Impact of Maxillomandibular Advancement Upon the Pharyngeal Airway Volume and the Apnea-hypopnea Index in the Treatment of Obstructive Sleep Apnea.

PROTOCOL VERSION 1.0
OCTOBER 30, 2017

RUNNING TITLE: OSAS-OS - Maxillomandibular Advancement in the Treatment of Obstructive Sleep Apnea

NCT No: NCT03796078

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Date: 30.10.2017

Version: V1.0

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Abstract:

Aim: To study the correlation between PAV (pharyngeal airway volume), the clinical indicators of OSA (obstructive sleep apnea) and the impact of orthognathic surgery on them.

METHODS: A prospective, descriptive, unicentric three-arm study carried out by a multidisciplinary team to evaluate the following parameters in patients receiving orthognathic surgery during the study period:

- First arm: patients with OSA treated in terms of bimaxillary orthognathic surgery
- Second arm: patients with OSA treated in terms by Maxillary surgery solely.
- Third arm: patients with OSA treated in terms of mandibular surgery solely.

Key Words: Orthognathic surgery; Three- dimensional analysis; Upper Airway; cone-beam; Obstructive Sleep Apnea Syndrome; Obstructive Sleep Apnea.

I. Introduction

Sleep apnea-hypopnea syndrome (OSA) is estimated to affect 5-20% of the general Spanish adult population, although a study by Duran et al. 1 reports figures of up to 26%, and it is 2-3 times more common in men than in women 1. In addition, statistics show that more than 50% of affections are not and will not be diagnosed. In Spain, according to studies carried out in different age subgroups, it is estimated that there are between 5 and 7 million people who suffer from sleep apnea 1,2.

It is dyssomnia with respiratory pauses secondary to partial (hypopnea) or complete (apnea) obstruction of the upper airway (UA) 3.

The upper airway is occluded due to a drop in muscle tone of the upper airway dilator muscles during sleep, leading to partial narrowing or complete obstruction. The direct consequences of these episodes are the repetitive decrease in blood oxygen saturation and transient and recurrent awakenings from sleep caused by increased respiratory effort, which causes a reduction in the quality of sleep 3. When all these disorders They are also accompanied by clinical manifestations, such as excessive daytime sleepiness (EDS), neuropsychiatric, metabolic, respiratory and cardiac alterations, we classify it as OSA 3,4.

Recent studies suggest that patients with undiagnosed OSA consume between 2-3 times more resources than the general population 1,2. Most of the costs are attributable to more days of hospital stay, more consultations in specialized care and an increase in the pharmacological treatment prescribed 2.

The diagnosis of OSA requires the recording of multiple physiological signals during sleep 1-3. The reference diagnostic test, considered as the standard pattern for the detection of OSA, is polysomnography (PSG) 1-8. This consists of recording brain activity, breathing, heart rate, muscle activity, snoring and blood oxygen levels while sleeping. It is a test indicated for different sleep disorders such as OSA; and it is done at night. Thus, PSG records repeated episodes of upper airway obstruction during sleep, and these episodes are measured with the apnea-hypopnea index (AHI) 1-8. An AHI greater than 5 per hour associated with symptoms not explained by another cause would lead to the diagnosis of the disease 1-4.

Currently, the standard treatment of patients with OSA is by means of a CPAP (continuous positive airway pressure) device, which has limited degrees of compliance and tolerance (less than 50%), due to the discomfort of the device 1,3 ,5-8.

However, advancement surgery of the maxillary-mandibular complex has shown a success rate of 86% 5-9,12-19. Several studies have also been carried out that support that advancement surgery of the maxillary-mandibular complex increases the volume of the upper airway through direct imaging with endoscopy or 3D imaging studies with CBCT (Cone Beam Computed Tomography), CT (Computed Tomography) or MRN (Magnetic Resonance) 20-22. These surgical procedures were previously considered aggressive techniques with long and heavy postoperative periods, but today, with the appearance of virtual planning protocols and minimally invasive surgical techniques, the surgical time for these procedures is around two hours, they are performed generally in a 24-h hospitalization regimen and the postoperative ones are very well tolerated by the vast majority of patients 20-22 .

Despite this, to date there are no published studies that relate the impact of the replacement surgery of each one of the jaws in the three dimensions of space and the 3D volumetric changes of the UA obtained with it, on the AHI and other indicators. clinics of patients with SAHS. For this reason, the objective of this project is to correlate each of the movements of the maxillomandibular complex in the three axes of space performed during orthognathic surgery, with the volume of the UA, the AHI and the clinical indicators of OSA.

II. *Objectives*

OBJECTIVES: To study the correlation between pharyngeal airway volume (PAV), the clinical indicators of obstructive sleep apnea (AHI, ESS), and the impact of orthognathic surgery on them.

During the study period:

- Record of the type, magnitude and direction of surgical movements of the maxillofacial complex made during the surgery (Day 0-Month 1).
- Assessment of PAS/PAV stability (relapse) at short term (1 month).

3D PAV assessment by cranial voxel-based superimposition protocol before and one month and 12 months after orthognathic surgery.

- Household polysomnography (PSG) registry/ apnea-hypopnea index (Day 0, Month 1 and Month 12). (AHI evaluation bu neurophysiologist)
- Assessment of the clinical indicators of obstructive sleep apnea at day 0, month 1 and month 12:, blood pressure (mm Hg) , and daytime hypersomnia test (Epworth sleepiness scale, ESS) (Day 0, Month 1 and Month 12).
- Record of body mass index (BMI) (cm/Kg2)

Main Objective:

• Evaluate the impact of orthognathic surgery (bimaxillary or monomaxillary) and its movements on the PAV and the clinical indicators of OSA.

Specific objectives:

- Interrelate the degree of dentofacial deformity with the IAH.
- Study the potential correlation between the volume of the VAS and the IAH.
- Correlate the type, direction and magnitude of the surgical movements of the maxillofacial complex with PAV/PAS increase Correlate the type, direction and magnitude of the surgical movements of the maxillofacial complex with the cure of OSA (household PSG AHI assessment) and the following clinical indicators of OSA: diurnal hypersomnia test (ESD, ESS).
- Evaluate negative effects of either maxillary or mandibular surgical movements in PAS/PAV increase and the cures of OSA.
- Evaluate negative effects of either maxillary or mandibular surgical movements in the improvement of the clinical symptoms and the cure of OSA.
- To study the possible effect of surgical complications on PAS/PAV stability at long term and the clinical symptoms of OSA.
- Demonstrate that maxillomandibular surgery is a defined, predictable and a definitive cure for OSA.
- Demonstrate that skeletal, linear, and cross-sectional volume parameters remain stable at long-term.
- Demonstrate that AHI and OSA-related parameters stay stable at long term after mono- or bimaxillary surgery.

Hypothesis

- **H1a:** Maxillomandibular advancement (orthognathic surgery) does correlate with the volume of the upper airway, at both short or long term.
- **H2a:** Maxillomandibular advancement (orthognathic surgery) does correlate with the clinical indicators of obstructive sleep apnea, at both short or long term.

Material and methods

METHODS: A prospective, descriptive, unicentric study carried out by a multidisciplinary team to evaluate the following parameters in patients undergoing orthognathic surgery at Maxillofacial institute Teknon medical center.

Study design:
A prospective single-center intervention study will be carried out by a multidisciplinary team made up of oral and maxillofacial surgeons, neurophysiologists, anesthesiologists and nurses, at the Maxillofacial Institute of the Teknon Barcelona Medical Center, together with the Department of Oral and Maxillofacial Surgery of the International University of Catalonia.

- First arm: patients with OSA treated in terms of bimaxillary orthognathic surgery
- Second arm: patients with OSA treated in terms by Maxillary surgery solely.
- Third arm: patients with OSA treated in terms of mandibular surgery solely.

Arms and Interventions

Arms	Assigned Interventions
Active Comparator: Bimaxillary surgery (MMA) Bimaxillary Orthognathic Surgery. MMA	Procedure/Surgery: Maxillomandibular advancement Treatment: Mono or Bimaxillary Orthognathic Surgery. The surgery of Reposition of the jaws is carried out under general anesthesia using minimally invasive techniques, the patient is extubated After surgery, antibiotics are prescribed during admission, anti-inflammatories, antiemetics and a local cold mask is applied of closed circuit at 17ºCelsius. The patient is discharged at 24 h. Other Names: • MMA (maxillomandibular advancement)
Active Comparator: monomaxillary surgery (Isolated MaxS) Monomaxillary surgery (Isolated MaxS)	Procedure/Surgery: monomaxillary surgery (isolated MaxS) Monomaxillary surgery (Isolated MaxS): The surgery of Reposition of the maxilla is carried out under general anesthesia using minimally invasive techniques, the patient is extubated After surgery, antibiotics are prescribed during admission, anti-inflammatories, antiemetics and a local cold mask is applied of closed circuit at 17ºCelsius. The patient is discharged at 24 h.
Active Comparator: monomandibullary surgery (Isolated MandS) Monomandibular surgery (Isolated MandS)	Procedure/Surgery: monomandibullary surgery (MandS) Monomandibullary surgery (Isolated MandS): The surgery of Reposition of the maxilla is carried out under general anesthesia using minimally invasive techniques, the patient is extubated After surgery, antibiotics are prescribed during admission, anti-inflammatories, antiemetics and a local cold mask is applied of closed circuit at 17ºCelsius. The patient is discharged at 24 h.

This research protocol has been accepted by the Ethics Committee (CEIC) of the Maxillofacial Institute of the Teknon Medical Center (Barcelona, Spain) (ANNEX V) and by the CEIC of the International University of Catalonia (Sant Cugat del Vallès, Barcelona, Spain). All enrolled subjects will receive detailed study information and will be offered to sign informed consent prior to the start of the study.

Reference population:
A total of 80 patients, over 18 years of age, surgically treated for dentofacial deformities by orthognathic surgery at the Maxillofacial Institute of the Teknon Medical Center, Barcelona, will be included in the study.

All subjects included in the study will undergo home portable PSG which will be evaluated by a specialist in neurophysiology. Portable devices have proven to be an acceptable alternative method for diagnosis in subjects with a high pretest probability of at least moderate or severe OSA, and who do not have cardiopulmonary impairment. In the event of upper airway obstruction, they will be evaluated together with the otorhinolaryngology service of the Teknon Medical Center, Barcelona.

Sample size:
It has been decided to include a sample of 80 patients in order to obtain statistically significant results. This sample size will allow us to complete the recruitment in 18 months.

To be included in the study, patients must meet the following criteria:

Inclusion Criteria:

1. Patients over 18 years of age who present any kind of dentofacial deformity candidates for orthognathic surgery
treatment.
2. Growth of the maxillofacial complex completed.
3. Patients without uncontrolled cardio-pulmonary disease.
4. Patients willing to understand the procedures of the study and that agree to give their signed informed consent.
5. Patients who commit to perform the postoperative controls for at least one postoperative year.
6. Patients with a good general condition of health, confirmed by pre-operative study and assessment by Anaesthesiology
(ASA).

Exclusion Criteria:

1. Patients with a clinical history in which any surgery would be contraindicated
2. Patients with any facial Syndromic malformation
3. Patients who have undergone chemotherapy or radiotherapy during the last 5 years, including area of head and neck.
4. Patients who refuse to accept the clinical conditions of the study and are not willing to sign the form corresponding
informed consent.
5. Patients who are expected to lack adherence to follow-up or to

Surgical Procedure

- Patients who meet the eligibility criteria and have given consent for inclusion in the study will be entered into the center's surgical protocol.
- Treatment: Mono or Bimaxillary Orthognathic Surgery. The jaw replacement surgery is carried out under general anesthesia using minimally invasive techniques, the patient is extubated after surgery, antibiotics, anti-inflammatories, and antiemetics are prescribed during admission and a closed circuit local cold mask is applied at 17ºC. The patient is discharged after 24 h.
    - First arm: patients with OSA treated in terms of bimaxillary orthognathic surgery
    - Second arm: patients with OSA treated in terms by Maxillary surgery solely.
    - Third arm: patients with OSA treated in terms of mandibular surgery solely.

Workplan

Initial Visit (T0):

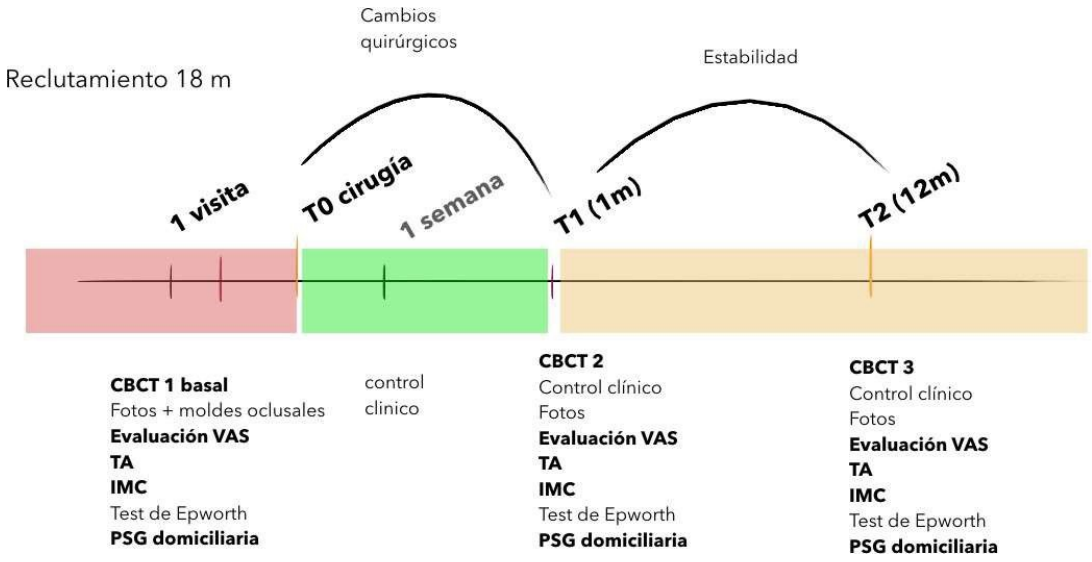
• Preoperative visit (T0) 1 week before surgery performed by the nursing team and staff:

- Explain the study and the procedure to be carried out, giving an information document to the patient and proceeding to sign the informed consent.
- Collection of demographic and clinical variables of interest.
- Record-taking according to the center's treatment protocol for case study and surgical planning: CBCT, intraoral scanning, photos, occlusal records. (Hernández-Alfaro PROTOCOL 2013) 24.
- Explanation of the treatment plan and surgery schedule.
- Assessment of BP**(blood preasure), BMI and Epworth Test(1).
    - ** BP is recorded on two occasions with a time interval of 5 minutes under the same conditions.
- Delivery and placement of the home PSG(1) device.

Follow-up visits (T1-T2):

- Visits carried out by the same team of surgeons who performed the initial visit and the intervention. Patients will be evaluated one month (T1) and 12 months (T2) after surgery. In each of these visits, the patient will be questioned and explored, with the aim of evaluating the post-surgical evolution and the possible appearance of early and late complications typical of the intervention. Apart from the clinical control, a photographic record, CBCT, BP**, BMI, Epworth test and PSG will also be carried out.

**** on two occasions with a time interval of 5 minutes, blood pressure is recorded under the same conditions**



Data collection: Radiological assessment.

It will be performed using cone beam computed tomography (CBCT). Two investigators with a high level of experience with 3D virtual image overlay techniques, using the Dolphin software (Dolphin Imaging 11.9 Premium, Chatsowrth, CA, USA), will assess the volume changes of the upper airway (naso-, gold - and hypo-pharynx) (Fig. 13), and the stability of the surgery in the long term (it is verified that there is no recurrence of the movements carried out during surgery). To ensure the precision of the measurements, fixed points at the base of the skull are taken as reference.

A CBCT will be performed at baseline, as well as one month and twelve months post-treatment.

The images of the three CBCTs of each patient are stored in iCat Vision, which are exported to the Dolphin software (Dolphin Imaging 11.9 Premium, Chatsowrth, CA, USA), in DICOM format with which the necessary measurements are carried out. to accurately quantify the movements produced in the jaws and the volume of the UA.

Outcome measurements:

- **Main variable:** Evaluation of the volume change of the upper airway and the amount and direction of movement of both jaws during jaw replacement surgery, comparing the measurements of the CBCT before (T0) and one month (T1) and 1 year (T2) of the jaw surgery.

- **Secondary variables:**

    - Evaluation of the increase in volume of the upper airway by means of CBCT one month and one year after jaw replacement surgery.
    - Evaluation of the clinical indicators of OSA by taking a BP, and daytime hypersomnia test (Epworth Test) one month and one year after jaw replacement surgery. The BMI is calculated to detect those changes in the AHI due to weight changes.
    - Presence of early or late surgical complications
    - Study of the stability of surgical movements of the jaws one month and one year after surgery by superimposing CBCT images.

Statistical analysis.

The descriptive analysis will include the most relevant statistics for each of the linear, angular and volumetric parameters, as well as patient profile variables and intervention characteristics: mean, standard deviation, minimum, maximum and median for the continuous and absolute frequencies and percentages for the categorical.

Using a Kolmogorov-Smirnov test, the adjustment to normal distribution of the different dimensions will be verified. Given the sample size, the objectives will be addressed from a parametric analysis approach.

The inferential analysis will include the following statistical methods:

For each group:

- ANOVA general linear model of repeated measures, to compare the evolution of the skeletal and volumetric parameters of the pathway throughout the follow-up. The multiple comparisons will be made with the

Bonferroni correction and will allow assessing the effects in the short term (T1-T0), stability (T2-T1) and long term (T2-T0).

- Pearson's linear correlation coefficient, to estimate the degree of association between volumetric and skeletal changes, also in the different periods (T0, T1 and T2).
- Independent samples t tests, Mann-Whitney and Kruskal-Wallis non-parametric tests to assess differences in volumetric changes according to aspects of the individual's profile and type of surgery.
- The level of significance used in the analyzes will be 5%.

Ethical Considerations.

The guidelines of the Declaration of Helsinki will be followed in all phases of treatment and written informed consent will be obtained from all subjects.

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