF: Acute respiratory failure

ASA: American Society of Anesthesiologists

BIS: Bispectral Index

BMI: Body Mass Index

COPD: Chronic Obstructive Pulmonary Disease

CPAP: Continuous Positive Airway Pressure

CRF: Case Report Form

ECG: Electrocardiogram

FiO2: Inspired Fraction of Oxygen

FRC: Respiratory Functional Capacity

ICU: Intensive Care Unit

MAC: Minimum Alveolar Concentration

ODI: Oxygen Desaturation Index

OSA: Obstructive Sleep Apnea

PACU: Post-Anesthesia Care Unit

PEEP: Positive End Expiratory Pressure

REM: Rapid Eye Movement

TOF: Train Of Four

UA: Upper airway

VAS: Visual Analogue Scale

2. ABSTRACT

Background: The prevalence of obstructive sleep apnea (OSA) in the general population ranges from 2 to 6% but the incidence is directly proportional to the age and weight. Few patients with confirmed diagnosis and only 5% receive treatment. The higher prevalence of OSA in the surgical population has been demonstrated in several studies as well as the increased surgical risk. A meta-analysis confirmed the increased complications (postoperative desaturation, acute respiratory failure, cardiac events and the need for transfer to ICU) in this population. When OSA is diagnosed preoperatively, the rate of postoperative pulmonary complications is low and not associated with OSA severity. The beneficial effect of CPAP on patients with OSA is known but its benefit is unknown in patients at high risk of OSA undergoing surgery to prevent these respiratory complications such as post-surgical desaturations.

Objective: To evaluate the effectiveness of CPAP vs ventimask postoperative in patients with high risk of OSA to prevent postoperative desaturations. The secondary objectives are to examine the reduction of postoperative hospital stay of these patients and to evaluate the prevalence of high risk of OSA in surgical population.

Methods: The design is a single-center, randomized, simple blind, and parallel-group trial will be performed between 2017 and 2019 in Dr. Josep Trueta University Hospital of Girona. 682 patients will be recluted during 2 years and randomized into two groups. 341 will receive CPAP therapy with an oxygen concentration of 50% and PEEP 8-10 cm H2O the first 24 hours after surgery and 341 patients will receive ventimask a 50% of oxygen concentration.

Key words: obstructive sleep apnea; surgery; postoperative complications; preoperative assessment; continuous positive airway pressure.

3. INTRODUCTION

Obstructive sleep apnea (OSA) is a serious condition characterized by repeated episodes of complete or partial obstruction of the upper airway. The episodes are accompanied by varying degrees of arterial desaturation and sympathetic activation. The result is sleep disruption, excessive daytime sleepiness, often snoring and cardiovascular dysfunction.

OSA is the most prevalent sleep disorder. In an epidemiological study, Young et al. noted that the prevalence of sleep apnea (defined as apnea-hypopnea index (AHI)) ≥ 5/h was 9% for women and 24% for men. However, the prevalence of Obstructive sleep apnea (OSA) (defined as AHI ≥ 5/h and daytime sleepiness) was 2% in women and 4% in men. (1)

This prevalence is directly increased by age and obesity, factors to which it is closely related. It has also been seen that a significant proportion of patients undergoing surgery are at high risk for OSA. (1)

An estimated 82% of men and 92% of women with moderate-to-severe sleep apnea have not been diagnosed. Curry out a correct preoperative diagnostic approach is important for both anesthesiologists and surgeons. Generally, OSA correlates with an increased presentation of patients with difficult airway and are at increased risk to having perioperative complications (including hypoxemia, pneumonia, pulmonary embolism, atelectasis, myocardial infarction, cardiac arrhythmias, and unanticipated admission to the ICU) (2)

The use of non-invasive ventilation such a continuous positive airway pressure (CPAP) produces a pneumatic resistance that increases the pharyngeal diameter and makes it difficult to collapse.

The appropriate use of CPAP reduces or eliminates daytime drowsiness, systemic hypertension, improves the symptoms of right heart failure and neurocognitive function. (7)

3.1 OVERVIEW OF OSA

3.1.1. TERMINOLOGIES

According to the American Academy of Sleep Medicine:

- The **Obstructive sleep apnea syndrome** is defined like intermittent and recurrent episodes of partial or complete obstruction of the upper airway during sleep despite the ventilator effort, causing hypoxemia, hypercapnia and sympathetic activation. The diagnosis of obstructive sleep apnea syndrome requires the presence of more than five episodes per hour and diurnal sequelae (such as excessive daytime sleepiness, fatigue and cognitive impairment); or cardiovascular comorbid conditions (such as hypertension, ischemic heart disease, or prior stroke). (3,4)
- **Apnea** in adults consists of periods of 10 seconds or more where airflow is obstructed. The arterial oxygen desaturation is >4% and this apnea period ends with a patient's micro-awakening. (3)
- **Hypopnea** is defined as periods of 10 seconds or more in which the airflow decreases at least 50% of the previous or baseline value. These episodes are accompanied by varying degrees of arterial oxygen desaturation (>3% y <4%) and sympathetic activation. (3)
- The **Apnea-Hypopnea Index (AHI)** measures the severity of apneas / hypopneas. AHI is defined as the sum of apneas and hypopneas divided by the hours of sleep. (1,3,5)

  Based on the AHI, the severity of OSA is classified by American Academy of Sleep Medicine as follows:

OSA severity	Adult criteria (AHI/hour)	Pediatric criteria (AHI/hour)
None/minimal	< 5	0
Mild	5-14	1-5
Moderate	15-29	6-10
Severe	≥ 30	>10

The severity of OSA as measured by the AHI may worsen in OSA patients during the postoperative period. (5–7)

- **Oxygen Desaturation Index**: Average of time during the episodes of desaturation, defining each desaturation as a period of> 10 seconds of durability where the oxygen saturation decreases> 4% on the average value of saturation patient the last 120 seconds. (3)

3.1.2. CLASSIFICATION OF APNEAS

According to its origin we can find three types of apneas:

- Obstructive (these are the most frequent and will be treated in this study): airflow interruption is caused by upper airway obstruction (UA) despite the fact that the ventilatory musculature tries to overcome this obstruction.

- Central (uncommon and not included in this study): the cessation or decrease of airflow occurs due to cessation or decrease of the activity of the ventilatory muscles.

- Mixed: apneas or hypopneas begin with a central mechanism and then the ventilatory muscles are activated becoming obstructive apnea.

3.1.3. EPIDEMIOLOGY

OSA is a very prevalent disease affecting 4-6% of men and 2-4% of women in the adult population and 1-3% of the child population (usually with tonsillar or adenoid hypertrophy). (5,8)

Age and sex are important influences. 27% percent of women and 43% of men ages 50 to 70 years old are estimated to have OSA versus 9% of women and
26% of men in the 30- to 49-years category. (5)

At present, with an aging population and increasing rates of obesity, the prevalence of OSA is likely to increase.

Numerous factors increase the risk of OSA: (2,9,10)

- Male sex
- Advanced age
- Obesity (about 50% of patients have a BMI> 30kg / m^2, this narrows the pharynx, as does the shortening of one or both jaws)

- Anatomical abnormalities: increased neck circumference, macroglossia, nasal obstruction, and craniofacial abnormalities, tonsillar and adenoidal hypertrophy.
- Alcohol (Precipitates and / or aggravates OSA)
- Tobacco (irritates and inflames UA)
- Drugs (benzodiazepines widely used in anesthesia decrease the tone of the UA)
- Body position (some patients only have OSA in the supine position)
- Other factors to consider are lack of physical exercise, gastroesophageal reflux (favors the collapse of the UA), hypothyroidism and acromegaly.

Importantly, OSA is common in patients who present for surgery, with estimates ranging from the prevalence of the general population to as high as 70% in select populations (eg, bariatric surgical patients). Estimating a real prevalence of OSA in the surgical population of 20%. (3)

Similar to the general population, most patients with OSA remain undiagnosed at the time of surgery.

3.1.4. PHYSIOPATHOLOGY AND COMPLICATIONS

Focusing on obstructive apneas, which are the only ones included in this study.
The pathophysiology of the underlying mechanisms of OSA and its complications is complex, multifactorial and not fully understood.
Stability in the UA caliber depends on the action of the oropharyngeal and abductor dilator muscles, which are normally activated rhythmically during each inhalation. The obstructive apneas are caused by UA closure by "suction" during sleep inspiration as the negative pressure of the inspiratory muscles (diaphragm and the intercostal muscles) exceeds the activity of the dilator muscle of the UA. These muscles have their own tone and are also managed by mechanoreceptors and chemoreceptors. The most important upper airway opener is the genioglossus muscle, which is activates in synchrony with the inspiratory muscles of respiration; it dilates the airway and prevents collapse. (8,11,12)

Factors favoring **collapse include narrowing of the upper airway** (anatomic factor), excessive loss of muscle tone (muscle factor), and defect in protective reflexes (neurological factor). (13,14)

Anatomical Factor:

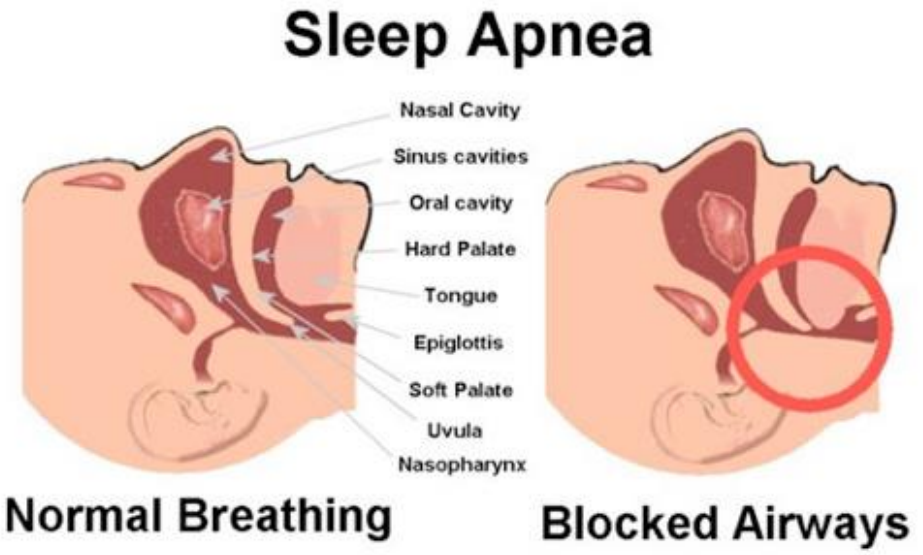
Due to several factors, the caliber of the UA narrows, generating a greater negative pharyngeal pressure during inspiration, this fact predisposes to the collapse of UA. These anatomical factors, in addition, modify the other two (muscular and neurological). One example of is the micrognathia, carries the base of the tongue backwards and this interferes with the muscular efficiency of the genioglossus. Obese individuals also tend to have lower lung volumes, especially lower functional residual capacity because the lungs are more compressed and cannot expand properly, a fact that negatively influences the size of the airway and its narrowing. Likewise, the fatty deposit between the muscle fibers reduces its contractile capacity.

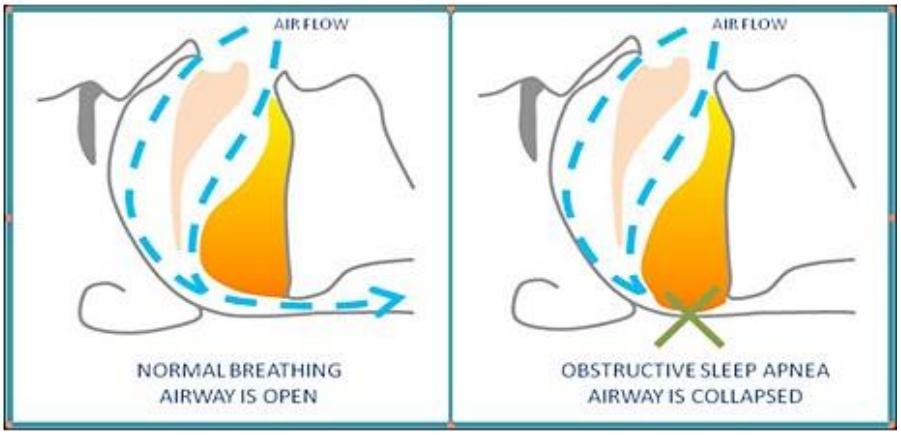
Muscle Factor:

In electromyographic studies has been demonstrated that the dilator muscles reduce or disappear their strength and the activity of the diaphragm is altered very little so leading to a closure of the UA, especially in patients with OSA. The presence of excessive compliance has been clearly demonstrated, which causes this pathway to be more collapsible or to require less negative pressure to do so. Factors of upper respiratory muscle function include abnormal muscle dilator activity and an alteration in the contraction diaphragm-dilator muscles ratio. Defects in the response of this musculature or incoordination between it and the diaphragm may be the cause of OSA.

In recent studies it has been concluded that the dilator muscles in OSA are the target of adaptive, immunohistochemical and metabolic trophic phenomena in response to stimulation. Although there is no evidence that sleep affects neuromuscular activity in OSA, the disappearance of compensatory hyperactivity in wakefulness and the reduced muscle contraction efficacy observed in some patients may explain the greater instability of sleep apnea-hypopnea characteristic of OSA.

These muscles appear to have a histological composition adapted to short contractions, making them more vulnerable to fatigue. In apneic patients, these muscles are continually requested and it has been suggested that they may present muscle injuries due to this overexertion.





Neurological factor:

It has already been pointed out that suppression of pharyngeal muscle activity in sleep is fundamental for OSA to produce a reduction in the UA caliber that makes it more vulnerable to collapse in inspiration. The anatomical factors predispose to apnea. Likewise, changes in the stability of the respiratory control system and the decrease in lung volume in sleep may also play a role. It is important to note that UA remains open during wakefulness and closes only during sleep (especially during the rapid eye movement phase). By extension, even in individuals with a narrowed UA, the disease is ultimately caused by the impact of the brain's sleep mechanisms on the process of control of the pharyngeal muscles, the tone of which is necessary and sufficient to maintain the UA open on waking.

Maintenance of UA efficacy will depend on correct coordination of synchronization and intensity of the inspiratory musculature and upper respiratory tract muscles.

The end result is snoring (which usually begin before the close of the UA), hypopneas or apneas, these snoring are an exaggerated inspiratory efforts to resolve this obstruction and / or hypoxemia cause a transient and usually unconscious awakening of the patient (arousal) that is responsible for the end of apnea. As a result of these repetitive micro-awakenings throughout the night the dream is fragmented and ceases to be reparative. (8,12)

Breathing is primarily controlled by central respiratory pacemakers in the medulla that interact with central and peripheral chemoreceptors. Central chemoreceptors in the medulla, pons, and cerebellum sense the pH of the central nervous system, which corresponds to the level (partial pressure) of carbon dioxide in the blood, whereas peripheral chemoreceptors, mainly in the carotid body, are primarily sensitive to changes in the oxygen concentration (partial pressure of arterial oxygen). The episodes of hypoxemia and hypercapnia sensitize chemoreceptors that increase the sympathetic response, which causes peripheral vasoconstriction. This fact generates a series of long-term effects that cause alterations in cardiovascular function (pulmonary hypertension, systolic-diastolic overload with congestive heart failure, arrhythmias and sudden death). (15)
Increased secretion of catecholamines also increases platelet aggregation favoring thrombotic processes. (11)

OSA has important pathophysiological consequences at level of: (8,9,11,12,16)

- Cardiovascular system: systemic hypertension resistant to treatment (by vasoconstriction caused by hypoxia) (63-83%). Systemic inflammation is also favored, with increased C-reactive protein and cytokines such as IL-6 and TNF-alpha, which results in endothelial dysfunction and atherosclerosis responsible for: congestive heart failure (up to 76%), heart disease Ischemic (38%), atrial fibrillation (49%), and other arrhythmias (58%).
- Metabolic: Diabetes Mellitus type II (36%), hypothyroidism (45%), is closely related to morbid obesity (50-90%).
- Cerebrovascular: cerebrovascular accident (stroke) (71-90%) due to endothelial dysfunction and atherosclerosis.

- Respiratory: the obstruction produces greater negative pleural pressures that increase the afterload, which may appear: pulmonary hypertension (77%), pulmonary edema, asthma (18%).

3.1.5. CLINIC

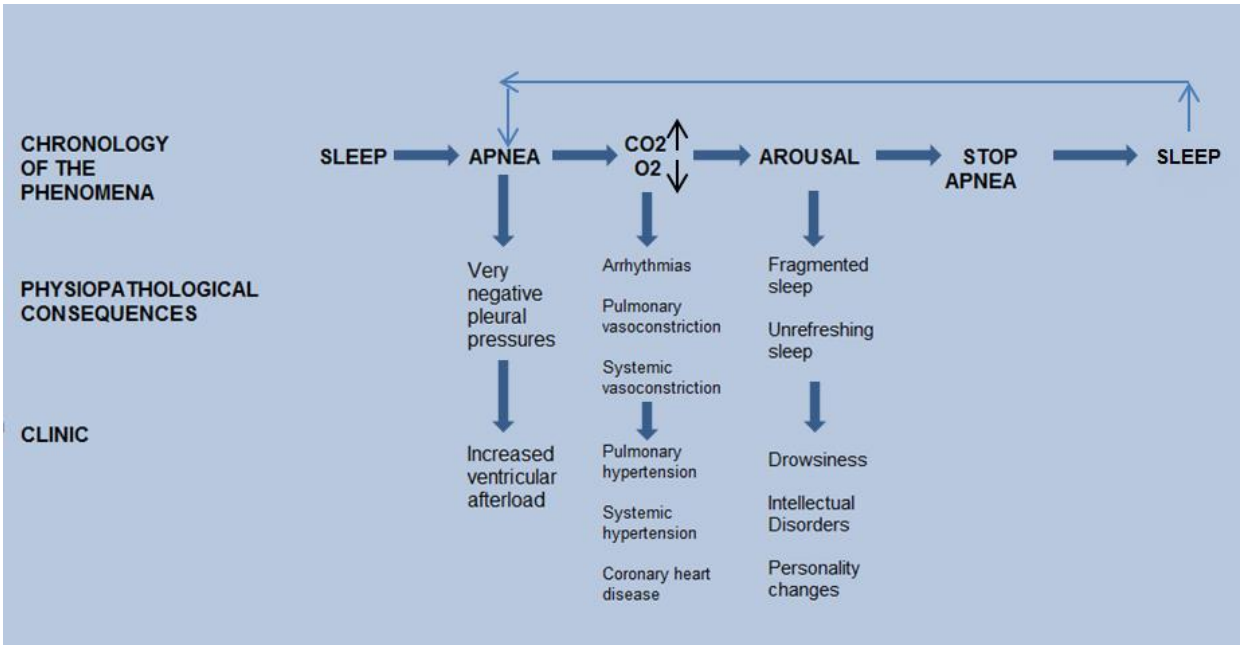
OSA is characterized by repetitive partial or complete collapse of the airway during sleep, which could lead to hypoxemia and/or hypercapnia with associated clinical signs and symptoms:

Daytime symptoms: sleepiness and / or unrepairable sleep sensation, morning headaches, chronic fatigue, dry mouth morning, diaphoresis, irritability, apathy, depression, decreased libido, memory loss, difficulty concentrating and traffic accidents (due to lack of concentration).

Nocturnal symptoms: snoring and witnessed breathing interruptions (apneas), or awakenings because of gasping or choking observed by the person with whom the patient shares bed, abnormal motor activity, enuresis (children) and nicturia (adults), nocturnal sweating, occasional insomnia, restless sleep and gastroesophageal reflux. Frequent awakenings and nightmares are commonly.

OSA is also associated with chronic upper airway inflammatory disorders, including sinusitis, allergic rhinitis, and asthma.

Apart from these symptoms, which can be very intrusive, OSA can lead to adverse health outcomes, including cerebrovascular disease, cardiovascular disorders (eg, hypertension, ischemic heart disease, arrhythmias, pulmonary hypertension, and congestive heart failure), metabolic syndrome, depression, and increased risk of accidents.



3.1.6. DIAGNOSIS

For a correct diagnosis in clinical practice should include: (8,9,12)

3.1.6.1. ANAMNESIS

- Adequate **anamnesis** to the patient and his bed partner. We will ask about the diurnal and nocturnal symptoms of this disorder.

3.1.6.2. PHYSICAL EXAMINATION

The otorhinolaryngological examination is important in a correct evaluation of the patient, although, as in the case of the clinic, the anatomic alteration is not related to the severity of OSA. The anatomical exploration of UA helps to understand the pathophysiology and also to evaluate other therapeutic options, in addition to the application of CPAP. An individualized case study will be achieved and, therefore, a much more correct therapeutic planning. This anatomical exploration may also predict possible future maladaptations to the use of CPAP. In some cases, CPAP compliance problems can reduce compliance.

- The first step is the visual examination of the patient, in which the morphotype (e.g., obesity, short neck) and facial constitution, especially maxillomandibular discordances, bad bites and mandibular alterations will be evaluated.
- Followed by an oral cavity examination, considering the lingual volume in relation to the cavity, the possible presence of tonsil hypertrophy and, finally, the increase of soft palate volume, its position in relation to the posterior wall or the presence of membranes that increase its surface.

  After an anatomical nasal examination with anterior rhinoscopy and nasal endoscopy that can scan both nostrils and rhinopharynx by bucking otorhinolaryngological alterations, the most frequent are septal deviations, polyposis and adenoid hypertrophies and, occasionally, retrognathism.
- Finally it is essential the endoscopic exploration of the UA using flexible endoscope, in order to discover the place of collapse. The problem has always resided in the fact that it is an exploration that is carried out under different conditions from those in which the disease develops (in wakefulness and with the patient sitting).

3.1.6.3. COMPLEMENTARY TEST

- Blood analysis: most of the time it will be normal but we can find polyglobulia or thyroid disorders (the presence of subclinical hypothyroidism (elevated TSH, Thyroid-Stimulating Hormone, with normal T3, triiodothyronine and T4, Thyroxine) is relatively frequent) in advanced disease phases. A metabolic and cardiovascular risk profile (glycaemia and lipids) is also important.

- Electrocardiogram: ask for suspicion of heart disease or high blood pressure.
- Simple chest x-ray: Required only on suspicion of heart or respiratory disease.
- Computed tomography: allows a very accurate evaluation of the UA and has been validated to measure the area of the pharyngeal section. Modern technologies allow for three-dimensional reconstructions, virtual images and dynamic studies. It has been observed that the UA has a smaller diameter in patients with OSA and the most important changes are the lateral diameters. The VAS is more distensible in patients with OSA than in the healthy ones.
- Magnetic resonance imaging: provides, like Computed Tomography, a three-dimensional image of UA. In addition, it gives us an idea not only of the fatty

tissue content, but also of the aqueous content. It has been shown that fatty contents are increased in patients with OSA and that they are located laterally. It has also been observed that the volume of fat around the pharynx correlates with the severity of OSA (apnea / hypopnea index).

- **Full polysomnographic study** is the gold standard test for OSA diagnosis (with registration of respiratory and neurophysiological signals during sleep). Polysomnography yields the apnea-hypopnea index (AHI) score (an index of sleep apnea severity), and an AHI score greater than 5/h indicates the presence of OSA. The AHI score is the basis of the ASA rating of OSA severity as mild (AHI, 6–20/h), moderate (AHI, 21–40/h), and severe (AHI, ≥41/h). Of note, the AHI score of the American Academy of Sleep Medicine Task Force differs slightly from the one published by ASA: no OSA (AHI, ≤4/h), mild OSA (AHI, 5–15/h), moderate OSA (AHI, 16–30/h), and severe OSA (AHI, ≥31/h) by ASA classification.

  The overnight polysomnography is a limited and expensive access study, it is not possible to use it in all cases, therefore it is also accepted the registration of respiratory profiles and oxygenation at night (without neurophysiological record) or, the simplest of all, nocturnal oximetry that analyzes oxyhemoglobin saturation continuously. The overnight oximetry has been proposed as an OSA screening tool, with overnight oxygen desaturation index (ODI) scores greater than 10 desaturations per hour resulting in 93% sensitivity and 75% specificity to detect moderate-to-severe OSA. Its disadvantage is that, in patients for whom there is a high index of suspicion, a negative oximetry reading still needs confirmatory polysomnography.

3.1.7. TREATMENT

The two basic pillars of this disease are: (8,12)

- Hygienic-dietary measures of sleep: to sleep sufficient hours with a regular schedule, alcoholic and tobacco abstinence, weight loss, treatment of nasal obstruction, to avoid supine position, suppressing central nervous system depressant drugs, physical exercise and treatment of gastroesophageal reflux if there is one.
- **CPAP**: Continuous positive airway pressure. CPAP pumps air under pressure into the respiratory tract of the lungs, keeping the trachea open during sleep.

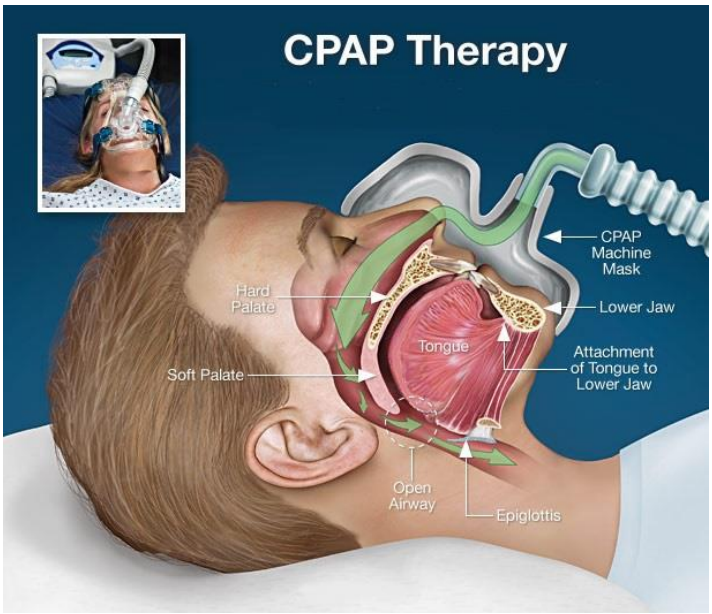
Forced air that is infused through CPAP prevents episodes of airway collapse that block respiration in people with obstructive sleep apnea and other respiratory problems. Its application through a nasal mask a positive pressure of 5-20 mmHg that is transmitted to the pharynx and prevents its collapse, improving symptoms, sleepiness, ability to drive vehicles, cognitive functions, mood, quality of life. (17)

CPAP is not a curative treatment. The main disadvantage is that it is uncomfortable for the patient and requires training time.

The mains indications of treatment are: (8,12)

- Patients with AHI> 30 with symptoms of OSA or notorious cardiovascular disease. Hygienic-dietary measures + CPAP.
- Patients with AHI between 10-30 and symptoms clearly secondary to OSA. Hygienic-dietary measures +/- CPAP.
- Patients with AHI> 30 without symptoms and without cardiovascular disease: Hygienic-dietary measures and reevaluation.

(ANNEX 3- INFORMATION ABOUT CPAP)



- Other options for selected cases are: maxillofacial surgery, otorhinolaryngology and prosthetics.

3.2. PREOPERATIVE SCREENING OSA

The high prevalence of undiagnosed OSA and its peri-surgical complications requires a reliable, efficient, and easily used screening test to make an early diagnosis and treatment. The overnight polysomnography is the gold standard test for diagnosis, but is very expensive and limited accessibility.

Various screening tools of easily assessed clinical signs and symptoms have been used to identify patients at high risk for OSA. All these screening questionnaire are used to screen OSA in surgical patients.

The Epworth Sleepiness Scale is a simple questionnaire that quantifies daytime sleepiness, a common symptom of OSA. Correlation of the Epworth Sleepiness Scale scores with OSA continues to be controversial.

The Berlin Questionnaire queries the history of snoring, excessive daily sleepiness, hypertension and takes into account demographic and anthropometric variables. It has positive and negative predictive values of 77.9 and 44.9% for OSA and 31.5 and 92.8% for severe OSA, respectively.

The STOP (snoring, tiredness, observed apneas, high blood pressure) and the STOP-BANG questionnaire includes for a total eight dichotomous (yes/no) questions related to the clinical features of sleep apnea (**S**noring, **T**iredness, **O**bserved apneas, high blood **P**ressure, **B**MI >35 kg/m2, **A**ge >50 years, **N**eck circumference >40 cm, and male **G**ender). For each question, answering “yes” scores 1, a “no” response scores 0, and the total score ranges from 0 to 8. The probability of moderate to severe OSA increases in direct proportion to the STOP-Bang score: score of ≥ 2 positives for STOP or ≥ 3 positives for STOP-BANG indicating high risk of OSA. (18,19)

The STOP-Bang questionnaire can be completed quickly and easily (usually within 1-2 min) and overall response rates are typically high (90-100%). The questionnaire has demonstrated a high sensitivity using a cutoff score of ≥ 3: 84% in detecting any sleep apnea (AHI > 5 events/h), 93% in detecting moderate to severe sleep apnea (AHI > 15 events/h), and 100% in detecting severe sleep apnea (AHI > 30 events/h). (18,20)

Corresponding specificities were 56.4%, 43%, and 37%. Scores and negative predictive values are 90% and 100%.

The 2006 ASA practice guidelines propose a 14-item screening tool that assesses OSA predisposing physical characteristics, signs of airway obstruction during sleep,

and somnolence. This tool has positive and negative predictive values of 72.1 and 38.2% for OSA and 27.9 and 90.9% for severe OSA, respectively.

Compared with polysomnography they still have low specificities and moderate predictive values, thus a negative result from these tools does not exclude the possibility of OSA.

Screening Techniques for Obstructive Sleep Apnea in Adults (3)

Variables	Berlin Questionnaire	ASA Checklist	STOP Questionnaire	STOP-Bang Questionnaire	Nocturnal Oximetry
Validation	Perioperative setting	Perioperative setting	Perioperative setting	Perioperative setting	Perioperative setting
Items (n)	10	14	4	8	—
High risk of OSA	Score ≥2 categories	Score ≥2 categories	Positive score ≥2	Positive score ≥3	ODI >10
			AHI ≥15		
Sensitivity (%)	78.6 (67.1–87.5)	78.6 (67.1–87.5)	74.3 (62.4–84.0)	92.9 (84.1–97.6)	93.3 (89.7–97.0)
Specificity (%)	50.5 (40.6–62.3)	37.4 (28.2–47.3)	53.3 (43.4–63.0)	43.0 (33.5–52.9)	74.6 (69.6–79.6)
			AHI ≥30		
Sensitivity (%)	87.2 (72.6–95.7)	87.2 (72.6–95.7)	79.5 (63.5–90.7)	100 (91.0–100.0)	100 (100–100)
Specificity (%)	46.4 (37.9–55.1)	36.2 (28.2–44.8)	48.6 (40.0–63.0)	37.0 (28.9–45.6)	58.6 (53.7–63.4)

Data are presented as mean percentage (95% confidence interval)

AHI, Apnea-Hypopnea Index; ASA, American Society of Anesthesiologists; OSA, obstructive sleep apnea; ODI, Oxygen Desaturation.

(ANNEX 2- STOP-Bang scale)

Because of its ease of use, efficiency and high sensitivity, the STOP-Bang questionnaire has been widely adopted and validated in various populations and medical conditions especially in surgical patients. (18)

3.3. PERIOPERATIVE COMPLICATIONS IN OSA PATIENTS

The perioperative period is a particularly dangerous time for patients with OSA.

General anesthetics, narcotics, and sedatives can worsen airway obstruction by enhancing upper airway muscle relaxation, reducing ventilation, and blunting arousal from sleep. Narcotics depress both the central response to hypercapnia and the peripheral response to hypoxia: at low doses they primarily decrease tidal volume; at higher doses they decrease the respiratory rate.

Changes in rapid eye movement (REM) sleep during the postoperative period can also put a patient with OSA at risk. Pain and postanesthetic effects can reduce REM sleep, which is followed by a rebound increase in REM sleep 3 to 5 days after surgery. This REM rebound can worsen OSA because REM sleep is normally accompanied by unstable breathing, worsening of airway muscle tone, and a decrease in the arousal response to hypoxia, hypercapnia, and airway occlusion. Adult and pediatric patients with OSA have been found to be highly sensitive to narcotics. (3,21)

Numerous studies have demonstrated that surgical patients with OSA pose a significant clinical challenge to health-care professionals because of OSA's associations with several comorbidities, including hypoxemia, aspiration pneumonia, pulmonary embolism, atelectasis, difficult intubation, increased emergent postoperative endotracheal intubation, need for postoperative ventilation, cardiovascular disease, heart failure, arrhythmias, hypertension, stroke, metabolic syndrome and unanticipated admission to the ICU. During the perioperative period, sleep is disrupted and the severity of sleep-disordered breathing is increased postoperatively in surgical patients with OSA. (2,21)

- Gupta et al. have shown an increased risk of postoperative complications (39% vs 18%), higher rate of transfer to ICU (24% vs 9%), and increased length of hospital stay in patients with obstructive sleep apnea compared with control subjects matched for age, sex, and body mass index (BMI). They also

demonstrated that OSA treated with CPAP decreased their complications and days of hospital stay. (22)

- Similarly, in another's case-control study, Liao et al. (23) and Memtsoudis et al. (7) also noted the same.
- In the same way, it was observed that patients at high risk of OSA (by the STOP-Bang questionnaire) had a higher rate of postoperative pulmonary and cardiac complications, as well as a longer hospital stay than those at low risk of OSA (19,6% vs 1,3%). (2)
- Hwang et al. Demonstrated, in a sample of 172 patients, that "Patients with an ODI 4% ≥ 5/h had a significantly higher rate of postoperative complications than those with ODI 4% < 5/h (15.4% vs 2.7%). Interestingly, the rate of postoperative complications increased with increasing ODI severity. Patients with an ODI 4% of 5-15 had a 13.8% incidence of complications, compared to 17.5% of those with an ODI 4% > 15." (ODI: Oxygen desaturation index ≥ 4%, calculated by nocturnal oximetry at the home before elective surgery) (24)

(ANNEX 1- STUDIES REPORTING)

OSA is affected by the surgical process in several points related with anesthesia and the surgery:

- General anesthesia decreases the activity of the UA dilating muscles (genioglossus muscle) in a dose-dependent manner, this favors collapse and obstruction of the UA. (25,26)
- Anesthetics decrease the "arousal" response that is a protective factor of apneas because it is responsible for finalizing them.
- Anesthetics, opioids, hypnotics and benzodiazepines decrease ventilation-minute because they alter the sensitivity to CO2 of chemoreceptors at the carotid bodies and by general depression of respiratory centers in the central nervous system. It depends on sex (seems to affect only women) and race. (27,28)
- General anesthesia is associated with significant alteration in pulmonary function and gas handling.

  Induction of anesthesia causes an immediate significant reduction in functional residual capacity of 16-20% in supine position. The reduction in functional residual capacity is correlated with age and chest wall elastance. It results in

airway closure, reduce lung compliance, and ventilation perfusion mismatch. The shape of the chest cavity changes because there is cephalic displacement of the diaphragm. This cause partial collapse of lung segments or atelectasis, which occurs in 90% of anesthetized patients. Loss of functional residual capacity, lung recruitment, airway closure, and airway obstruction predispose patients to hypoxemia. (28)

- The stress of surgery, pain and drugs to alleviate that pain favor increased synthesis of inflammatory substances such as cortisol, TNF-alpha, IL-6, IL-1, which decrease REM sleep on days 1 and 2 after surgery. After the first two days of surgery, a "REM sleep rebound" during recovery nights 3 to 5 increases the likelihood of hypoxemia and other complications. (29–31)
- The risk of complications also depends on the type of surgery and the duration of the surgery, with the risk of abdominal and cardiac surgeries. (2)

As a consequence of these alterations, the presence of OSA was significantly associated with: (2)

- Higher odds of desaturation: In a group of 1764 patients with OSA 189 desaturated (10.71%) versus a group of 1881 patients without OSA where only 105 desaturated (5.58%); OR 2.27, 95% CI 1.20-4.26, P=0.01. (21)
- Greater ICU transfer: In a group of 2062 patients with OSA 105 were transferred to the ICU (5.09%) versus a group of 3681 patients without OSA where only 58 were transferred to the ICU (1.57%); OR 2.81, 95% CI 1.46-5.43, P=0.002. (21)
- Postoperative acute respiratory failure (ARF) was more frequent in patients with OSA compared with those without OSA although there was a significant variation in the reporting of ARF between studies: In a group of 1680 patients with OSA 33 had a ARF (1.96%) versus other group of 3421 patients without OSA which only 24 had ARF (0.70%); OR 2.43, 95% CI 1.34-4.39, P=0.003. (21)
- Higher length of stay.
- Difficult intubation.
- Prolonged orotracheal tubing (need for orotracheal tubing for more than 48 hours).

- Prolonged mechanical ventilation (need for mechanical ventilation for more than 48 hours for the treatment of acute respiratory failure).
- Difficult extubation, because a situation of laryngeal edema and laryngospasm occurs when the endotracheal tube is removed in these patients. To minimize its appearance has been recommended to extubate the patient when fully awake and with the maximum possible elevation of the head.(18,32)
- Increased sensitivity to opioids and postoperative upper airway obstruction.

3.4 PERIOPERATIVE MANAGEMENT OF PATIENTS WITH HIGH RISK OF OSA

Recently, the increase in postoperative pulmonary complications due to the high prevalence of OSA and its importance for anesthesiologists and surgeons have led the European Society of Anesthesiology and the American Society of Anesthesiology to initiate clinical studies aimed at establishing peri-surgical management strategies in these patients. The lack of evidence behind the guideline recommendations and the significant cost of guideline implementation have created a dilemma between potentially improved postoperative adverse events and increased health-care resource utilization. (2,3,11,33,34)

A. **Preoperative Preparation**: Adequate identification of patients at high risk of OSA through:
   - Detailed anamnesis to him and his family: history of airway difficulty with previous anesthetics, hypertension, or other cardiovascular problems, and other congenital or acquired medical conditions.
   - Physical examination: should include an evaluation of the airway, nasopharyngeal characteristics, neck circumference, tonsil size, and tongue volume.
   - The use of screening questionnaires such as the STOP-Bang.

   This evaluation may be initiated in a preanesthesia clinic (if available), always a few weeks before surgery.

B. **Intraoperative Preparation**: include:
   - Choice of anesthesia technique (general anesthesia with a secure airway is preferable to deep sedation without a secure airway, it is preferred the use of regional anesthesia when will be possible).

- Airway management (patients previously treated with CPAP or an oral appliance, consider using these modalities during sedation).
- Patient monitoring (ventilation should be continuously monitored by capnography or another automated method if feasible because of the increased risk of undetected airway obstruction in these patients).

C. **Postoperative Preparation**:

- Postoperative analgesia (reduces or eliminates the use of systemic opioids).
- Oxygenation (the use of lonely oxygen should be discouraged as it inhibits the stimulation of hypoxemia on the respiratory centers and this causes a decrease in the protective micro-awakenings, and could aggravate CO2 retention; its prefers initiation of nasal CPAP or noninvasive positive pressure ventilation and if the patient was already using CPAP at home put him in the hospital as well).
- Patient positioning (avoid if possible the supine position).
- Monitoring (In the critical care unit, by telemetry or by properly trained personnel during the period of time the patient is most at risk (first week after surgery) and must be continuous).

3.5. EFFECTS OF CPAP ON POSTOPERATIVE OUTCOMES IN SURGICAL PATIENTS WITH HIGH RISK OF OSA

Nasal application of CPAP is the most widely used treatment for OSA because of its efficacy and low level of invasiveness. CPAP acts as a pneumatic splint to prevent occlusion of the airway during sleep, thereby significantly reducing apneas and hypopneas and the associated hypoxic and hypercapnic events. CPAP has

been shown unequivocally to alleviate the symptoms of OSA including: amelioration of excessive daytime sleepiness, restoration of quality of life, improvement in vigilance, concentration and memory, lessening of fatigue, reduction in health care usage, and a decrease in traffic accidents.

The efficacy of CPAP has not been established in the perioperative setting. There is insufficient evidence from the literature to evaluate whether the perioperative use of CPAP may reduce adverse events in OSA patients undergoing surgery. It is not known whether CPAP can reduce the risk of perioperative cardiorespiratory events in OSA patients when the upper airway is further compromised by sedation, anesthesia or

analgesia. There are no randomized controlled studies that specifically address this issue. The following is a summary of the possible potential beneficial effects of CPAP in OSA patients undergoing surgery.

Acute effect of CPAP on Hemodynamics: In general, acute elevation in arterial blood pressure is a common adverse event in OSA patients. The efficacy of long-term CPAP treatment in reducing arterial blood pressure in OSA patient's not undergoing surgery has been demonstrated. Acute CPAP use for 1–3 days in nonsurgical OSA patients with hypertension can lead to a reduction of arterial blood pressure (systolic blood pressure from 125 ± 15 mm Hg to 120 ± 10 mm Hg, diastolic pressure from 86 ± 16 mm Hg to 83 ± 12 mm Hg). However, there is no available evidence from randomized controlled studies.

With regards to cardiac rhythm abnormalities, CPAP treatment reduces the number of apnea associated cardiac arrhythmias and the beneficial effects of CPAP on sinus arrest and episodes of heart block during sleep have been reported. In a study of 17 patients, CPAP treatment reduced the number of arrhythmias from 1575 to 165 episodes per night ($P < 0.01$).These studies provide preliminary support for the use of CPAP for perioperative cardiac rhythm abnormalities among OSA surgical patients. (35)

CPAP has been shown to improve cardiac function with long-term use but evidence of a beneficial cardiovascular effect with short-term CPAP use is required. A favorable hemodynamic effect within a few minutes of application suggests a potential role for postoperative CPAP.

Acute effect of CPAP on respiratory function: There are studies have shown that perioperative use of CPAP leads to a reduction in the rate of postoperative pulmonary complications. In 200 patients who developed hypoxemia immediately after undergoing major abdominal surgery, the use of postoperative CPAP at 7.5 cm H2O plus supplemental oxygen using a helmet interface led to a reduction in the incidence of endotracheal intubation, pneumonia, infection, and sepsis when compared with supplemental oxygen alone. (38)

In summary, well-designed research studies on the postoperative effect of CPAP in OSA surgical patients are lacking.

4. JUSTIFICATION OF STUDY

The prevalence of OSA in surgical population is higher than in the general population, 22-41% compared to 13-6% respectively. Although a prevalence of OSA of 22-41% is estimated in the surgical population only one of five this patients are diagnosed and very few of these patients are receiving treatments. (3)

Despite advances in anesthesia and surgery this patients with OSA suffered a lot of adverse postoperative events. Many studies have been demonstrated that patients with OSA undergoing elective surgery under general anesthesia have a higher risk of respiratory complications (2,5,15,16), which increases the morbimortality of the patient and health costs for the greater number of days in the hospital, as well as the resources used for its recovery. (22–24,36,37)

There are many strategies and different treatment for to decrease the risk of postoperative complications. Among the different treatment to improve the respiratory function is CPAP, it is highly effective in controlling symptoms of OSA in general population. Reducing nocturnal events and improving day sleepiness cognitive function and decrease arterial blood pressure.

The current lack of scientific evidence makes no agreement between the different studies on the effectiveness of postoperative CPAP in reducing the risk of postoperative respiratory events in OSA patients undergoing major surgery. (10,33,37,38)

This study is important because it aims to be demonstrating the benefit of the use of CPAP after surgery with general anesthesia in the reduction of desaturation events and improve oxygenation in the surgical patients with OSA. The reduction in the desaturation events are important to avoid futures respiratory complications and perhaps the reduce time hospitalization.

Actually no data are available to evaluate the impact of preoperative OSA screening and corresponding perioperative care measures on perioperative outcomes.

For to screening the patients we will use the STOP-Bang scale because is a sensitive, easy, cheap, fast and sensitive, to stratify the risk of OSA in patients undergoing laparoscopic abdominal major surgery under general anesthesia. This screening, which

is currently not done in pre-anesthetic consultations of Josep Trueta University Hospital, is important in two aspects:

1. It allows us to know a more accurate value of the prevalence of OSA. Given all patients undergoing surgery would not be able to perform a Polysomnography (gold standard technique for diagnosis) because we would saturate the Sleep´s Units, patients with a high risk of OSA in this screening (STOP-Bang result> 5) would be candidates for polysomnography after surgery.

2. Knowing that it is a patient with a high risk of OSA alerts us and makes us take greater care with this patient during the perioperative process in order to avoid possible respiratory complications.

In brief, the aim this trial is to demonstrate that effective OSA screening in the preoperative period may be important to reduce futures complications in the postoperative in regarding we applied a strategies such as CPAP during in the early hours after surgery.

5. QUESTION, HYPOTHESIS AND OBJECTIVES

5.1. QUESTION:

Can the use of postoperative CPAP in patients at high risk of OSA reduce desaturation episodes after elective laparoscopic abdominal major surgery under general anesthesia?

5.2. HYPOTHESIS:

Primary Hypothesis:

- Using CPAP 24 hours after elective laparoscopic abdominal major surgery under general anesthesia reduce episodes of early desaturation compared to current management.
  Since hemoglobin desaturation is a possible predictor of subsequent pulmonary complications such as pulmonary hypertension, atelectasis and acute respiratory failure.

Secondary Hypothesis:

- Given OSA is being underdiagnosed, to determine a more accurate prevalence of OSA using the STOP-Bang scale for screening in surgical patients, bringing the prevalence of OSA to a more real value and decreasing the number of undiagnosed cases.
- Using postoperative CPAP, in patients at high risk for OSA undergoing elective laparoscopic abdominal major surgery under general anesthesia, we can reduce the length of hospital stay.

5.3. OBJECTIVES:

Main Objective:

- To evaluate the efficacy of CPAP in the first day after major elective surgery with general anesthesia compared with oxygen therapy with mask in patients with high risk of OSA to prevent the occurrence of hemoglobin desaturations.

To observe later if decreasing the number of hemoglobin desaturations also decreases the incidence of respiratory complications.

Secondary objectives:

- To determine a more real incidence than the current OSA in surgical patients by means of the STOP-Bang scale (and subsequent confirmation with polysomnography in patients at high risk).
- To evaluate the efficacy of CPAP in patients with high risk of OSA undergoing elective surgery with general anesthesia to reduce the length of hospital stay compared to current management.

6. MATERIALS AND METHODS

6.1. STUDY DESIGN

This project will be an early prospective, single center, randomized, single blind (results analyzer), parallel-group trial that compare use of CPAP versus non-use of CPAP, in patients with high risk of OSA undergoing laparoscopic abdominal major surgery.

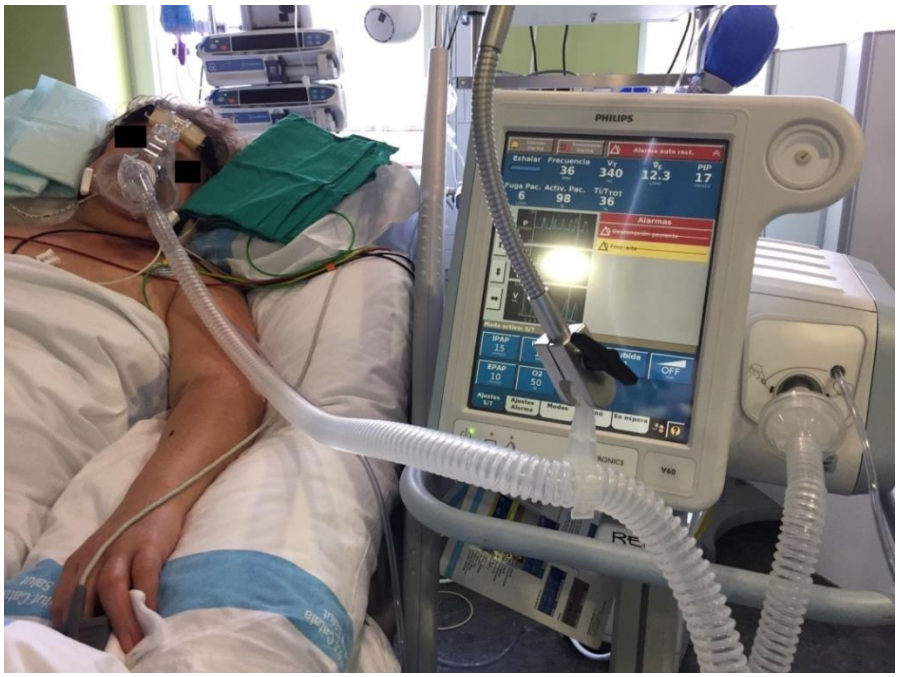
The patients will be randomly divided in two groups (1:1 ratio), the randomization will be performed with a randomized electronic procedure.

The first group, **CPAP group**, will use CPAP with 50% oxygen or FiO2 (fraction of inspired oxygen) at 0.5 and PEEP 8-10 cm H2O during 24 hours after surgery and then, they will receive ventimask (oxygen concentration of 50%) during 24 more hours. **(ANNEX 3 – CPAP)**

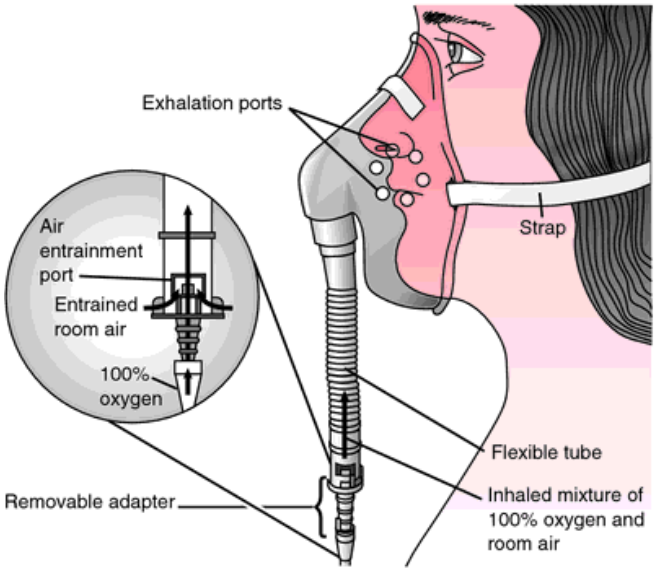
The second group, **non-CPAP group**, will receive oxygen therapy with ventimask at a concentration of 50% oxygen during 48 hours after surgery. **(ANNEX 4 –Ventimask)**

Both groups will be submitted to the same techniques of respiratory physiotherapy before and after surgery.

For the monitoring of the two groups, will be performed a strict oxygen control with pulse-oximeter during the first 48 hours after surgery (accepting as desaturation the level of oxygen under 92%) to try to avoid a bias.



CPAP



VENTIMASK

This will be a simple blind trial: patients and the medical professional that will perform the procedure will be aware of the type of treatment they will be receiving. In order to reduce the bias of the simple blind trial, the statistical consultants will not have access to this information.

This study will be carried out in a single center, the Josep Trueta University Hospital of Girona (it is a third level hospital), specifically in the anesthesia department.

6.2. STUDY POPULATION

The patients of the study would be men and women up to 18 years old that they are going to undergo laparoscopic abdominal major surgery. During the surgery, both groups will receive general anesthesia.

The estimated time of recruitment is 2 years. They will be recruited when they visit the pre-anesthetic consultation before surgery and complete all the following inclusion and exclusion criteria. After signing the informed consent and join the trial, patients will be randomly assigned to 1 of 2 groups:

- Group I, CPAP group: CPAP with an oxygen concentration of 50% and PEEP of 8-10 cm H2O.
- Group II, non-CPAP group or control group, which receive oxygen to 50% of concentration with a ventimask.

The duration of both interventions is 48 hours.

6.2.1. INCLUSION CRITERIA:

All individuals must meet all of the inclusion criteria in order to be eligible to participate in the study.

- Male or female, aged between 18-80 years of age.
- Provision of signed and dated informed consent form.
- Patients with a high risk of OSA by the STOP-Bang scale. (Score > 5 in the STOP-Bang scale).
- Laparoscopic major abdominal programmed surgery.

6.2.2. EXCLUSION CRITERIA:

An individual who meets any of the following criteria will be excluded from participation in this study:

- Minor, thoracic, or cardiac surgery.
- Emergency surgery.
- ASA IV patient´s or unstable disease at the time of surgery.
- Active respiratory process at the time of surgery.
- Patients with chronic renal failure.
- Pregnancy or lactation.
- Laparotomy major abdominal programmed surgery.
- Surgery time greater than 6 hours.
- Known allergic reactions to drugs used in anesthesia / analgesia.
- Exercise tolerance less than 4 in metabolic equivalents, METS.
- Need for blood transfusion during surgery.
- Patient carrying a nasogastric tube at the time of surgery.
- Procedures in which only local or peripheral nerve anesthesia was used.
- Outpatient procedures, defined as those requiring less than a 1-day stay for a patient alive at discharge.

6.2.3. PARTICIPANT WITHDRAWAL OR TERMINATION

REASONS FOR WITHDRAWAL OR TERMINATION

- Patient withdrawal criteria: Participants are free to withdraw from participation in the study at any time upon request. Patient withdrawal from

this study is not expected to be excessive because of the short duration of the study and the interventions are not very harmful.

- Protocol withdrawal criteria:

An investigator may terminate participation in the study if:

- Any clinical adverse event, laboratory abnormality, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant, (eg, onset of more episodes of hypoxia, onset of complications such as pneumotorax, etc.).
- The participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.
- The protocol requirements are not met, for example that he does not tolerate CPAP and uses it less than 18 hours.

HANDLING OF PARTICIPANT WITHDRAWALS OR TERMINATION

In this trial, many patients are not expected to be lost or withdrawn because it is a very short study (of only two days) and the use of CPAP is quite tolerable.

Patients withdrawn from the study will not be replaced; it is assumed that 10% of patients will be withdrawn.

6.3. SAMPLE

6.3.1. STRATEGIES FOR RECRUITMENT

Patients will be recruited at the department of ambulatory pre-anesthesia in the Josep Trueta University Hospital of Girona, where:

- Patients undergoing laparoscopic major abdominal surgery under general will first be identified.

- The 8 questions of the STOP-Bang scale will be performed and the risk of having OSA will be stratified. Only patients with a STOP-Bang value> 5, who are considered to be at high risk, will be chosen.

Patients were recruited until a sample of 682 patients (non-probabilistic method) was obtained, 341 for the CPAP group, and 341 for the non-CPAP group (probabilistic method).

6.3.2. SAMPLE SIZE

Sample size calculations were performed using power calculator GRANMO.

Accepting an alpha risk of 0.05 (i.e., significant a P< 0.005), and a beta risk of 0.2 in a two-sided test, 341 subjects are necessary in first group (CPAP group) and 341 in the second (non-CPAP group) to find as statistically significant a proportion difference, expected to be of 0.1071 in group 1 and 0.05 in group 2, with a reason between the samples equal 1. It has been anticipated a drop-out rate of 1% so it is a very short trial in time and little harmful to the patient. We use the ARCSINUS approximation.

So, the total amount of participants needed for the study is 682.

An Information sheet **(ANNEX 8)** for participants of the project will be given to the candidate and if the patient agrees with it, he or she will sign the informed consent form **(ANNEX 9)** and informed consent to anesthesia **(ANNEX 10).**

We estimate a relative risk of 0.55 according to the results of previous studies in patients with OSA. According to a metaanalysis published in British Journal of Anaesthesia in 2012: OSA was significantly associated with higher odds of desaturation: of 1764 patients with OSA, 189 desaturated (10.71%) versus 1881 patients without OSA, where they only desaturated 105 (5.58%); OR 2.27, 95% CI 1.20–4.26, P=0.01. It is also important the ICU transfer, of 2062 patients with OSA, 105 were transferred to UCI (5.09%) versus 3681 patients without OSA, where they only were transferred to UCI 58 (1.57%); OR 2.81, 95% CI 1.46–5.43, P=0.002. **(21)**

We expect similar results in high risk of OSAS patients. Subgroup analyses had similar conclusions as main analyses.

6.3.3. ESTIMATED TIME OF RECRUITMENT

No data have been published on the actual incidence of OSA undergoing major laparoscopic abdominal surgery. But using the statistics collected by the Josep Trueta University Hospital of Girona, where the number of all surgical procedures (stratified by type of surgery (urgent or programmed surgery) and anesthesia) is collected and

estimating that 20% of the surgical population is OSA, we have established a time of sample recruitment. (2,3)

(ANNEX 12 – TABLE WITH NUMBER OF SURGERIES PERFORMED ANNUALLY IN THE TRUETA HOSPITAL)

If we want to study a total of 682 patients at high risk for OSA, we have to design a unicentric study and in approximately 2 years we can obtain this number of patients. This is a non-probabilistic, consecutive and competitive sampling. The center will apply the inclusion criteria of subjects until the estimated sample size is completed. Patients will go to the outpatient clinic of Anesthesiology of the Josep Trueta University Hospital as they would normally and there would be applied the screening with the STOP-Bang scale.

An information sheet **(ANNEX 8)** will be provided for project participants and if the patient agrees with it, they will sign the informed consent form **(ANNEX 9)** and informed consent to anesthesia **(ANNEX 10).**

6.3.4. MEASURES TO MINIMIZE BIAS

ENRROLLMENT AND RANDOMIZATION PROCEDURES

All patients who will undergo major non-emergency laparoscopic abdominal surgery under general anesthesia who have a STOP-Bang score greater than 5 (high risk of OSAS) admitted to the outpatient clinic of Anesthesia of the Josep Trueta University Hospital, who meet the criteria for entering the study, who, after having been well informed (patient information sheet, (**ANNEX 8**) will accept the informed consent (**ANNEX 9**) and the informed consent to anesthesia (**ANNEX 10**), and they had learned to make a correct respiratory physiotherapy, will be eligible for the clinical trial.

The statistician builds a randomization sequence using statistical software (SPSS).

They will be included in one of the following 2 groups:

- CPAP group: with oxygen to 50% of concentration and PEEP of 8-10 cmH2O.
- Non-CPAP group: with a ventimask with oxygen to 50% of concentration.

This will provide a probabilistic sampling, a simple random sampling. From each patient we will obtain a code that will provide the semicritical care unit and the nursing team

responsible for the care and surveillance of these patients. This code will allow you to know in which group each patient is assigned, so that the treatment equipment can be properly prepared.

Assignments will be known by the investigation/treatment team as it is an open-trial but nobody in the team will have decided in which approach the patient should have been included. The only one who is blinded to the randomization assignment will be responsible for analyzing the data collected (specialist statistician).

It is correct to perform it as an open clinical trial because we are comparing very similar treatments for patients in whom no treatment or monitoring is currently applied (we are only including new perioperative management guidelines in patients with suspected disease, the disease is not confirmed).

6.4. VARIABLES

6.4.1. INDEPENDENT:

- The use of **Continuous Positive Airway Pressure (CPAP)**.

Independent variable will be the use of CPAP or ventimask during 48 hours after laparoscopic abdominal major surgery under general anesthesia. We will consider this variable as a dichotomous nominal qualitative one (yes or no), differentiating between patients who have received CPAP or ventimask.

- ACQUISITION: Will be used the equipment of CPAP available in the service of Rehabilitation of the Josep Trueta University Hospital, as well as the oxygen masks that will be used in the control group. This service is also equipped with the pulse oximeters with which we will control the hemoglobin saturation.
- ADMINISTRATION AND DURATION OF THERAPY: The first group, **CPAP group**, will be used CPAP (nasal-buccal mask) with 50% oxygen concentration or FiO2 (fraction of inspired oxygen) at 0.5 and PEEP 8-10 cm H2O during 24 hours after surgery.

  The second group, **non-CPAP group**, will receive oxygen therapy with ventimask (nasal-buccal mask) at a concentration of 50% oxygen during the same 24 hours after surgery.

  Both techniques will be initiated at most 30 minutes after extubation in the postanesthesia care unit via noninvasive ventilators.

After the first 24 hours after surgery, both groups will remain 24 more hours with Ventimask and continuous monitoring with pulsi-oximeter.

Both groups will be submitted to the same techniques of respiratory physiotherapy before and after surgery.

- TRACKING OF ADHERENCE: The follow-up of these patients will be performed through continuous supervision of the nursing staff in charge of this study and the continuous monitoring of oxygen saturation of the hemoglobin by a pulse-oximeter that both groups carry during the 48 hours after the surgery.
- ADVERSE EFFECTS:

- Bad adaptation to the machine: to avoid it, the patient is taught to use the machine before surgery. If during the trial the patient is unable to tolerate CPAP as minimum 18 hours, he/she will be withdrawn from the study.
- Dryness in the mouth can be caused by CPAP itself or breathing through the mouth at night. A CPAP machine that has a thermal humidifier can help alleviate this side effect.
- Allergies and irritation of the skin by the CPAP mask is one of the side effects of the treatment. CPAP masks can cause skin allergies or skin irritation. If this happens, try to look for another type of mask if it is not possible to remove the mask to the patient.

6.4.2. DEPENDENT:

6.4.2.1. Primary dependent variable:

- The **incidence of desaturation.**

Description: The diagnosis of desaturation will be done with the pulse oximeter, considerer as desaturation a saturation of hemoglobin ≤ 94%.

It will be measured as a dichotomous nominal qualitative variable (yes or no).

To evaluate the efficacy of our first objective, we will keep the patients belonging to both groups with a pulse oximeter 48 hours after surgery and note the number of times they desaturate (considering desaturation as a decrease in hemoglobin saturation ≤ 94%).

It is important to register the number of desaturation because they can be predictors of the future respiratory complications that appear in the patients with high risk of OSA, the greater the number of desaturations the greater the risk of hypoxemia, metabolic

changes, development of pulmonary hypertension and ischemic cardiac and cerebral events. (14, 29)

6.4.2.2. Secondary dependent variable:

- **Severity and duration of the desaturations**.

Description: Controlled with the pulse oximeter.

It will be measure as a discrete quantitative variable (% desaturated hemoglobin).

We will also collect the duration of each desaturation expressed in seconds of time.

- The **prevalence of high risk of OSA in surgery patients**.

Description: The diagnosis of high risk of OSA will be done with the STOP-Bang scale **(ANNEX 2)**. A case of high risk of OSA is defined as a result greater than 5 in this scale.

It will be measured as a dichotomous nominal qualitative variable (yes or no).

It is useful to establish a reliable screening method for the recognition of patients at high risk for OSA before surgery. Since it has been shown that there is a high incidence of OSA patients among surgical patients (and about 80-90% are undiagnosed) and that these patients have an increased risk of complications after surgery and anesthesia. (13)

The STOP-Bang scale has demonstrated high sensitivity with medium specificity. (31)

6.4.3. COVARIABLES

All of them are descriptive analysis, obtained from the clinical history, or recorded in the "Case report form" created for the study.

- **Age:** 18-80 years of age. This is one of the most influencing factors in OSA, so it is essential to stratify patients before randomization. Is a discrete quantitative variable. It will be expressed in years.
- **Gender:** is a dichotomous nominal qualitative variable. It will be assessed by male or female.
- **Body Mass Index (BMI):** is a continuous quantitative variable. It will be expressed in kg/m².
- **Diabetes Mellitus:** is a dichotomous nominal qualitative variable. It will be expressed by yes or no.
- **Arterial hypertension:** is a dichotomous nominal qualitative variable. It will be expressed by yes or no.

- **Smoking:** Smoking status will be categorized as former, current or non-smoker, so it is a dichotomous nominal qualitative variable. It will be expressed by yes or no.
- **ASA scale:** This is a scale used to estimate the risk posed by anesthesia for the different states of the patient. Is a discrete quantitative variable. It will be measured as numbers (I, II, III, IV). **(ANNEX 5)**
- **Use of pre-study CPAP:** is a dichotomous nominal qualitative variable. It will be expressed by yes or no.
- **Time of surgery:** is a quantitative discrete variable. It will be expressed in hours.
- **Hospital stay time:** is a quantitative discrete variable, will be expressed in days.
- **Basal oxygen saturation on arrival at operating room:** It is important to know the basal saturation of oxygen on arrival at operating room because it can help us to get an idea of how it will behave afterwards. It will be measure as a discrete quantitative variable (% desaturated hemoglobin).
- **Morphine bolus number:** required by the patient during the 48-hour study to relieve pain. It is a quantitative discrete variable. It will be measured as numbers: (1, 2, 3, etc).
- **VAS scale:** this scaled is used to measure the pain perceived by the patient. It is a quantitative discrete variable and will be expressed in centimeters. **(ANNEX 7)**

6.5. INTERVENTIONS

6.5.1. STUDY PROCEDURES

A) Pre-anesthesia consultation in the outpatient

- **Medical history:**

- We must apply the STOP-Bang scale of 8 questions to stratify patients according to their risk of OSA, this is not currently done in these consultations in Girona. **(ANNEX 2)**
- The patients with a result in the STOP-Bang scale> 5, we must deepen the clinical interview looking for that it does not fulfill any criterion of exclusion.

- Collect the data of the covariables: age, sex, BMI, smoker, diabetic, arterial pressure.
- To perform the ASA questionnaire **(ANNEX 5)** to estimate the risk posed by anesthesia for the different states of the patient.
- Discard chronic respiratory processes such as chronic obstructive pulmonary disease with spirometry.
- Electrocardiogram.
- Physical examination: weight, height, Airway examination like modified Mallampati scale. The modified Mallampati scale is a scale used by anesthetists to predict the difficulty of intubation. **(ANNEX 6)**

• **Laboratory test**: General blood analysis with:

- Hematology: hemoglobin, hematocrit, white blood cells with differential count and platelet count.
- Coagulation: Quick time, partial thromboplastin time activated and fibrinogen.
- Biochemistry: creatinine, Blood Urea Nitrogen (BUN) and ions: sodium, potassium and glucose.

• **Collection of informed consent:**

After being well informed of all the issues related to the study **(Information sheep- ANNEX 8)** if the patient agrees, informed consent will be collected from participation in the study **(Informed consent- ANNEX 9)**. It is important that both informed consent is correctly signed by the patient.

B) Respiratory physiotherapy, in outpatient consultations. (39)

Patients selected for the trial will receive a respiratory physiotherapy class where they will be taught to do breathing exercises. Pre- and post-surgical respiratory therapy aims to prevent and / or treat respiratory complications due to or stimulated by the surgical process, through respiratory exercises, directed cough, early mobilization and efficacious analgesia with or without an incentive inspired. The main objective is to favor the respiratory function and the drainage of tracheobronchial secretions.

- **The preoperative** Respiratory care should be started in the preoperative period, identifying patients at risk, susceptible to respiratory complications and initiating the treatment of reversible factors that may respond to treatment. Start respiratory physiotherapy exercises, as it serves as training of the respiratory muscles.

Indication of prophylactic measures from preanesthetic consultation
1. Smoking cessation (at least 12-24 h) and enolism
2. Antibiotic treatment if respiratory superinfection occurs
3. Introduction or adequacy of bronchodilator treatment
4. Fluidization of secretions, favoring fluid intake
5. Initiation, except for specific contraindications, of frequent respiratory physiotherapy exercises
6. Treatment of heart failure and arrhythmias
7. Physical exercise as prophylaxis of deep venous thrombosis
8. Premedication should be avoided in many patients by replacing it with good information
9. Thromboprophylaxis
10. Consider prevention of chronic pain in patients at risk.

- **The postoperative**: The primary goal will be to restore pulmonary expansion and facilitate the removal of secretions.

The exercises are:

1. Diaphragmatic respiration: This technique has as a function to help the patient to elevate the diaphragm by increasing pulmonary expansion and improving ventilation of the pulmonary bases.
2. Puckered lips: This technique has the function of avoiding the collapse of the distal airway and its premature closure, as well as reducing dyspnea. It is mainly indicated in patients with Chronic Obstructive Pulmonary Disease.
3. Pulmonary Insufflation: (Technique with Inspired Inspiraometer). This technique has the function of providing a prolonged maximum inhalation, allowing the alveoli to expand and helping to eliminate secretions from the respiratory passages. These devices are used as one of the measures to treat and prevent perioperative pulmonary complications by increasing lung volume, favoring drainage of secretions and improving gas exchange. Its function is to encourage (encourage) the patient to make long and deep inspirations.
4. Vibration: This technique has the function of favoring the elimination of bronchial secretions, especially in those patients in whom percussion is contraindicated, or

postural drainage cannot be performed due to mobility problems. It can be used along with postural drainage to help release secretions. It consists of the gentle and rhythmic pressure of the hands on the thorax of the patient, when it is in phase of expiration, by means of this technique it is possible to increase the speed of the exhaled air in order to dislodge the secretions.

5. Percussion: This technique has the function of mobilizing secretions by striking the chest wall rhythmically, with hollow hands transmitting an impulse.
6. Assisted cough: This technique has the function of provoking expectoration in the patient through the previous stimulation of the cough. An effective cough is characterized by deep and deep sound, while ineffective has a sharp sound.
7. Postural drainage: This technique has the function of getting secretions drained by gravity to the bronchi and trachea, until they can be expelled by the cough.

6.5.2. PERIOPERATIVE MANEGEMENT (0-24 HOURS)

6.5.2.1. PREOPERATIVE MANEGEMENT

In the outpatient pre-anesthesia consultation (within 28 days prior to surgery).

- Obtain informed consent with the patient's signature in writing.
- Obtain demographic information, medical history, medication history, alcohol and tobacco use history.
- Review medical history to determine eligibility based on inclusion/exclusion criteria, discard acute illnesses or uncontrolled / unstable chronic processes.
- Perform medical examinations needed to determine eligibility based on inclusion/exclusion criteria.
- Collect blood for: hematology, coagulation and biochemistry.
- Record vital signs.
- All patients will visit the respiratory physiotherapy unit where they will learn respiratory exercises. Also once they enter the study, all patients will be explained using CPAP and will be tested with each.
- Provide participants with the necessary instructions for major laparoscopic abdominal surgery with general anesthesia.

6.5.2.2. INTRAOPERATIVE MANEGEMENT

All subjects undergo general anesthesia using a standardized approach based on a preexisting evidence-based clinical practice guideline:

1. Basic monitoring: ECG, pulse oximeter, capnography, blood pressure, BIS (normal values for correct deep sleep is between 40-60), TOF (for a good neuromuscular blockade, 90% of nerve fibers must be blocked).

   They will be given a urinary catheter that will last up to 48 hours after the surgery as a minimum, the doctor will assess the removal of the catheter after the clinical trial.

2. Pain control: dorsal epidural catheter (prior to the induction phase).
3. Preinduction Pressure Support (7–10 cm H2O/10 cm H2O) administered via the anesthesia machine (Datex-Ohmeda), positioning in the ramped position (with the external auditory meatus located at the level of the anterior chest wall).
4. Anesthesic induction: with midazolam (1mg), propofol (1–2 mg/kg), fentanyl (2-3 µg/kg), atropine (0.1mg/kg), and rocuronium (0.6-0.8 mg/kg total body weight).
5. Intubation: direct view laryngoscopy, oxygen (FIO2 50%) air.
6. Anesthesic maintenance: desflurane (MAC 0.9-1 and BIS 40-60), and rocuronium´s bolus and remifentanil in continuous perfusion (0.1-0.2 microg/kg/min) for maintenance anesthesia and patients received volume-controlled ventilation, with tidal volume (6 ml/kg ideal body weight) and a respiratory rate of 12 breaths per minute and/or intraoperative PEEP (7 cm H2O, greater for body mass index of greater than 50) for maintenance airway.
7. Anesthesic edduction: reversion of muscle relaxation with Bridion (sugammadex 100 mg / dl) to achieve TOF greater than 90%.
   A bolus was performed on the dorsal epidural catheter of bupivacaine (0.125%), adrenaline (0.02) and fentanyl (70 microgr).
   Administer intravenous paracetamol (1 g / 6 h).
8. Extubation: after reversal, patients will be extubated if they be able to obey commands and are taking tidal volumes of at least 400 ml with a respiratory rate of fewer than 20 breaths per minute. Will be extubated in the semi-incorporated position after complete reversal of neuromuscular blockade.
   Both groups will be extubated and oxygenated with a nasal mask with a concentration of 50% oxygen, 4-6 l/min oxygen.

- BIS: Bispectral Index™ (BIS™) monitoring systems enable anesthesia professionals to access processed EEG information as a measure of the effect of certain anesthetics during the care of patients they select to monitor. The clinical impact of BIS™ monitoring has been demonstrated in a variety of randomized controlled trials that reveal the potential for BIS monitoring to facilitate improvements—including patient safety—in anesthesia care.
- TOF: Train-Of-Four monitor is a peripheral nerve stimulator, is used to assess neuromuscular transmission when neuromuscular blocking agents (NMBAs) are given to block musculoskeletal activity. By assessing the depth of neuromuscular blockade, peripheral nerve stimulation can ensure proper medication dosing and thus decrease the incidence of side effects.
- MAC: Minimum alveolar concentration is the concentration of a vapour in the lungs that is needed to prevent movement (motor response) in 50% of subjects in response to surgical (pain) stimulus. MAC is used to compare the strengths, or potency, of anaesthetic vapours.

6.5.2.3. POSTOPERATIVE IMMEDIATE MANEGEMENT

All subjects receive this ventilatory support during transport to the postanesthesia care unit (PACU) and in the PACU until change to postoperative CPAP or ventimask.

On arrival to the PACU, all subjects will be connected to continuous monitors of vital signs, analgesia will be administered via dorsal epidural catheter that administers continuous perfusion of bupivacaine (0.125%), adrenaline (1: 200000) and Fentanyl (2 µg / ml) and paracetamol (1gram). This catheter will be used for 48 hours after surgery (only for the duration of the test).

For the pain, we will use the Visual Analogue Scale (VAS scale, EVA in Spanish, if the patient has a VAS score greater than 3, administer morphine bolus (2 mg). **(ANNEX 7)**

In a maximum period of 30 minutes from the end of the surgery:

- **Non-CPAP group** subjects will be oxygenated with ventimask with of 50% oxygen.
- **CPAP group** subjects will be oxygenated with the Ventilador Respironics V60 CPAP system (Respironics California, Inc) with a concentration of 50% oxygen and PEEP of 8-10 cm H2O.

CPAP will be continued on the postoperative night for a minimum of 18 h and only will be discontinued 24 h after extubation.

6.5.3. POSTOPERATIVE MANEGEMENT (24-48 HOURS)

Follow-up 24 hours after surgery:

- Patients will be monitored continuously, cardiorespiratory monitoring, temperature and blood pressure.
- The blood test measurement: (hematology, coagulation and biochemistry) will be done to 12 and 24 hours after surgery.
- Evaluate the pain with the VAS´s scale to 4, 8 and 24 hours after surgery, and if the patient has a VAS score greater than 3 the nurse will administer him/her morphine bolus (2 mg).
- Record adverse events as reported by participant or observed by the responsible nursing team.
- Record vital signs, results of the hemoglobin saturation recorded with the pulse oximeter by the nurse.
- Receive a respiratory physiotherapy session.
- Remove the CPAP to the CPAP group and add ventimask, thus, both groups (CPAP´s group and ventimask´s group) will receive 50% oxygen with ventimask from 24 to 48 hours after surgery.
- Record participant's adherence to treatment program.

Final Study Visit 48 hours after surgery:

- Patients will be monitored continuously, cardiorespiratory monitoring, temperature and blood pressure.
- The blood test measurement: (hematology, coagulation and biochemistry) will be done to 48 hours after surgery.
- Evaluate the pain with the VAS´s scale to 48 hours after surgery, and if the patient has a VAS score greater than 3 the nurse will administer him/her morphine bolus (2 mg).
- Record adverse events as reported by participant or observed by the responsible nursing team.
- Record vital signs, results of the hemoglobin saturation recorded with the pulse oximeter by the nurse.
- Receive a respiratory physiotherapy session.

- Remove the pulse oximeter from the patient.
- Explain the end of the study and the results obtained in your case.

6.6. JUSTIFICATION OF SENSITIVE PROCEDURES

There are no studies demonstrating the benefit of CPAP regarding the use of any ventilatory support in patients at high risk of OSA, a main limitation is that the risk of OSA is not measured in a patient who is going to undergo major surgery.

Due to this lack of scientific evidence of CPAP superiority regarding the non-use of CPAP, one group is justified in using CPAP and the other using ventilatory support with a nasal mask. (11,17)

6.7. DATA COLLECTION

Referring to patient information, we recorded: age, sex, BMI, patient´s comorbidities as smoking, diabetes, blood pressure, ASA, postoperative reported pain scores (VAS), number of times the patient received morphine´s bolus, number of times hemoglobin desaturation and severity of these.

The collection of data will be prospectively extracted from medical records. We will create, for the development of the study, a case report form (CRF) **(Data colletion sheet- ANNEX 11)**.

Every day a nurse from the nursing team assigned to the trial will complete the CRF. The data will be collected upon arrival of the patient from quirophan to the semicritical unit (PACU), at 4 hours, 8, 24 and 48 hours after surgery. Every Friday will review the data for the whole week.

Every Monday, the hospital's anesthetist will email the CRF for the whole week to the statistician. The CRF will not show the names of patients or any data that can relate to them, only the identification code that we assigned to the beginning of the study, this way we ensure that the specialist in statistics is blind.

The statistician will enter the data into a database.

Being a study in a single hospital we avoid the bias that could be produced by variability between hospitals or equipment.

6.8 OTHER ACTIVITIES FROM THE STUDY

- **Pilot experiment**

Before starting the clinical trial, a pilot experiment will be conducted for two months to evaluate the CRF, the possible difficulties for obtaining the data and analyzing the correct coordination between hospitals.

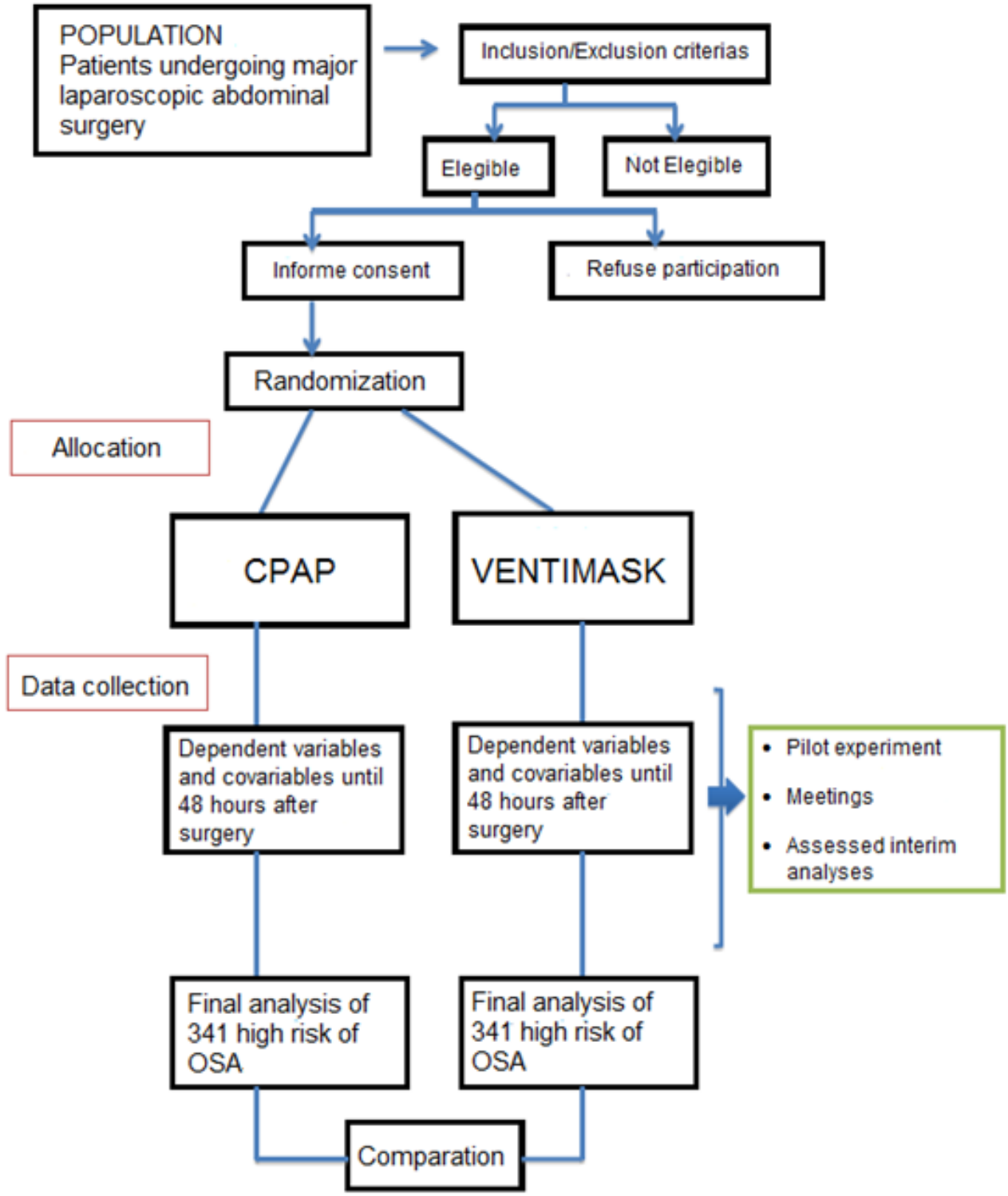
- **Meetings**

We will organize 5 meetings with the anesthesiologist, the study coordinator and the statistical specialist. The aim of the meetings (before and after the pilot experiment, at the end of the first year, and at the end of second year of data collection) will be to ensure the correct operation of the study (we specify the specific objectives of each meeting in the work plan). At the end of the study, another meeting will be done to analyze and interpret results. We ensure a permanent communication between doctors and the study coordinator.

- **Assessed interim analyses**

At the 100, 200, 400, 600, enrolled patients, the statistical specialist will analyze the data obtained from the outcomes (Desaturation number, desaturation severity and possible adverse events) with the objective to stop the study if he find differences clinically relevant between the groups. Finally he will realize the statistical analysis from all the data, when we enrolled 682 patients.

6.9. SUMMARY OF THE PROGRESS OF THE SUBJECTS



6.10. TASK AND RESEARCH TEAM

- The nurse: 2
  - Monitor the patient 24 hours a day until 48 hours after surgery.
  - Note the number of desaturations and the severity of these daily.
  - Note the occurrence of any adverse effects.
  - Perform VAS scales.
  - Administer the drugs required by the patient.
- The neumologist:
  - Will be responsible for monitoring the occurrence of possible postoperative respiratory complications.
- The respiratory physiotherapist:
  - He will give 3 sessions of respiratory physiotherapy to each patient: the first one before surgery, the second at 24 hours after surgery and the third at 48 hours after surgery.
- The Anesthesiologist: 2
  - The entire process of anesthesia during surgery
  - Treatment of post-surgical pain.
  - Data collection weekly (CRF for the whole week) and sent to the statistician.
- The Statistical specialist:
  - Design randomization program.
  - Assessed interim analysis at the 100-200-400-600 enrolled infants.
  - Statistical analysis.
- The study coordinator:
  - He/she is the responsible for the correct operation of the study, the coordination and to get and convey the data from the hospitals to the statistical specialist.
  - Interpret and analyze results.

7. STATISTICAL ANALYSIS

The study includes all participants who have fulfilled 75% of the time established with CPAP or oxygen mask, that is, at least 18 hours out of 24 established.

In the **univariate analysis**, we will define variables as categorical or continuous.

- Categorical variable will be described as percentages and proportions.

- Quantitative variables will be described, with means ± standard deviation (the variables with normal distribution) and with median and interquartile range (25-75) (the variables with skewed distribution).

In the **bivariate analysis**, we must compare our independent, considering it as a dichotomous nominal qualitative one (CPAP or non-CPAP) which each one of the dependent variables:

- Incidence of desaturation: it is a dichotomous nominal qualitative variable (yes = desaturation, if hemoglobin´s saturation ≤94%; no= no desaturation). We will need the x2 test to compare with independent variable.
- Severity and durations of desaturations: is a discrete quantitative variable, so in order to compare it with the independent one, we will need the statistic Mann-Whitney U test. In order to correlate the results from Severity and Incidence of desaturation, we will apply Mann-Whitney U test too.
- The prevalence of OSA with STOP-Bang screening, it is a nominal qualitative variable, so in order to compare it with the independent one, we will need the x2 test. In order to correlate the results from Incidence of desaturation, we will need the x2 test and to compare with severity of desaturation, we will need the Mann-Whitney U test.

The **multivariate analysis** will be performed with the finality of introducing possible covariates and confounding factors. The analysis will be done with a logistic regression test will be used to estimate odds ratio and 95% confidence intervals. It will be used to assess the relationship between different outcome measures and the effect of CPAP, after adjustment for the potentially confounding effects.

All statistics analysis will be carried out with the Statistical Package for Social Science (SPSS). To manage computed data, Microsoft Excel tool will be used. P value of <0.05 will be considered to indicate statistical significance. Analysis will be done in intention to treat and the results may be stratified for the different hospitals.

8. LIMITATIONS

Making a revision of our protocol, there are some limitations that should be taking into consideration because can interfere in our research. The most important limitations are explained below:

- As a result of the administration conditions of the different treatments, it is impossible to make a double-blind trial because both patients and the professionals will be aware about the treatment group in which the patient is. To minimize this bias, the statistician will not be aware of which participant belongs to each group.
- It is important to make a clear and precise awareness of the importance of the disease that may be present and the added risks involved in surgery. We must also explain the inability of the doctors or nurses responsible for changing the group. With this we try to increase adherence to the treatment.
- The other important limitation is that the patient must adapt to the use of CPAP, which in some cases are not able to tolerate it and respect the established hours of use. This study requires a lot of patient participation (they have to go to the hospital several times, understand how to use new devices, etc.).

  To minimize the losses due to this cause we must explain to the patient the operation of the machine and practice its use with it, in order to adapt the patient to CPAP. Before excluding a patient from the study, we will try to call you to come to the appointment.
- Regarding the questionnaire used (STOP-Bang), is a validated questionnaire to have proved to be useful for assess the risk of suffer from OSA. Is a screening scale, does not make a diagnosis of certainty.

  So that patients with a high risk of OSA according to the STOP-Bang scale should undergo polysomnography after the study to confirm the diagnosis of OSA.
- The STOP-Bang scale has some questionable items, such as:

  - The patient makes apneas while sleeping
  - The patient snores

  Some patients or their bed partners may not appreciate these parameters correctly. To minimize this error we accepted as high risk of OSA a result greater than 5.

9. ETHICAL ASPECTS

This clinical trial has been designed following the Declaration of Helsinki (last update October 2013). This protocol will be sent to the Clinical Research Ethics Committee (CEIC) of the Josep Trueta University Hospital of Girona to be evaluated. The modifications of the protocol will be made in case the CEIC considers it necessary. After local approval of the protocol by the CEIC, the study must be approved by the Spanish Association of Medicines and Sanitary Products (AEMPS) with the EudraCT application before beginning the trial.

The research project will be carried out in accordance with Spanish legislation related to clinical trials: "Law 29/2006 of July 26, on guarantees and rational use of medicines and medical devices

- RD 1/2015, of July 24, on Biomedical Research, which regulates the use of medication and sanitary products.
- RD 1591/2009 of October 16 and 1616/2009 of October 26: research with sanitary products "
- The right of health protection will be respected as per article 43 of the Spanish Constitution of 1978. Patients have the right to leave the trial at any time with no impact on the health care they receive. All patients will be insured for harm and damages that might result from the investigation.

Concerning about the patients, all of them will be given the patients information sheet **(Annex 5)** with all the information about the clinical trials. Once the information has been delivered and understudied, the patients will be asked to sign the informed consent **(Annex 6)** in order to be enrolled in our trial. The principle of autonomy will be respect in all the process.

According to the Spanish Organic Law 15/1999, de 13 de diciembre, de Protección de Datos de Carácter Personal and the later Spanish Legislative Royal Decree 1720/2007, del 21 de Diciembre, all the information of the patients (name, surnames, clinical history, etc) will be confidential and the anonymity will be guaranteed in all the trial process. The participants will have the right to consult, modify and delete their personal data from their personal life.

All the investigators will have to declare no conflict of interest.

10. WORK PLAN AND CHRONOGRAM

The research team will be composed by: one study coordinator (SC), 2 anesthesiologists (Anes), nurse specialized in semi-intensive care (Nur), pneumologist (Pneu), Respiratory physiotherapist (R.phy) and one statistical specialist (SS).

The duration of the clinical trial it will be 3 years, and it will be organized according the following steps. The trial has been designed in 5 phases:

- **PHASE 1 COORDINATION: (6 months)**

1. Design the protocol (2 months) it will be do it for the anesthesiologist of this project and it will take two months: reading bibliography, establishing hypothesis, objectives and defining the population. .

2. Initial meeting for coordination (4 months):

- Selection of the Nur, Pneu and R.phy. The protocol it will be discussed with the members of the study to make sure that everyone agrees with the procedures and they will do the chronogram. The CRF have been understood in order to be followed by all of them.
- Previous to start the clinical trial, we must register it in AEMPS webpage through eudraCT application in order to obtain the nº solicitude.
- Finally the Anes must be obtained the ethical approval of the protocol from the CEIC from Josep Trueta University Hospital.

2. Database creation by the SS.

- **PHASE 2: RECRUITMENT, INTERVENTIONS AND DATA COLLECTION. (24 months)**

4. Recruitment of patients: A competitive and consecutive non-probabilistic sampling will be performed at anesthesiologist outpatient visits by the Anes. The estimated time of recruitment will be 2 year (It can be modified; the objective is to enroll 681 patients with high risk of OSA undergoing major laparoscopic abdominal surgery under general anesthesia). Because the sampling is consecutive non-probabilistic, so the process will be continuous: informed consent, randomization, surgery, 48-hours data collection in postoperative period.

5. Data collection (24 months): once the patients are enrolled in the study, the interventions and data collection will be done by Nur daily and every Monday, the anesthetist, will be in charge of picking up the CRF for the whole week and sending it by email to the SS. During this period, Pneu and R.phy will be available to help the research team with any doubt about the health status of patients.

6. Pilot experiment (2 months): to detect problems, mistakes of the CRF and possible failure of coordination. (SC, Anes, Nur, Pneu, R.phy).

7. Meeting 2: the objective will be to discuss if there is any improvement of the CRF and coordination, before starting the data collection. (SC, Anes, SS).

8. Meeting 3 (12 months after initiate data collection) and Meeting 4 (24 months after initiate data collection). The aim will be to solve problems, check the quality of the data collected, and to check that the protocol has been followed. Another activity will be interpreting the preliminary results from the interim analyses and quantifying the number of patients with the objective to determine the real duration of the study. (SC, Anes, SS).

- **PHASE 3: DATA ANALYSIS AND RESULTS INTERPRETATION (4 months)**

9. Statistical Analysis, it will be done by the SS. Finally, the statistical will sent these results to the main investigators, in order to interpret and discuss them.

10. Meeting 5 (after statistical analysis) with the objective to interpret and discuss the results from the statistical analysis. (SC, Anes, SS).

- **PHASE 4: PUBLICATION AND DISSEMINATION OF THE RESEARCH FINDINGS (6 months)**

12. Publication (SC, Anes, SS) and dissemination (SC) of the research findings (6 months). Write and edit the results to publish them and assist to conference to disseminate the findings.

10.1. CHRONOGRAM SCHEME

Year	2017				2018				2019				2020	
Months	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dic	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dic	Jan-Mar	Apr-Jun	Jul-Sep	Oct-Dic	Jan-Mar	Apr-Jun
First phase: Protocol preparation and coordination (SC and SS)														
Protocol design														
Initial meeting														
Chronogram														
Authorizations														
Data base creation														
Second phase: Recruitment, intervention and data collection (SC, Anes, Nur, Pneu, R.phy, SS)														
Patient recruitment														
Pilot experiment														
Meeting 2														
Intervention														
Follow-up														
Data collection														
Meeting 3														
Meeting 4														
Third phase: Statistical analyses and discussion of the results (SC, Anes and SS)														
Analysis														
Meeting 5														
Discussion														
Fourth phase: Results publishing and dissemination (Anes)														
Final report														
Publishing														
Congress														

11. FEASIBILITY

Since the clinical trial is carried out at the Josep Trueta University Hospital (third level hospital), all the members work there previously (the study will be carried out by the staff of this Hospital), it would only be necessary to hire a statistician outside the hospital who will analyze the data blindly (he will not know Which group of patients belongs each data).

The hospital will provide the needed informatics equipment for the data collection, an informatics room will be transferred to our statistician for the analysis of the data.

Interventions will be performed by the same team. All of them will have a large experience administrating the two treatment options.

Anesthesiologists, the pulmonologist, respiratory physiotherapist and nurses will receive their usual salaries at the hospital, moreover the material both CPAP, oxygen masks and pulse oximeters will belong to the hospital's facilities (no extra purchase). For that reason only the specialist in statistics will have to be paid.

In Spain there are between 1,200,000 and 2,150,000 patients with relevant OSAS, but it has been estimated that the prevalence of OSA among the surgical population is greater than in the general population, and about 80% are undiagnosed. This study would approach the diagnosis of OSA to many of that 80%. In addition OSA is associated with a greater number of periquirurgical complications, these could be reduced with a special management such as postoperative CPAP.

Estimating a prevalence of OSA of 5% and taking into account that almost 2000 non-urgent major surgeries under general anesthesia are performed at the Josep Trueta University Hospital, we calculated that we would need about 682 patients and we could recruit them in approximately two years.Because there are not a real OSA register in surgycal population, this is just an approximation based on the prevalence of diagnosis OSA of Europe. We cannot predict exactly the number of patients that will come to our surgeries and it is possible that not every patient meet the inclusion criteria. For these reasons, is possible that the recruitment period will have to be prolonged.

We know that is difficult to enroll 682 high risk of OSA for our study, but the relevance of the study and the possible impact of the results, justifies the efforts. The OSA patients are a population more vulnerable and increasingly present in our society.

12. BUDGET

- Firstly, referring to the **personnel**: We will hire a statistical specialist for make easier and reliable the randomization. He or she will code patients too. The estimated salary will be 35€/hour and more or less 60 hours will be needed. So, the total estimated cost will be 2100€. The nurse responsible for collecting data on a continuous basis of each patient will be encouraged with 15 €/hour, estimating that the hours that will take to collect the daily data of the 682 patients will be approximately 200 hours (3000€ in summary). The anesthesiologist will also receive a salary of 15 € / h for collecting the data at the end of the week and delivering them to the statistician, it is estimated that he will spend 100 hours there (1500€ in total). The physician outpatient visits are not included in the budget, because they are visits that are done in the usual clinical practice. The respiratory physiotherapist and the pneumologist are also part of the hospital staff so they will receive their normal salary.
- Secondly, the **materials**: All the material used, CPAP, oxygen masks and pulse oximeters belong to the hospital, so there is no cost. The blood tests are performed routinely in PACU in patients after surgery so we will not be included in the budget.
- Finally, established **taxes** are AEMPS authorization, publishing and inscription price for Spanish Congress of Anesthesiology. Other taxes are accommodation and travels.

	Cost	Quantity	Total
Staff costs			
Statistical Specialist	35 €/h	60 h	2.100 €
Nurse	15 €/h	200 h	3.000 €
Anesthesiologist	15 €/h	100 h	1.500 €
AEMPS authorization	1.500 €	1	1.500 €
Anesthesia congress	800 €	1	800 €
Publication and dissemination cost			
Approximated cost of publication	1.500 €	1	1.500 €
Travels, Accomodations of meeting	800 €	1	800 €
TOTAL =			**12.700€**

13. CONFLICT OF INTEREST

The authors declare no conflict of interest.

14. IMPACT OF THE PROJECT

If the results are relevant and our hypotheses are validated, CPAP could start to be used routinely as preventive treatment of respiratory complication after surgery in high risk of OSA patients. It can be a change in the medical practice.

We will also introduce the use of a screening technique (STOP-Bang scale) for patients with OSA, since this disease is very frequent among the surgical population and in 80% of cases it is not diagnosed.

On one hand, it will be a positive change, because the preventive treatment with CPAP is cheap and its continuous use has been shown to be effective in patients diagnosed with OSA.

Therefore, if these results are similar in high risk of OSA (no confirmed diagnosis), we can prevent the incidence of hemoglobin desaturations and possibly posterior respiratory complications, and this would reduce the expenditures in the ICUs.

On the other hand, the economic burden of OSA is substantial, owing to prolonged hospital stays, surgical reinterventions and the possible complications (such as death, acute fail respiratory, atelectasis, or the pulmonary hypertension). There are no studies from the economic impact of OSA in surgery in Spain, but, if this study is feasibility, it will lead to a decrease of respiratory complications events post-surgery which will need less hospital attention. Not only the inpatient care will significant decrease but also that the days of hospital stay and the transfer to emergency units will be less used in this patients by the prevention with CPAP.

We consider that, now is the most appropriate time for carrying out the study and consequently according to the results, implement or not the routine use of CPAP to prevent hemoglobin desaturation in the Spanish patients with high risk of OSA.

15. BIBLIOGRAPHY

1. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The Occurrence of Sleep-Disordered Breathing among Middle-Aged Adults. N Engl J Med [Internet]. 1993 Apr 29 [cited 2017 Jan 3];328(17):1230–5. Available from: http://www.ncbi.nlm.nih.gov/pubmed/8464434

2. Vasu TS, Grewal R, Doghramji K. Obstructive sleep apnea syndrome and perioperative complications: a systematic review of the literature. J Clin Sleep Med [Internet]. 2012 Apr 15 [cited 2017 Jan 5];8(2):199–207. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22505868

3. Wolfe RM, Pomerantz J, Miller DE, Weiss-Coleman R, Solomonides T. Obstructive Sleep Apnea: Preoperative Screening and Postoperative Care. J Am Board Fam Med [Internet]. 2016 Mar 1 [cited 2016 Nov 29];29(2):263–75. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26957384

4. Qaseem A, Dallas P, Owens DK, Starkey M, Holty J-EC, Shekelle P, et al. Diagnosis of Obstructive Sleep Apnea in Adults: A Clinical Practice Guideline From the American College of Physicians. Ann Intern Med [Internet]. 2014 Aug 5 [cited 2016 Nov 27];161(3):210. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25089864

5. Chung F, Memtsoudis SG, Ramachandran SK, Nagappa M, Opperer M, Cozowicz C, et al. Society of Anesthesia and Sleep Medicine Guidelines on Preoperative Screening and Assessment of Adult Patients With Obstructive Sleep Apnea. Anesth Analg [Internet]. 2016 Aug [cited 2016 Dec 22];123(2):452–73. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27442772

6. Busha BF, Strobel RJ, England SJ. The length-force relationship of the human genioglossus in patients with obstructive sleep apnea. Respir Physiol Neurobiol [Internet]. 2002 Apr [cited 2017 Jan 8];130(2):161–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12380006

7. Memtsoudis S, Liu SS, Ma Y, Chiu YL, Walz JM, Gaber-Baylis LK, et al. Perioperative Pulmonary Outcomes in Patients with Sleep Apnea After Noncardiac Surgery. Anesth Analg [Internet]. 2011 Jan [cited 2016 Dec 27];112(1):113–21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21081775

8. Harrison TR, Longo DL. Harrison : principios de medicina interna [Internet]. México: McGraw-Hill Interamericana; 2012 [cited 2017 Jan 27]. Available from: http://cataleg.udg.edu/record=b1330876~S10*cat

9. Chung SA, Yuan H, Chung F. A Systemic Review of Obstructive Sleep Apnea and Its Implications for Anesthesiologists. Anesth Analg [Internet]. 2008 Nov [cited 2016 Dec 31];107(5):1543–63. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18931212

10. Sánchez, Navarro G. Síndrome de apnea obstructiva del sueño . Implicaciones y complicaciones. Jorn Científica Actual en Anestesiol y Med preioperatoria. 2011;1–6.

11. Barimboim E. Apnea del sueño como factor de riesgo en intervenciones quirúrgicas. Rev Am Med Respir. 2014;14(3):272–9.

12. Farreras Valentí P, Rozman C, Cardellach F, Domarus A von. Medicina interna [Internet]. Barcelona : Elsevier; 2016 [cited 2017 Jan 27]. Available from: http://cataleg.udg.edu/record=b1385345~S10*cat

13. Canet J, Gallart L. Predicting postoperative pulmonary complications in the general population. Curr Opin Anaesthesiol [Internet]. 2013;26(2):107–15. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23407151%5Cn

14. Canet J, Gallart L, Gomar C, Paluzie G, Vallès J, Castillo J, et al. Prediction of Postoperative Pulmonary Complications in a Population-based Surgical Cohort. Anesthesiology [Internet]. 2010 Dec [cited 2016 Dec 23];113(6):1338–50. Available from: http://www.ncbi.nlm.nih.gov/pubmed/21045639

15. Gögenur I, Rosenberg-Adamsen S, Lie C, Carstensen M, Rasmussen V, Rosenberg J. Relationship between nocturnal hypoxaemia, tachycardia and myocardial ischaemia after major abdominal surgery. Br J Anaesth. 2004;93(3):333–8.

16. Fassbender P, Herbstreit F, Eikermann M, Teschler H, Peters J. Obstructive Sleep Apnea-a Perioperative Risk Factor. Dtsch Arztebl Int [Internet]. 2016 Jul 11 [cited 2016 Nov 27];113(27–28):463–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/27476705

17. Pelosi P, Jaber S. Noninvasive respiratory support in the perioperative period. Curr Opin Anaesthesiol [Internet]. 2010;23(2):233–8. Available from:

http://eutils.ncbi.nlm.nih.gov/entrez/eutils/elink.fcgi?dbfrom=pubmed&id=20019602&retmode=ref&cmd=prlinks%5Cnpapers2://publication/doi/10.1097/ACO.0b013e328335daec

18. Chung F, Yegneswaran B, Liao P, Chung SA, Vairavanathan S, Islam S, et al. STOP Questionnaire. Anesthesiology [Internet]. 2008 May [cited 2016 Dec 23];108(5):812–21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18431116

19. Seet E, Chua M, Liaw CM. High STOP-BANG questionnaire scores predict intraoperative and early postoperative adverse events. Singapore Med J. 2015;56(4):212–6.

20. Chung F, Yang Y, Brown R, Liao P. Alternative Scoring Models of STOP-Bang Questionnaire Improve Specificity To Detect Undiagnosed Obstructive Sleep Apnea. J Clin Sleep Med [Internet]. 2014 Sep 15 [cited 2016 Dec 23];10(9):951–8. Available from: http://www.ncbi.nlm.nih.gov/pubmed/25142767

21. Kaw R, Chung F, Pasupuleti V, Mehta J, Gay PC, Hernandez A V. Meta-analysis of the association between obstructive sleep apnoea and postoperative outcome. Br J Anaesth [Internet]. 2012 Dec 1 [cited 2017 Jan 4];109(6):897–906. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22956642

22. Gupta RM, Parvizi J, Hanssen AD, Gay PC. Postoperative Complications in Patients With Obstructive Sleep Apnea Syndrome Undergoing Hip or Knee Replacement: A Case-Control Study. Mayo Clin Proc [Internet]. 2001 Sep [cited 2016 Dec 7];76(9):897–905. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11560300

23. Liao P, Yegneswaran B, Vairavanathan S, Zilberman P, Chung F. Postoperative complications in patients with obstructive sleep apnea: a retrospective matched cohort study. Can J Anesth Can d'anesthésie [Internet]. 2009 Nov 23 [cited 2016 Dec 7];56(11):819–28. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19774431

24. Hwang D, Shakir N, Limann B, Sison C, Kalra S, Shulman L, et al. Association of Sleep-Disordered Breathing With Postoperative Complications. Chest [Internet]. 2008 May [cited 2016 Nov 25];133(5):1128–34. Available from: http://www.ncbi.nlm.nih.gov/pubmed/18339794

25. Eastwood PR, Platt PR, Shepherd K, Maddison K, Hillman DR. Collapsibility of

the upper airway at different concentrations of propofol anesthesia. Anesthesiology [Internet]. 2005 Sep [cited 2016 Dec 27];103(3):470–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16129969

26. Hillman DR, Walsh JH, Maddison KJ, Platt PR, Kirkness JP, Noffsinger WJ, et al. Evolution of Changes in Upper Airway Collapsibility during Slow Induction of Anesthesia with Propofol. Anesthesiology [Internet]. 2009 Jul [cited 2016 Dec 27];111(1):63–71. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19512872

27. Bailey PL, Pace NL, Ashburn MA, Moll JW, East KA, Stanley TH. Frequent hypoxemia and apnea after sedation with midazolam and fentanyl. Anesthesiology [Internet]. 1990 Nov [cited 2016 Dec 5];73(5):826–30. Available from: http://www.ncbi.nlm.nih.gov/pubmed/2122773

28. Bailey PL, Lu JK, Pace NL, Stat M, Orr JA, White JL, et al. Response To Hypoxia. N Engl J Med. 2000;1228–34.

29. Lin E, Calvano SE, Lowry SF. Inflammatory cytokines and cell response in surgery. Surgery [Internet]. 2000 Feb [cited 2017 Jan 6];127(2):117–26. Available from: http://www.ncbi.nlm.nih.gov/pubmed/10686974

30. Ni Choileain N, Redmond HP. Cell Response to Surgery. Arch Surg [Internet]. 2006 Nov 1 [cited 2017 Jan 7];141(11):1132. Available from: http://www.ncbi.nlm.nih.gov/pubmed/17116807

31. Knill RL, Moote CA, Skinner MI, Rose EA. Anesthesia with abdominal surgery leads to intense REM sleep during the first postoperative week. Anesthesiology [Internet]. 1990 Jul [cited 2017 Jan 7];73(1):52–61. Available from: http://www.ncbi.nlm.nih.gov/pubmed/2360740

32. Nagappa M, Liao P, Wong J, Auckley D, Ramachandran SK, Memtsoudis S, et al. Validation of the STOP-Bang Questionnaire as a Screening Tool for Obstructive Sleep Apnea among Different Populations: A Systematic Review and Meta-Analysis. Arias-Carrion O, editor. PLoS One [Internet]. 2015 Dec 14 [cited 2016 Dec 23];10(12):e0143697. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26658438

33. American Society of Anesthesiologist. Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea. Anesthesiology [Internet]. 2014 Feb [cited 2016 Dec 23];120(2):268–86. Available from:

http://www.ncbi.nlm.nih.gov/pubmed/24346178

34. Hedenstierna G, Edmark L. Effects of anesthesia on the respiratory system. Best Pract Res Clin Anaesthesiol. 2015;29(3):273–84.

35. Belozeroff V, Berry RB, Sassoon CSH, Khoo MCK. Effects of CPAP therapy on cardiovascular variability in obstructive sleep apnea: a closed-loop analysis. Am J Physiol Heart Circ Physiol [Internet]. 2002 Jan [cited 2017 Jan 30];282(1):H110-21. Available from: http://www.ncbi.nlm.nih.gov/pubmed/11748054

36. Vasu TS, Doghramji K, Cavallazzi R, Grewal R, Hirani A, Leiby B, et al. Obstructive Sleep Apnea Syndrome and Postoperative Complications. Arch Otolaryngol Neck Surg [Internet]. 2010 Oct 18 [cited 2016 Dec 9];136(10):1020. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20956751

37. Güldner A, Kiss T, Serpa Neto A, Hemmes SNT, Canet J, Spieth PM, et al. Intraoperative Protective Mechanical Ventilation for Prevention of Postoperative Pulmonary Complications. Anesthesiology. 2015;123(3):692–713.

38. Güldner A, Pelosi P, de Abreu MG. Nonventilatory strategies to prevent postoperative pulmonary complications. Curr Opin Anaesthesiol [Internet]. 2013;26(2):141–51. Available from: http://www.ncbi.nlm.nih.gov/pubmed/23385322

39. Balsera BC, Sánchez LM, Gómez ÓG, Moyano NG, Cabra PD, López RG-, et al. Descripción de un protocolo de sioterapia respiratoria a pacientes sometidos a cirugía abdominal alta . Description protocol chest physiotherapy to patients undergoing upper abdominal surgery . 2015;45–52.

16. ANNEX

16.1. ANNEX 1- STUDIES REPORTING ASSOCIATION BETWEEN OBSTRUCTIVE SLEPP APNEA AND PERIOPERATIVE COMPLICATIONS (2)

Table1—Studies reporting association between obstructive sleep apnea and perioperative complications

Author	Type of Study	Number of Patients	Diagnosis of OSAS	Type of Surgeries	Complications	Results
Gupta et al.[96]	Case control study	101 patients with OSA and 101 matched controls	Polysomnography (PSG)	Orthopedic (hip or knee replacement)	Reintubation, hypoxemia, acute hypercapnia, myocardial infarction, arrhythmia, delirium, and ICU transfer	Patients with OSA had higher rate of postoperative complications (39% vs 18%). These patients also had increased hospital length of stay.
Auckley et al.[105]	Historical cohort study	81 patients with completed Berlin Questionnaire	Berlin Questionnaire	Elective surgery (type of surgeries is not included in the abstract)	Hypoxemia, hypercapnia, reintubation, atelectasis, pneumonia, arrhythmia, thromboembolism	Patients with high-risk of sleep apnea based on the Berlin Questionnaire had a higher rate of postoperative complications (20% vs 4.5%).
Sabers et al.[106]	Case control study	234 patients with OSA and 234 matched controls	Polysomnography	Non-otorhinolaryngologic outpatient surgical procedures	Unplanned hospital admission, bronchospasm, upper airway obstruction, hypotension, atrial fibrillation, pulmonary edema	No significant difference in the rate of unplanned hospital admissions (23.9% vs 18.8%) or other adverse events (2.1% vs 1.3%)
Kaw et al.[100]	Case control study	37 patients with OSA and 185 matched controls	Polysomnography	Cardiac	Encephalopathy, postoperative infections, and ICU length of stay	Patients with sleep apnea had higher rate of encephalopathy, postoperative infections (mediastinitis), and increased ICU length of stay.
Hwang et al.[102]	Historical cohort study	172 patients underwent home nocturnal oximetry	Home nocturnal oximetry	Abdominal, ENT, Thoracic, Vascular, Gyn, Neurosurgical, Urologic, Cardiothoracic, and Orthopedic	Arrhythmia, hypoxemia, atelectasis, GI bleed, pneumonia, pulmonary embolism,	Patients with ODI4% ≥ 5/h had a higher rate of postoperative complications than those with ODI4% < 5/h (15.3% vs 2.7%).
Gali et al.[104]	Prospective cohort study	693 patients with completed Flemons Criteria and SACS score	Flemons Criteria and SACS score	Orthopedic, Gyn, ENT, Urologic, Thoracic, Plastics, Neurosurgery, General abdominal	Arrhythmia, MI, ICU admission, pneumonia, need for the ventilator support	Postoperative respiratory events were associated with high SACS and PACU events
Liao et al.[95]	Retrospective matched cohort study	240 patients with OSA and 240 matched controls	International Classification of Disease (ICD-9) codes	Cardiac, ENT, Orthopedic, Spine, Urologic, General, Gyn, and Plastic	Hypoxemia, pulmonary edema, bronchospasm, arrhythmia, confusion	Patients with OSA had a higher incidence of postoperative complications (48% vs 36%)
Vasu et al.[16]	Historical cohort study	135 patients with completed STOP BANG Questionnaire	STOP BANG Questionnaire	Orthopedic, Abdominal, Head and Neck, ENT, Gyn, Vascular, Cardiothoracic	Hypoxemia, pneumonia, pulmonary embolism, atelectasis, hypotension, atrial fibrillation	Patients with high-risk of sleep apnea based on STOP BANG Questionnaire had a higher rate of postoperative complications (19.6% vs 1.3%) and the hospital length of stay.

PSG, polysomnography; ICU, Intensive Care Unit; SACS, Sleep Apnea Clinical Score; PACU, Postanesthesia Care Unit.

Table 1 continues on the following page

Table1 (*continued*)—Studies reporting association between obstructive sleep apnea and perioperative complications

Author	Type of Study	Number of Patients	Diagnosis of OSAS	Type of Surgeries	Complications	Results
Stierer et al.[107]	Prospective cohort study	A cohort of 2139 patients who underwent ambulatory surgical procedure	Probability of OSA based on demographic and questionnaire including Maislin index score	Orthopedic, ENT, Gyn, Plastic, Neurologic, Urologic, and general outpatient surgical procedures	Unplanned hospital admission, hypoxemia, cardiac arrhythmia, re-intubation, re-admission within 24 h of discharge, and need for lung ventilation	Increased propensity for OSA was not associated with unplanned hospital admission. However, it was associated with difficult intubation, increased oxygen requirement, and intraoperative tachycardia with increased need for labetalol or metoprolol.
Memtsoudis et al.[101]	Case control study	58358 orthopedic patients with OSA and 45547 general surgery patients with OSA were matched for controls in 1:3 manner	International Classification of Disease (ICD-9) codes	Orthopedic and general surgery	Aspiration pneumonia, pulmonary embolism, need for intubation and mechanical ventilation, ARDS	Patients with sleep apnea undergoing orthopedic and general surgeries were at a higher risk of aspiration pneumonia, ARDS, and the need for intubation and mechanical ventilation.
Kaw et al.[103]	Cohort study	471 patients who underwent non-cardiac surgery within 3 years of PSG	Patients with an apnea-hypopnea index (AHI) ≥ 5/h were defined as OSA, and those with AHI < 5 as controls	Non-cardiac surgery	Atrial fibrillation, respiratory failure, hypoxemia, delirium, transfer to ICU, congestive heart failure, myocardial infarction, hospital length of stay	Patients with OSA had a higher rate of postoperative hypoxemia (12.4% vs 2.1%), transfer to ICU (6.7% vs 1.6%), any complication (14.2% vs 2.6%), and hospital length of stay.

PSG, polysomnography; ICU, Intensive Care Unit; SACS, Sleep Apnea Clinical Score; PACU, Postanesthesia Care Unit.

16.2. ANNEX 2- STOP-Bang SCALE (18)

Cuestionario STOP-Bang actualizado

Si	No	
♣	♣	**¿Ronquidos?** ¿**Ronca fuerte** (tan fuerte que se escucha a través de puertas cerradas o su pareja lo codea por roncar de noche)?
♣	♣	**¿Cansado/a?** ¿Se siente con frecuencia **cansado, fatigado, o somnoliento** durante el día (por ejemplo, se queda dormido mientras conduce)?
♣	♣	**¿Lo observaron?** ¿Alguien lo **observó dejar de respirar o ahogarse/con dificultad para respirar** mientras dormía?
♣	♣	**¿Presión?** ¿Tiene o está recibiendo tratamiento para la **presión arterial alta**?
♣	♣	**¿Índice de masa corporal de más de 35 kg/m^2?**
♣	♣	**¿Tiene más de 50 años?**
♣	♣	**¿El tamaño de su cuello es grande? (Medido alrededor de la nuez o manzana de Adán)** Si es hombre, ¿el cuello de su camisa mide 17 pulgadas/43 cm o más? Si es mujer, ¿el cuello de su camisa mide 16 pulgadas/41 cm o más?
♣	♣	**Sexo = ¿Masculino?**

Criterios de calificación para la población en general

- **Bajo riesgo de AOS (Apnea Obstructiva del Sueño):** Sí a 0-2 preguntas
- **Riesgo intermedio de AOS (Apnea Obstructiva del Sueño):** Sí a 3-4 preguntas
- **Alto riesgo de AOS (Apnea Obstructiva del Sueño):** Sí a 5-8 preguntas o si respondió "sí" a 2 o más de las primeras 4 preguntas y es del sexo masculino o si respondió "sí" a 2 o más de las primeras 4 preguntas y su IMC es más de 35 kg/m^2 o si respondió "sí" a 2 o más de las primeras 4 preguntas y la circunferencia de su cuello es: (17"/43cm en hombres, 16"/41cm en mujeres)

Predictive Performance of Combination of Two Items From STOP and One From Bang for Identifying Patients With Moderate to Severe Obstructive Sleep Apnea (Apnea-Hypopnea Index > 15)

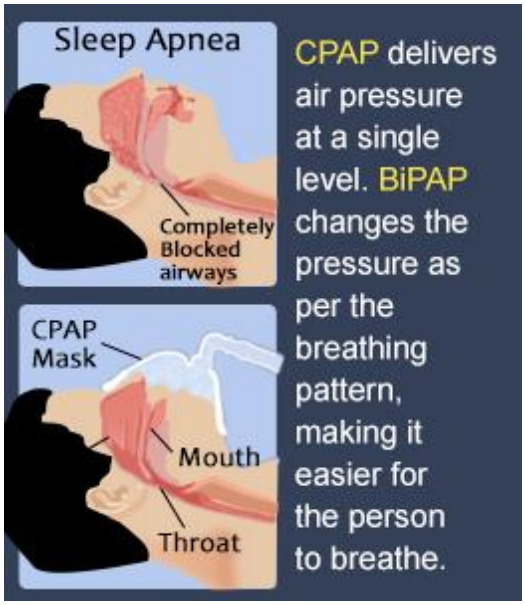
Cutoff	Sensitivity	Specificity	PPV	NPV
STOP-Bang ≥ 3	87.3 (81.8-91.6)	30.7 (25.7-36.1)	43.8 (38.8-48.8)	79.7 (71.5-86.4)
STOP ≥ 2 + Bang ≥ 1	71.6 (64.7-77.8)	46.1 (40.5-51.7)	45.0 (39.5-50.7)	72.4 (65.7-78.4)
STOP ≥ 2 + BMI > 35 kg/m^2	20.8 (15.4-27.2)	85.0 (80.6-88.7)	46.1 (35.4-57.0)	63.5 (58.7-68.0)
STOP ≥ 2 + Neck > 40 cm	33.5 (27.0-40.6)	79.0 (74.1-83.3)	49.6 (40.8-58.4)	65.8 (60.8-70.5)
STOP ≥ 2 + male gender	40.1 (33.2-47.3)	76.8 (71.8-81.3)	51.6 (43.4-59.8)	67.5 (62.4-72.3)
STOP ≥ 2 + age > 50 y	59.4 (52.2-66.3)	56.1 (50.5-61.6)	45.5 (39.3-51.8)	69.1 (63.1-74.7)

Data are presented as average (95% CI). Bang = BMI, age, neck circumference, and male gender; NPV = negative predictive value; PPV = positive predictive value; STOP = snoring, tiredness, observed apnea, and high BP. (Adapted with permission Chung et al.[43])

16.3. ANNEX 3 – CPAP (17)

Continuous Positive Airway Pressure (CPAP) is a type of noninvasive respiratory support, it is a form of ventilator assistance that is applied to the patient through an external interface, such as a facial, nasal, or head appliance. Select groups of surgical patients may have a higher risk of postoperative pulmonary complications (PPCs) due to intrinsic patient characteristics, such as obesity, or specific to the surgical procedure. In such settings, CPAP could improve outcomes by avoiding the increased cost and higher mortality associated with respiratory failure that can follow PPC.

The most critical aspect of delivery of noninvasive respiratory support is the external nonsealed patient-ventilator interface. Consequentially, air leaks of variable amount are common and depend on mask fitting as well as patient facial characteristics. Leaks interfere with ventilator functioning and contribute to patientventilator asynchrony. The ventilators dedicated for Noninvasive respiratory support rely on turbine-driven bi-level pressure generators to guarantee the desired inspiratory and expiratory pressures. Patients inspire through a single limb circuit, whereas expiration occurs through a controlled-leak valve, which is usually placed in proximity to the mask to limit the amount of rebreathing. External oro-nasal masks are the most commonly used patient-ventilator interfaces in the acute setting, due to their perceived increased tolerability. Indeed, device intolerance can limit the effectiveness of CPAP, leading to recurrent hypoxemia and hypercapnia. Mask application can lead to complications such as skin ulcerations and necrosis. An alternate approach is use of a semi-rigid helmet with a soft collar fitting to deliver CPAP, which is accomplished without a ventilator.

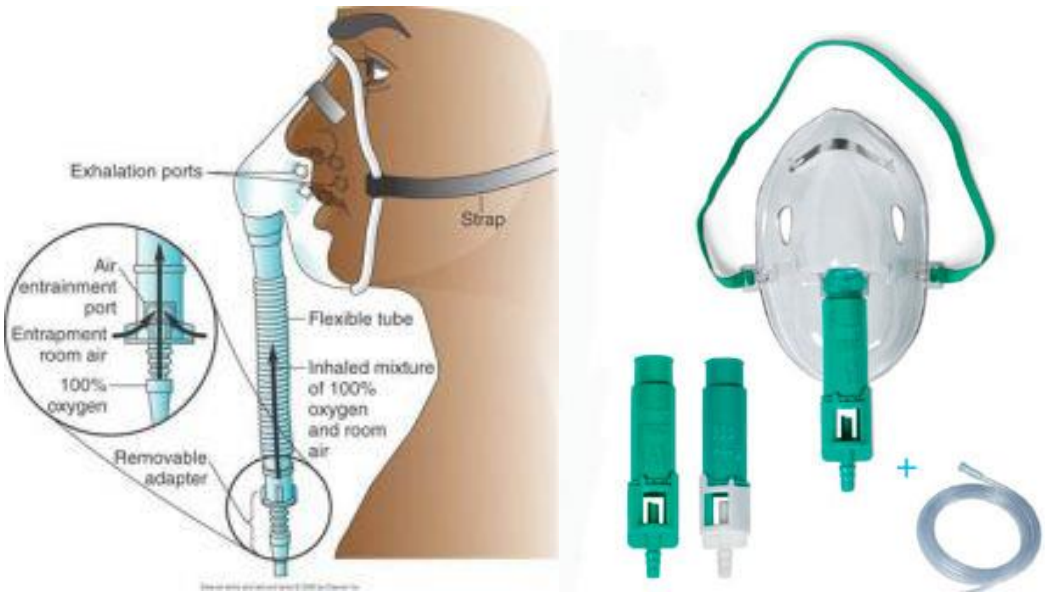


16.4. ANNEX 4 – VENTIMASK

Venturi mask (Ventimask): is a high flow oxygen therapy device:

- They allow us to administer oxygen at different concentrations, corresponding to each concentration a determined amount of liters per minute.

- Allows the administration of an exact concentration of oxygen, allowing FiO2 levels of between 24-50%, with an amount of liters per minute that oscillates between 3-15 liters. This system follows the Bernoulli principle, ie the device mixes oxygen with ambient air through holes of different diameter.



16.5. ANNEX 5 – ASA SCALE (CLASSIFICATION REGARDING ANESTHETIC RISK)

ASA PS Classification	Definition	Examples, including, but not limited to:
ASA I	A normal healthy patient	Healthy, non-smoking, no or minimal alcohol use
ASA II	A patient with mild systemic disease	Mild diseases only without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30 < BMI < 40), well-controlled DM/HTN, mild lung disease
ASA III	A patient with severe systemic disease	Substantive functional limitations; One or more moderate to severe diseases. Examples include (but not limited to): poorly controlled DM or HTN, COPD, morbid obesity (BMI ≥40), active hepatitis, alcohol dependence or abuse, implanted pacemaker, moderate reduction of ejection fraction, ESRD undergoing regularly scheduled dialysis, premature infant PCA < 60 weeks, history (>3 months) of MI, CVA, TIA, or CAD/stents.
ASA IV	A patient with severe systemic disease that is a constant threat to life	Examples include (but not limited to): recent (< 3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or ESRD not undergoing regularly scheduled dialysis
ASA V	A moribund patient who is not expected to survive without the operation	Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction
ASA VI	A declared brain-dead patient whose organs are being removed for donor purposes	

16.6. ANNEX 6 – MALLAMPATI CLASSIFICATION

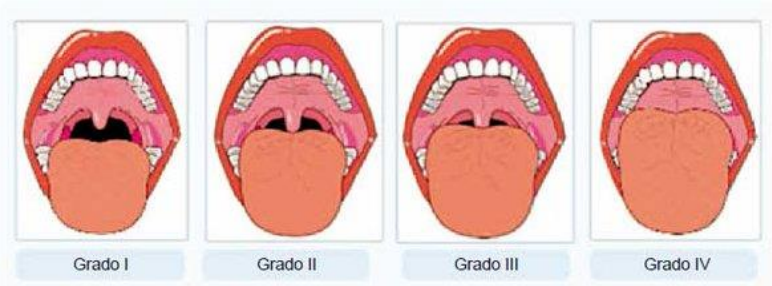
Score Mallampati to try to predict a probable difficult intubation. Its application may be useful in patients with probable OSA. It is performed simply with the patient in a seated position and maximum oral opening without phonation. Evaluates in four degrees the vision capacity of the oropharynx and used by anesthetists to predict the difficulty of intubation (**Mallampati classification**):

- **Class I**: you can see the soft palate, the jaws, the uvula and the tonsillar pillars.

- **Class II**: the soft palate, the jaws and the uvula can be seen partially. The uvula contacts the base of the tongue.

- **Class III**: the soft palate and the base of the uvula can be seen.

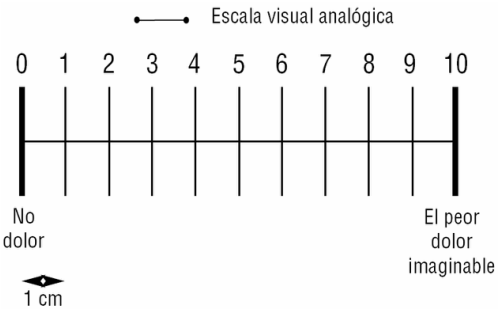
- **Class IV**: you can only see hard palate and the rest is out of sight.



16.7. ANNEX 7 – VAS SCALE

VISUAL ANALOGUE SCALE – (VAS) EVA in Spanish.

It allows measuring the intensity of the pain with the maximum reproducibility between the observers. It consists of a horizontal line of 10 centimeters, at the ends of which are the extreme expressions of a symptom. In the left one is located the absence or less intensity and in the right the greater intensity. The patient is asked to mark on the line the point that indicates the intensity and is measured with a millimeter rule. The intensity is expressed in centimeters or millimeters.



16.8. ANNEX 8 – INFORMATION SHEET

HOJA DE INFORMACIÓN AL PACIENTE

TÍTULO DEL ENSAYO CLÍNICO: Can the use of postoperative CPAP in patients at high risk of OSA reduce desaturation episodes after surgery? Clinical trial, unicentric, randomized, with simple blind and parallel design.

INTRODUCCION: Nos dirigimos a usted para informarle sobre un estudio de investigación en el que se le invita a participar. El estudio ha sido aprobado por el Comité Ético de Investigación Clínica del Hospital Universitari de Girona Dr.Josep Trueta y la Agencia Española del Medicamento y Productos Sanitarios (AEMPS), de acuerdo a la legislación vigente, el Real Decreto 223/2004, de 6 de febrero, por el que se regulan los ensayos clínicos con medicamentos. Nuestra intención es tan solo que usted reciba la información correcta y suficiente para que pueda evaluar y juzgar si quiere o no participar en este estudio. Para ello lea esta hoja informativa con atención y nosotros le aclararemos las dudas que le puedan surgir después de la explicación. Además, puede consultar con las personas que considere oportuno.

PARTICIPACIÓN VOLUNTARIA: Debe saber que su participación en este estudio es voluntaria y que puede decidir no participar o cambiar su decisión y retirar el consentimiento en cualquier momento, sin que ello altere la relación con su médico ni se produzca perjuicio alguno en su tratamiento.

DESCRIPCIÓN DEL ESTUDIO: La apnea obstructiva del sueño es una enfermedad respiratoria. Su incidencia está directamente relacionada con la edad y el peso. Como no se realiza un adecuado diagnóstico ni tratamiento en las personas previamente diagnosticadas, actualmente es una causa importante de morbilidad y menos importante mortalidad en las UCIs hospitalarias, particularmente en los pacientes sometidos a cirugía mayor.

El uso de CPAP de manera continua ha demostrado mejorar la calidad de vida en población general con diagnóstico de SAOS. El objetivo de nuestro estudio es evaluar la eficacia del uso de CPAP versus mascarilla naso-bucal de oxígeno (Ventimask) en la reducción de las desaturaciones de hemoglobina (Saturación ≤ 94%), número de días de estancia hospitalaria, mortalidad relacionada con el SAOS. Para ello se ha diseñado este ensayo clínico donde se administrará de forma aleatoria el CPAP o la mascarilla naso-bucal de oxígeno (Ventimask). Al ser un proceso aleatorizado todos los pacientes tienen las mismas probabilidades de recibir CPAP o Ventimask.

PROCEDIMIENTOS DEL ENSAYO: Todos los pacientes se someterán a una sesión de fisioterapia respiratoria antes de la cirugía con un facultativo especializado del hospital. Se pondrá el CPAP con una demora de máximo 30 minutos tras finalizar la cirugía, en el grupo de

máscara de oxígeno también se empezará como mucho 30 minutos después y se mantendrá durante las 24 primeras horas tras la cirugía. El CPAP se administrará con una concentración de oxígeno al 50% y una PEEP de 8-10 mm H2O. La mascarilla de oxígeno contendrá una concentración de flujo del 50% de oxígeno pero sin el aporte de una presión continua.

BENEFICIOS Y RIESGOS DERIVADOS DE SU PARTICIPACIÓN EN EL ESTUDIO: Este estudio pretende ser una referencia, para iniciar el tratamiento preventivo con CPAP en los pacientes con alto riesgo de SAOS que se someten a cirugía. Se realizarán análisis evaluadores internos durante el transcurso del estudio, para asegurar que no hay diferencias clínicamente relevantes entre los dos grupos de estudio. CPAP no describe efectos secundarios. Aun así el estudio se realiza en pacientes con alto riesgo de SAOS, no con diagnóstico confirmado, por lo que no se pueden garantizar la ausencia de efectos adversos. Los pacientes que reciban CPAP así como el grupo control recibirán monitorización para detectar posibles efectos secundarios como la mala adaptación a la máquina o irritación en la piel.

SEGURO: Según lo establecido en el RD 223/2004, el promotor del ensayo ha contratado una póliza de responsabilidad civil que cubre los posibles daños y perjuicios que le pudiera ocasionar su participación en el ensayo clínico.

COMPENSACIÓN ECONÓMICA: Su participación en el estudio no le supondrá ningún gasto. Usted no tendrá que pagar por el CPAP ni recibirá una compensación económica.

CONFIDENCIALIDAD: El tratamiento, la comunicación y la cesión de los datos de carácter personal de todos los sujetos participantes se ajustará a lo dispuesto en la Ley Orgánica 15/1999, de 13 de diciembre de protección de datos de carácter personal. De acuerdo a lo que establece la legislación mencionada, usted podrá ejercer los derechos de acceso, modificación, oposición y cancelación de datos, para lo cual deberán dirigirse a su médico del estudio. Los datos recogidos para el estudio estarán identificados mediante un código y solo su médico del estudio/colaboradores podrán relacionar dichos datos con usted y con su historia clínica.

En el caso de que se produzca esta cesión, será para los mismos fines del estudio descrito y garantizando la confidencialidad como mínimo con el nivel de protección de la legislación vigente en nuestro país. El acceso a su información personal quedará restringido al médico del estudio/colaboradores, autoridades sanitarias (Agencia Española del Medicamento y Productos Sanitarios), al Comité Ético de Investigación Clínica y personal autorizado por el promotor, cuando lo precisen para comprobar los datos y procedimientos del estudio, pero siempre manteniendo la confidencialidad de los mismos de acuerdo a la legislación vigente.

Si usted decide retirar el consentimiento para participar en este estudio, ningún dato nuevo será añadido a la base de datos y puede exigir la destrucción de todas las muestras identificables previamente retenidas para evitar la realización de nuevos análisis.

16.9. ANNEX 9- INFORMED CONSENT

HOJA DE CONSENTIMIENTO INFORMADO AL PACIENTE

TÍTULO DEL ESTUDIO: Can the use of postoperative CPAP in patients at high risk of OSA reduce desaturation episodes after surgery?

Yo, Sr/Sra ……., con DNI ……

Confirmo que:

- He leído y he entendido la Hoja de Información para el Paciente y el formulario de Consentimiento Informado. Entiendo que podré conservar una copia de ambos.

- He tenido la oportunidad de hacer cualquier pregunta sobre el estudio y he obtenido una respuesta satisfactoria.

He hablado con (nombre del investigador/médico) ……

- He entendido que mi participación es totalmente voluntaria y que puedo abandonar el estudio en cualquier momento por cualquier razón y sin que suponga ningún tipo de consecuencia en mi futura atención sanitaria.

- En consecuencia doy permiso al personal del estudio para que consulte mi historia clínica con fines de verificación de datos y mi información recopilada durante el estudio. Siempre en conformidad con la Ley Orgánica 15/1999, de 13 de diciembre, sobre protección de datos de carácter personal.

En consecuencia, doy mi conformidad para participar en este estudio.

☐ SI ☐ NO

Permito que la información que se obtenga de este estudio sea utilizada en investigaciones futuras relacionadas con enfermos de SAOS.

☐ SI ☐ NO

Permito que la información sea introducida en la base de datos del hospital.

☐ SI ☐ NO

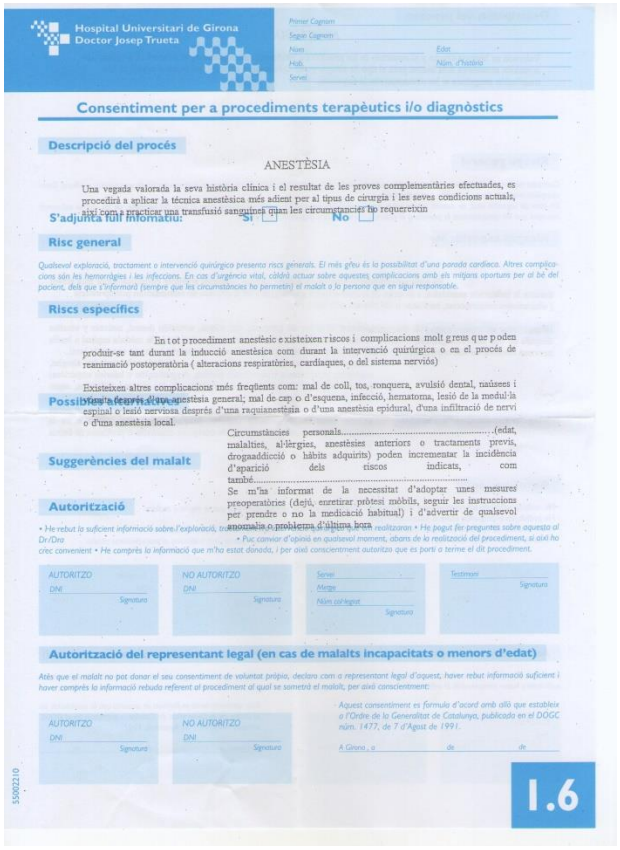
Firma del padre/madre/tutor del participante:

Fecha: __ __ / __ __ / __ __

Firma del investigador:

Fecha: __ __ / __ __/ __ __

16.10. ANNEX 10 - INFORMED CONSENT OF ANESTHESIA



Hospital Universitari de Girona Doctor Josep Trueta

Consentiment per a procediments terapèutics i/o diagnòstics

Descripció del procés

ANESTÈSIA

Una vegada valorada la seva història clínica i el resultat de les proves complementàries efectuades, es procedirà a aplicar la tècnica anestèsica més adient per al tipus de cirurgia i les seves condicions actuals, així com a practicar una transfusió sanguínia quan les circumstàncies ho requereixin

S'adjunta full informatiu: Sí ☐ No ☐

Risc general

Qualsevol exploració, tractament o intervenció quirúrgica presenta riscs generals. El més greu és la possibilitat d'una parada cardíaca. Altres complicacions són les hemorràgies i les infeccions. En cas d'urgència vital, caldrà actuar sobre aquestes complicacions amb els mitjans oportuns per al bé del pacient, dels que s'informarà (sempre que les circumstàncies ho permetin) el malalt o la persona que en sigui responsable.

Riscs específics

En tot procediment anestèsic existeixen riscos i complicacions molt greus que poden produir-se tant durant la inducció anestèsica com durant la intervenció quirúrgica o en el procés de reanimació postoperatòria (alteracions respiratòries, cardíaques, o del sistema nerviós)

Existeixen altres complicacions més freqüents com: mal de coll, tos, ronquera, avulsió dental, naúsees i vòmits després d'una anestèsia general; mal de cap o d'esquena, infecció, hematoma, lesió de la medul·la espinal o lesió nerviosa després d'una raquianestèsia o d'una anestèsia epidural, d'una infiltració de nervi o d'una anestèsia local.

Possibles alternatives

Suggerències del malalt

Circumstàncies personals.....(edat, malalties, al·lèrgies, anestèsies anteriors o tractaments previs, drogaadicció o hàbits adquirits) poden incrementar la incidència d'aparició dels riscos indicats, com també.....

Se m'ha informat de la necessitat d'adoptar unes mesures preoperatòries (dejú, endreçar pròtesi mòbils, seguir les instruccions per prendre o no la medicació habitual) i d'advertir de qualsevol anomalia o problema d'última hora

Autorització

• He rebut la suficient informació sobre l'exploració, tractament o intervenció quirúrgica que se'm va a realitzar • He pogut fer preguntes sobre aquesta al Dr./Dra • Puc canviar d'opinió en qualsevol moment, abans de la realització del procediment, si així ho crec convenient • He comprès la informació que m'ha estat donada, i per això conscientment autoritzo que es porti a terme el dit procediment.

AUTORITZO	NO AUTORITZO	Servei / Metge / Núm col·legiat	Testimoni
DNI / Signatura	DNI / Signatura	Signatura	Signatura

Autorització del representant legal (en cas de malalts incapacitats o menors d'edat)

Atès que el malalt no pot donar el seu consentiment de voluntat pròpia, declara com a representant legal d'aquest, haver rebut informació suficient i haver comprès la informació rebuda referent al procediment al qual se sometrà el malalt, per això conscientment:

Aquest consentiment es formula d'acord amb allò que estableix a l'Ordre de la Generalitat de Catalunya, publicada en el DOGC núm. 1477, de 7 d'Agost de 1991.

AUTORITZO	NO AUTORITZO
DNI / Signatura	DNI / Signatura

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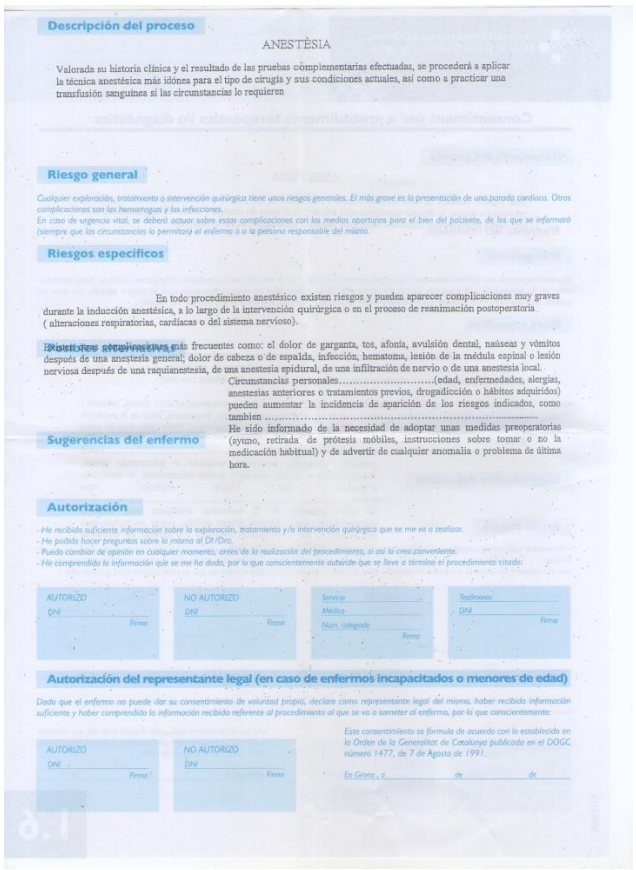

Descripción del proceso

ANESTÈSIA

Valorada su historia clínica y el resultado de las pruebas complementarias efectuadas, se procederá a aplicar la técnica anestésica más idónea para el tipo de cirugía y sus condiciones actuales, así como a practicar una transfusión sanguínea si las circunstancias lo requieren

Riesgo general

Cualquier exploración, tratamiento o intervención quirúrgica tiene unos riesgos generales. El más grave es la presentación de una parada cardíaca. Otras complicaciones son las hemorragias y las infecciones.
En caso de urgencia vital, se deberá actuar sobre estas complicaciones con los medios oportunos para el bien del paciente, de los que se informará (siempre que las circunstancias lo permitan) al enfermo o a la persona responsable del mismo.

Riesgos específicos

En todo procedimiento anestésico existen riesgos y pueden aparecer complicaciones muy graves durante la inducción anestésica, a lo largo de la intervención quirúrgica o en el proceso de reanimación postoperatoria (alteraciones respiratorias, cardíacas o del sistema nervioso).

Existen otras complicaciones más frecuentes como: el dolor de garganta, tos, afonía, avulsión dental, náuseas y vómitos después de una anestesia general; dolor de cabeza o de espalda, infección, hematoma, lesión de la médula espinal o lesión nerviosa después de una raquianestesia, de una anestesia epidural, de una infiltración de nervio o de una anestesia local.

Sugerencias del enfermo

Circunstancias personales.....(edad, enfermedades, alergias, anestesias anteriores o tratamientos previos, drogadicción o hábitos adquiridos) pueden aumentar la incidencia de aparición de los riesgos indicados, como tambien .....

He sido informado de la necesidad de adoptar unas medidas preoperatorias (ayuno, retirada de prótesis móbiles, instrucciones sobre tomar o no la medicación habitual) y de advertir de cualquier anomalia o problema de última hora.

Autorización

- He recibido suficiente información sobre la exploración, tratamiento y/o intervención quirúrgica que se me va a realizar.
- He podido hacer preguntas sobre la misma al Dr./Dra.
- Puedo cambiar de opinión en cualquier momento, antes de la realización del procedimiento, si así lo creo conveniente.
- He comprendido la información que se me ha dado, por lo que conscientemente autorizo que se lleve a término el procedimiento citado.

AUTORIZO	NO AUTORIZO	Servicio / Médico / Núm. colegiado	Testimonio
DNI / Firma	DNI / Firma	Firma	DNI / Firma

Autorización del representante legal (en caso de enfermos incapacitados o menores de edad)

Dada que el enfermo no puede dar su consentimiento de voluntad propia, declara como representante legal del mismo, haber recibido información suficiente y haber comprendido la información recibida referente al procedimiento al que se va a someter al enfermo, por lo que conscientemente:

Este consentimiento se formula de acuerdo con lo establecido en la Orden de la Generalitat de Catalunya publicada en el DOGC número 1477, de 7 de Agosto de 1991.

AUTORIZO	NO AUTORIZO
DNI / Firma	DNI / Firma

En Girona , a de de

16.11. ANNEX 11 - DATA COLLECTION SHEET (CRF)

PATIENT IDENTIFICATION NUMBER: ___ ___ ___ ___ ___

AGE: SEX:

MEDICAL INFORMATION:

- BMI:
- Diabetes:
- ASA:
- Time of surgery
- Smoker:
- Blood hypertension:
- CPAP pre-study:
- Basal hemoglobin saturation:

IN THE OPERATIVE ROOM: Desaturation episodes:

NUMBER												
SEVERITY												
TIME OF DURATION												
TIME OF DAY (H)												

24 HOURS AFTER SURGERY: Desaturation episodes:

NUMBER												
SEVERITY												
TIME OF DURATION												
TIME OF DAY (H)												

48 HOURS AFTER SURGERY: Desaturation episodes:

NUMBER												
SEVERITY												
TIME OF DURATION												
TIME OF DAY (H)												

OTHER DATES:

- Days of hospital stay:
- Development of respiratory complications (if so, indicate which and why they appear):
- Death:

16.12. ANNEX 12 – NUMBER OF TRUETA SURGERIES

Tipo de anestesia		Intervenciones totales	IQ programadas convencional	IQ urgentes	IQ CMA	IQ C. menor
CB/TR00196	Anestesia General	**1.776**	1.386	275	113	2
CB/TR00273	Anèstesia general balancejada	**322**	236	60	26	
CB/TR00274	Anèstesia general endovenosa	**13**	10	1	2	
CB/TR00470	Anestèsia Inhalatòria	**6**	2		4	
CB/TR00194	Anestèsia Local	**144**	20	5	119	
CB/TR00197	Anestèsia Locoregional	**21**	13	5	3	
CB/TR00281	Anestesia locoregional abdominal	**4**	3	1		
CB/TR00284	Anestesia locoregional craneo facial	**1**	1			
CB/TR00279	Anestesia locoregional de membre inferio	**19**	13	4	2	
CB/TR00278	Anestesia locoregional de membre superio	**25**	15	5	5	
CB/TR00282	Anestesia locoregional genitourinari/per	**14**	9	5		
CB/TR00283	Anestesia locoregional oftalmologica	**168**	1		167	
CB/TR00199	Anestesia Otros	**4**			3	1
CB/TR00195	Anestèsia Sedación	**202**	24	8	170	
CB/TR00198	Anestesia tecnicas combinadas	**125**	119	3	3	
CB/#	Arcos de rayos X	**6.824**	1.952	2.275	1.773	824
CB/TR00275	Bloqueix neuroaxial intradural	**752**	572	132	48	
CB/TR00276	Bloqueix neuroaxial epidural	**38**	17	21		
CB/TR00215	Locoregional + Sedació	**80**	23	2	54	1
CB/TR00287	Sedació endovenosa	**73**	10	13	50	
CB/TR00286	Sedació inhalatoria	**3**	1		2	
Resultado total		**10.614**	4.427	2.815	2.544	828

This document has been facilitated by the technical secretary of the Josep Trueta University Hospital and includes the number of surgeries performed in that hospital in 2015, and stratifies them according to the type of anesthesia used. We have based this document to estimate sample collection time, estimating that 20% of the surgical population is at high risk for OSA and choosing surgeries with general anesthesia and that are not urgent, adding a **total of 1753 surgeries**:

- General anesthesia: 1.386 no-emergency surgery.
- Balanced general anesthesia: 236 no-emergency surgery.
- General intravenous anesthesia: 10 no-emergency surgery.
- Anesthetics Inhalation: 2 no-emergency surgery.
- Anesthesia combined techniques: 119 no-emergency surgery.