Universitat Internacional de Catalunya
Facultat d'Odontologia

Tesis doctoral

Three-dimensional Impact of orthognathic surgery on the upper airway and the apnea-hypopnea index.

María Giralt Hernando

PhD Thesis

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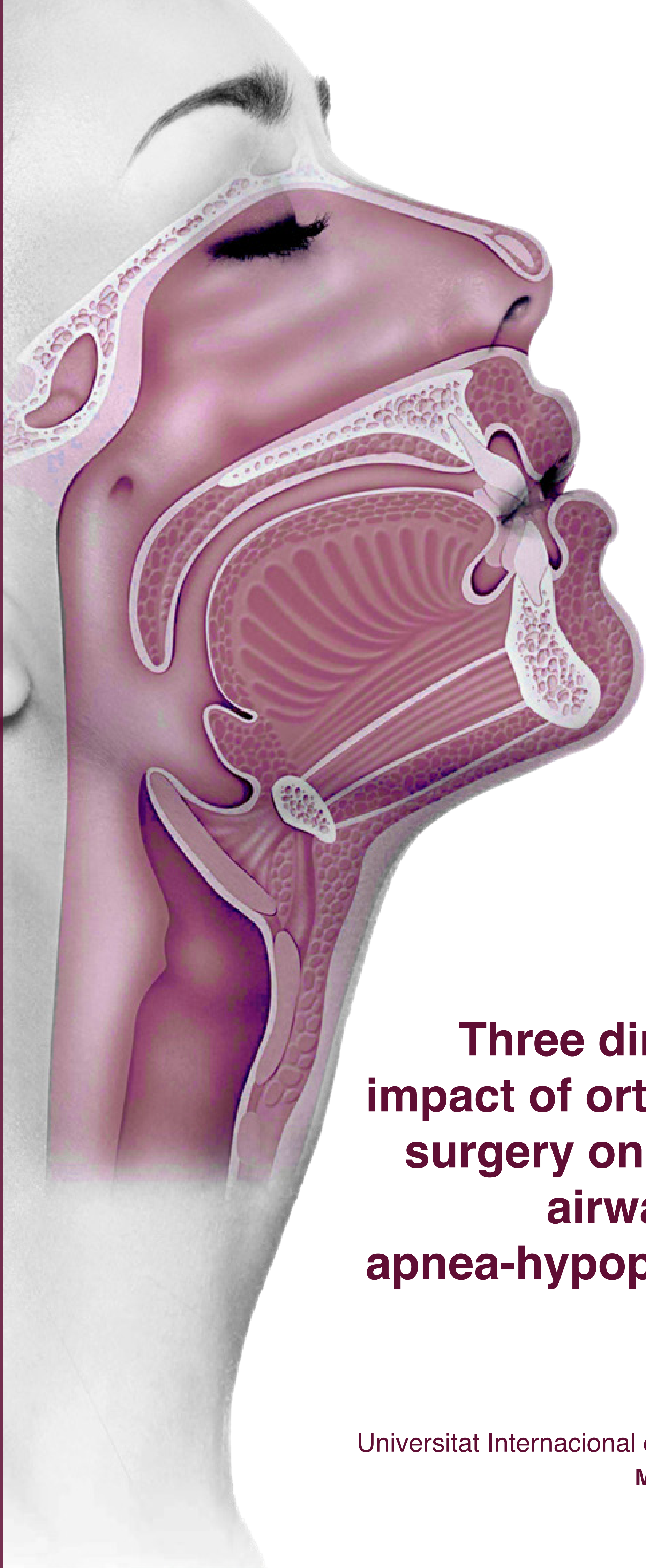

Three dimensional impact of orthognathic surgery on the upper airway and the apnea-hypopnea index

Universitat Internacional de Catalunya, 2021

Maria Giralt-Hernando

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A mis padres,
mi hermano y mis abuelos

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8.3 Approval of the PhD thesis project by the health Health Sciences Doctoral Academic Committee (Comisión Académica de Doctorado, CAD)

8.4 Approval of the PhD Thesis project by the Ethics in Research Committee (Comité d'Ética de Recerca, CER)

8.5 Approval of the PhD Thesis project by the Teknon Medical Center Ethics Committee of Clinical Investigation (Comité Ético de Investigació Clínica, CEIC)

8.6 International PhD mention approval certificate by the Pontifical Catholic University of Rio Grande do Sul (PUCRS), coordinated by the tutor prof. Dr.Rogerio Belle de Oliveira.

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Preliminary remarks

The present PhD investigation is a compendium of five related publications broadening the current state-of-the art and long-term three-dimensional effects of orthognathic surgery on the upper airway (UA) and the sleep-related disorders, such as the Obstructive Sleep Apnea-hypopnea syndrome (OSA).

Hence:

- Original PDF published or pre-print versions of the articles as they appear in in their respective journals are provided in Appendix I.

- Abbreviations, original figures from already published papers, captions to illustrations and tables have not been merged in the manuscript, as they belong to already published articles. However, new added figures in this PhD investigation have been standardized in each section throughout the whole text.

- Both generals' introduction and discussion references have been merged. Hence, each publications' individual reference list and captions to figures can be consulted separately in journal PDF format in Appendix I.

This PhD project, coordinated by Prof. Dr. Federico Hernández-Alfaro and Dr. Adaia Valls-Ontañón at the Universitat Internacional de Catalunya, started in January 2018 as a three-year program, and was granted by the competitive pre-doctoral fellowship ID: FI_B200134 by the AGAUR (Agencia de Gestió d'ajudes Universitàries i d'investigació) of the Generalitat de Catalunya.

Thus:

- Approval and concession of the FI-predoctoral fellowship received by AGAUR is provided in Appendix II.

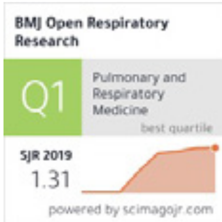
List of papers

Paper I

Title: Impact of surgical maxillomandibular advancement upon pharyngeal airway volume and the apnoea–hypopnea index in the treatment of obstructive sleep apnoea: systematic review and meta-analysis.

Authors: Giralt-Hernando M, Valls-Ontañón A, Guijarro-Martínez R, Masià-Gridilla J, Hernández-Alfaro F.

Journal: BMJ Open Resp Res.



DOI: 10.1136/ bmjresp-2019-000402.

Year: 2019 - Published.

Paper II

Title: Variation between natural head orientation and Frankfort horizontal planes in orthognathic surgery patients: 187 consecutive cases.

Authors: Hernández-Alfaro F, Giralt-Hernando M, Brabyn PJ, Haas Jr O, Valls-Ontañón A.

Journal: Int. J. Oral and Maxillofac.Surg.

DOI: 10.1016/j.ijom.2021.02.011.

Year: 2021 Published In-Press.

Paper III

Title: What are the surgical movements in orthognathic surgery that most affect the upper airways? A three-dimensional analysis.

Authors: Giralt-Hernando M, Valls-Ontañón A, Haas Jr O, Masià-Gridilla J, Hernández-Alfaro F.

Journal: Journal of Oral and Maxillofacial Surgery.

DOI: 10.1016/j.joms.2020.10.017.

Year: 2020 Published In-Press.

Paper IV

Title: Airway volume changes after orthognathic surgery in patients with down syndrome: a diagnostic-therapeutic algorithm.

Authors: Hernández-Alfaro F, Montes-Fernández-Micheltorena P, Molins-Ballabriga G; Giralt-Hernando M, Mayoral-Trias A, Valls-Ontañón A.

Journal: Journal of Otolaryngology - Head & Neck Surgery.

DOI: 10.24966/OHNS-010X/100054.

Year: 2021 Published.

Paper V

Title: Orthognathic surgery as first line treatment to cure obstructive sleep apnea (OSA): A Pilot study.

Authors: Giralt-Hernando M, Valls-Ontañón A, Haas Jr O, Zamora-Almeida G, Anitua E Hernández-Alfaro F.

Journal: Int. J. Oral and Maxillofac.Surg.

DOI: ---

Year: under Peer review.

List of Abbreviations

2D: Two-dimensional
3D: Three-dimensional
A: cephalometric point A
AASM: American Association for Sleep Medicine
Adv: maxillary advancement
AHI: apnea-hypopnea index
ANOVA: Analysis of variance
ANS: Anterior nasal spine
B: cephalometric pint B
BimaxS: Bimaxillary surgery
BMI: Body mass index
BSSO: Bilateral sagittal split osteotomy
CBCT: Cone-beam computed tomography
CCT: controlled clinical trial
CCW: counterclockwise rotation
CI: confidence interval
CONSORT: Consolidated Standards of Reporting Trials
CPAP: continuous positive airway pressure
CR: cure rate
CSA: cross-sectional axial area
CT: Computed tomography
CT90%: cumulative time spent with SpO2 < 90%
CW: clockwise rotation
d: statistical size effect
DFD: dentofacial deformities
MonomaxS: monomaxillary surgery
MOP: mandibular occlusal plane
MW: Mann-Whitney test
N: sample
Na: Nasion
NA: not assessed
DICOM: Digital Imaging and Communications in Medicine
DS: Down Syndrome
e-CRF: electronic report form
e.g.: in example
e/h: events per hour
EDS: excessive daytime sleepiness
EEG: electroencephalogram
ESS: Epworth Sleepiness score
F: Female
FH: Frankfort Horizontal
Fig.: Figure
GP: Genioplasty
HS: Hyoid suspension
HSAT: Home sleep apnea test
Hypo-: Hypopharynx
i.e.: in example
ICC: intraclass correlation coefficient
IQR: interquartile range
IRB: Institutional review board
KW: Kruskal-Wallis test
LF1: Le Fort I osteotomy
LSpO2: Lowest oxygen saturation
M: Male
Mand: mandible
Max: maxilla
mCSA: minimum cross-sectional axial area
Mm: millimeters
MonomandS: monomandibular surgery
Pog: Pogonion
PRISMA: The Preferred Reported Items for Systematic Reviews and Meta-Analyses
PSG: polysomnography
RCT: Randomized clinical trial

Naso-: Nasopharynx
NHO: natural head orientation
NHP: natural head position
NIV: noninvasive ventilation
NR: not reported
ODI: oxygen desaturation index
Oro-: oropharynx
OS: orthognathic surgery
OSA: obstructive sleep apnea
PA: pharyngeal airway
Palatal Expansion
PAS: posterior airway space
PAV: pharyngeal airway volume
PG: domiciliary polygraphy
PNS: Posterior nasal spine
RDI: respiration disturbance index
Sag.: Sagittal
SARPE: Surgically Assisted Rapid
SD: Standard deviation
SR: Systematic Review
SSR: surgical success rate
STROBE: Strengthening the Reporting of Observational Studies in Epidemiology
UA: upper airway
UI-STP: upper incisor soft-tissue nasion plane
UPPP: uvulopalatopharyngoplasty
VBS: voxel-based superimposition
Vs: versus

Summary of the main definitions with regard to sleep parameters according to the American Association of Sleep Medicine (AASM) AASM (Chicago Criteria 1999 and updated 2020 guidelines):

- *Apnea: cessation of airflow for at least 10 seconds*
- *Hypopnea (AASM recommended definition, updated January 2020): ≥ 3% (accepted 4%) oxygen desaturation from pre-event baseline and/or the event is associated with an arousal.*

- *Obstructive sleep apnea (OSA): sleep-related breathing disorder characterized by respiratory pauses secondary to partial (hypopneic) or complete (apneic) obstruction of the pharyngeal airway with a duration of at least 10 seconds.*

- *Apnea-hypopnea index (AHI): number of episodes of apnea and hypopnea per hour of sleep.*

- *OSA severity:*
  · Mild OSA: AHI ≥ 5 e/h
  · Moderate OSA: AHI ≥ 15 e/h
  · Severe OSA: AHI ≥ 30 e/h

- *Arousal: abrupt change of brain activity during sleep ((measured by EEG). Also known as change from deep sleep (REM; rapid eye movement) to light sleep (N-REM: non-rapid eye movement).*

- *Arousal (micro-arousals) index: number or frequency of sleep disruptions and awakening per hour of sleep (i.e: the more arousals, the more tired a patient is likely to feel).*

- *Excessive daytime sleepiness (EDS) in terms of the Epworth Sleepiness score (ESS): self-administered subjective questionnaire to assess daytime sleepiness.*

  · Score assessment:
  · 0 to 10 = normal range of sleepiness
  · 11 to 14 = mild sleepiness
  · 15 to 17 = moderate sleepiness
  · 18 to 24 = severe sleepiness

- *CPAP adherence: > 4 hours of night use of CPAP during 70% of the nights.*

- *CT 90%: cumulative time spent with SpO2 < 90%.*

- *Oxygen desaturation index (ODI): normal blood oxygen level (saturation) between 96 - 97%.*

- *OSA Success rate: final AHI threshold of < 20 e/h and its reduction by 50%.*

- *OSA Cure rate: final AHI threshold of < 5 e/h.*

- *Respiration disturbance index (RDI): number of respiratory disturbances (obstructive apneas, hypopneas, and respiratory event–related arousals (RERA)) per hour.*

01

GENERAL INTRODUCTION

1.1. Importance of the three-dimensional study of the upper airway in the context of orthognathic surgery and the sleep-breathing disorders (SBD) in patients with dentofacial deformities (DFD).

Obstructive sleep apnea (OSA) is a dyssomnia characterized by respiratory pauses secondary to partial (hypopnea) or complete (apnea) obstruction of the upper airway (UA) during sleep, with a duration of at least 10 seconds [1]. According to the latest updated version 2.6 of the American Association of Sleep Medicine (AASM), the hypopnea involves a reduction of the airflow and > 3% of oxygen desaturation, while apnea implies a cessation of the oro-nasal airflow for at least 10 seconds of duration [2]. As a result, the pharyngeal airway (PA) is occluded due to the fall in the muscle tone of the dilator muscles during sleep, which leads to its partial narrowing or total obstruction. The direct consequences of these episodes are the repetitive decrease in blood oxygen saturation (SatO2) with snoring and recurrent sleep arousals caused by increased respiratory effort, which causes a reduction in sleep quality [2].

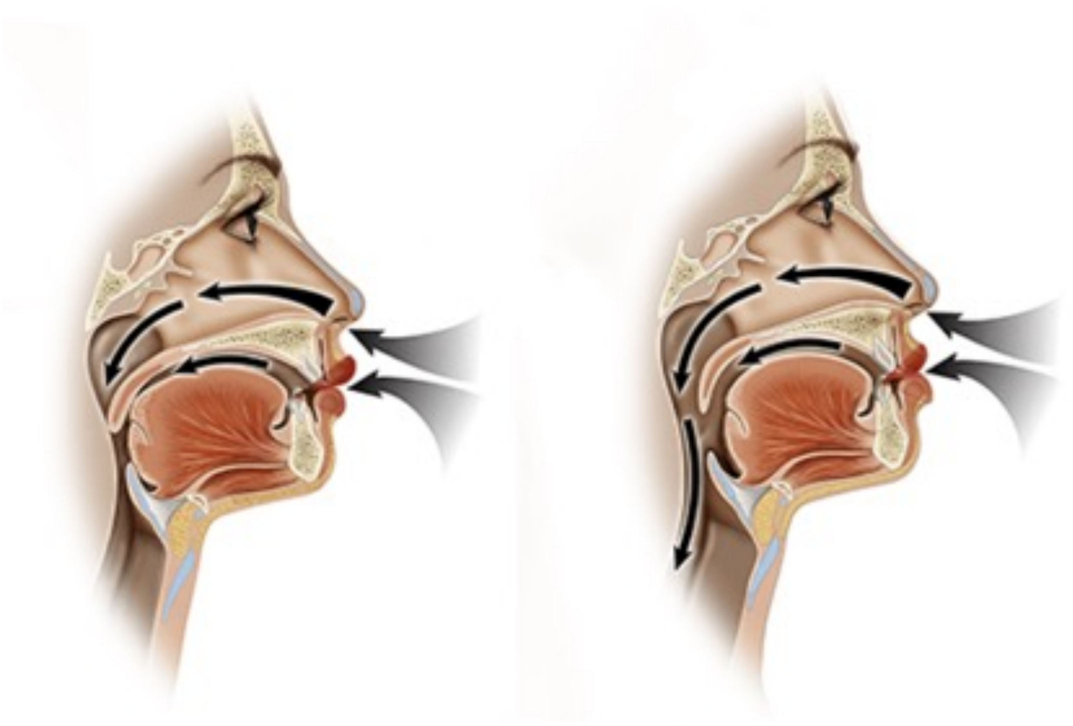


Figure 1. Schematic illustration of the naso-pharyngeal airflow when obstruction of the upper airway and in healthy patients.

When all these affections are accompanied by clinical manifestations, such as excessive daytime sleepiness (ESD), neuropsychiatric, metabolic, respiratory and cardiac alterations, we classify it as OSA [3]. However, systemic arterial hypertension (AT) and heart failure may occur, thus increasing the mortality risk produced by OSA [4].

It is estimated that systemic OSA syndrome affects from 5-20% of the general Spanish adult population, although other authors reported figures of up to 26%, and is 2-3 times more common in men than in women [5]. In Spain, according to studies in different age subgroups, it is estimated that there are between 5 and 7 million people suffering from OSA, where > 50% of these systemic affections run undiagnosed [6]. Recent studies [5] suggest that patients with undiagnosed OSA consume 3 times more resources than the general population [5]. These costs are related to more days of hospital stay, more consultations in specialized care and an increase in the prescribed pharmacological treatment [6].

For years, polysomnography (PSG) has been considered the gold standard diagnostic test registration by means of the apnea-hypopnea index (AHI), among other multiple physiological signals [7]. However, the latest consensus from the AASM has equated the use of home sleep apnea test (HSAT) - also known as house-hold polygraphies - when detecting mild to moderate OSA manifestations [2,7] . However, continuous positive airway pressure (CPAP) stays as the first line treatment armamentarium when dealing with OSA, although its low rates of adherence and tolerance (defined as > 4 hours of night use of CPAP for 70% of nights), not reaching 50% [8].

In this context, patients with different dentofacial deformities (DFD) – class I, II or III [9] and/or with maxillary or mandibular hypoplasia - are more prone to suffer from a chronic sleep-breathing disorder (SBD); and then, inheriting the systemic consequences of obstructive OSA syndrome [10]. Indeed, orthognathic surgery (OS) by means of maxillomandibular advancement (MMA) combined or not with orthodontics has solidly proven to improve and cure OSA clinical objective and subjective symptoms with a surgical success rate (SSR) of 86%[10]. Besides, OS aims to reestablish the facial harmony and correct the different DFD, while repositioning the maxillomandibular complex and achieving a long-term bone and soft tissue stability [11].

1.2. Importance of the three-dimensional virtual surgical planning and orientation in terms of orthognathic surgery.

Three-dimensional (3D) cone-beam computed tomography (CBCT) technologies play a major role in virtual surgical planning and outcome assessment [12]. In this context, it is important to highlight that head positioning of the patient and posture is a key factor in surgical planning for OS and airway assessment, since it influences the antero-posterior perception of the maxillomandibular complex [13]. Thus, clinicians should be able to reliably reproduce the natural head position (NHP) of the patient at the time of UA assessment in different third-party softwares. For decades, two-dimensional (2D) cephalometric measurements were used to assess the UA. However, thanks to the new emerging technologies, 3D assessment and pre- and post-operative evaluation, in terms of superimposition, are strongly recommended to avoid volumetric, linear and cross-sectional measurement error [14]. This protocols enables unbiased analysis of the surgical and volumetric outcomes based on softwares that had solidly demonstrated accuracy and precision, and avoids complex, technically demanding and time-consuming measurements [12]. This PhD investigation exemplifies and validates such recommended methods.

1.3. Clinical relevance of this project

CPAP is acknowledged to be the gold standard treatment for OSA, though the reported adherence failure rate reaches 46-83% over the long term. However, different surgical procedures have therefore been proposed, of which MMA has been shown to be the most effective option for treating OSA in selected patients, with an 86% SSR. However, to our knowledge, no previous studies have examined the relationship between the impact of 3D skeletal movements performed during OS on the pharyngeal airway volume (PAV)- and PSG-related parameters of DFD patients with mild, moderate to severe OSA, at long-term.

02

AIMS

2.1 General aim

The general aim described in this thesis was to reliably evaluate and assess the 3D-clinical effect of OS on both the UA and the long-term cure of OSA by means of the AHI.

2.2 Specific aims

Therefore, a number of different studies were designed and performed:

- to review the state-of-the art regarding the impact of maxillomandibular advancement (MMA) on the PAV and the AHI in the surgical treatment of OSA **(Paper I)**.

- to evaluate the importance of head position in terms of virtual surgical planning for orthognathic surgery - to demonstrate the variation between the Natural Head Orientation (NHO) and the Frankfort horizontal (FH) surgical planes in patients with an underlying dentofacial deformity (DFD). The secondary objectives were to correlate this angle variation between patients' DFD and the impact of counterclockwise rotation (CCW) after orthognathic surgery **(Paper II)**.

- to assess the effect of maxillary and mandibular 3D movements (isolated or jointly) on the PAV (nasopharynx, oropharynx, and hypopharynx) and the minimum cross-sectional area (mCSA) on a 3D basis. The secondary objectives were to correlate the magnitude, type, and direction of these skeletal movements with the airway dimension gain or impairment and their stability or relapse at 12-month follow-up **(Paper III)**.

- to describe and validate a proposed surgical protocol to maximize the airway volume when narrowing of the UA is the main concern in patients with DFD **(Papers III, IV and V)**.

- to validate a protocol and algorithm for the surgical management of dento-facial deformities in Down syndrome (DS) patients with OSA **(Paper IV)**.

- to study the success predictors and to correlate the effects of OS as the first line treatment to cure OSA (in terms of AHI and sleep patient-centered parameters) on a 3D basis over the short and long term **(Paper V)**.

03

RESULTS

3.1

3.1 Paper one

Impact of surgical maxillomandibular advancement upon pharyngeal airway volume and the apnoea–hypopnea index in the treatment of obstructive sleep apnoea:

A systematic review and meta-analysis

Giralt-Hernando M, Valls-Ontañón A*, Guijarro-Martínez R, Masià-Gridilla J, Hernández-Alfaro F

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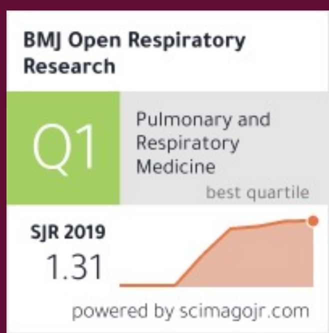
* Both authors contributed equally



ABSTRACT

Background. A systematic review was carried out on the effect of surgical maxillomandibular advancement (MMA) upon pharyngeal airway (PA) dimensions and the apnea-hypopnea index (AHI) in the treatment of obstructive sleep apnea (OSA), with the aim of determining whether increased PA in the context of MMA is the main factor conditioning the subsequent decrease in AHI.

Methods. A search was made of the PubMed, EMBASE, Google Scholar and Cochrane databases. A total of 496 studies were identified. The inclusion criteria were a diagnosis of moderate to severe OSA; MMA success evaluated by polysomnography (PSG); reporting of the magnitude of MMA achieved; PA increase; and a minimum follow-up of 6 months.

Results. Following application of the eligibility criteria, 8 articles were included. Meta-regression analysis showed MMA to significantly increase both pharyngeal airway volume (PAV) (mean 7.35 cm3 (range 5.35 – 9.34)) and pharyngeal airway space (PAS) (mean 4.75 mm (range 3.15 – 6.35)) and ensure a final AHI score below the threshold of 20 (mean 12.9 events/hour).

Conclusion. Although subgroup analysis showed MMA to be effective in treating OSA, more randomized trials are needed to individualize the required magnitude and direction of surgical movements in each patient, and to standardize the measurements of linear and nonlinear PAV parameters.

Keywords: “Orthognathic surgery”, “Obstructive Sleep Apnea Syndrome”, “Obstructive Sleep Apnea”, “Upper Airway”, “Oximetry”.

INTRODUCTION

Obstructive sleep apnea (OSA) is defined as a sleep-related breathing disorder characterized by respiratory pauses secondary to partial (hypopneic) or complete (apneic) obstruction of the pharyngeal airway (PA), with a duration of at least 10 seconds [1]. The PA is occluded due to a loss of muscle tone of the dilator muscles during sleep, which leads to its narrowing or total obstruction [1,2]. As a result, there are repetitive oxygen desaturations (SatO2) with snoring, unrefreshing sleep, fatigue and excessive daytime sleepiness (EDS) [1,2]. Systemic arterial hypertension and heart failure may subsequently develop, with a significant increase in mortality risk [1,2]. Overall, OSA may also have a social impact in terms of poor quality of life, days of work lost and traffic accidents [2].

It is estimated that OSA affects 5-20% [3] of the general adult population, though some authors report figures of up to 26% [3,4]. Nevertheless, the statistics show that over 50% of all cases go undiagnosed [3]. The disorder is three times more common in men than in women [3,4].

The diagnosis of OSA requires the recording of multiple physiological signals during sleep [4]. In this regard, polysomnography (PSG) is considered the gold standard for diagnosing the disease [4]. Polysomnography records brain activity, breathing, heart rate, muscle activity, snoring, blood oxygen levels while resting/sleeping and repeated episodes of PA obstruction, which are measured by the apnea-hypopnea index (AHI) [4]. In addition, the guidelines of the American Academy of Sleep Medicine (AASM) [4] indicate that either PSG or home sleep apnea testing (HSAT) can be used for the diagnosis of uncomplicated OSA in adults, although standard sleep channels are not monitored in the latest devices (e.g., electroencephalogram [EEG]) [4].

Different methods are currently used for treating OSA patients [5]. Continuous positive airway pressure (CPAP) is considered the gold standard in this regard. However, CPAP non-adherence rates of 46-86% have been reported [5] (adherence being defined as > 4 hours of night use of CPAP during 70% of nights) [6]. Different alternative treatments are available to expand the PA, such as uvulo-palato-pharyngoplasty (UPPP), tonsillectomy, adenoidectomy, hyoid suspension (Hs) or hyothyroidopexy [5], though the cure rate (CR) (defined as a final AHI < 5 events / hour) does not exceed 40%, and the results do not hold up over time [7,8].

Since Guilleminault [7] first described maxillomandibular advancement (MMA) as an effective treatment for OSA patients with a retrusive facial profile in 1976, several studies have confirmed its benefits [7,8]. Many publications have demonstrated that MMA moves the anterior pharyngeal wall forwards, resulting in enlargement of the PA and, consequently, a decrease in AHI [1,3,8,9-11]. Some authors have concluded that the efficacy of MMA is equivalent to that of CPAP use over the long term [5, 7, 10]. Accordingly, MMA with or without adjunctive surgical procedures is the most effective and predictable surgical treatment option for patients diagnosed with moderate to severe OSA, with a 50% and 86% cure and surgical success rate, respectively (SR, defined as final AHI < 20 events / hour, and its reduction by 50%) [8]. Thus far, a mean MMA of 10-12 mm has been described as the standard advancement required to treat moderate to severe adult OSA patients [7,11-13]. Mean linear maxillary and mandibular advancements of 8.07 ± 2.60 mm and 10.8 ± 2.34 mm, respectively, have been reported in the literature[13]. However, the magnitude of MMA required at the time of surgery in order to cure OSA depends on the patient dentofacial characteristics (e.g., retrognathia, maxillary hypoplasia, micrognathia, etc.), among other factors [5, 8,11,12].

Recent studies have evaluated PA enlargement after MMA, reporting significant changes in PA volume (PAV) (a mean 80.43% volume gain), related to a mean decrease in AHI of 83.01% ($p < 0.001$) [13]. These volumetric parameters are usually quantified using cone beam computed tomography (CBCT) [2,5,8,9,10,14,15], since the use of three-dimensional (3D) computer-aided planning technology with CBCT compared to conventional planning with two-dimensional (2D) cephalometry has proven to be more accurate at treatment planning and follow-up and thus more beneficial for the patient [16]. Nowadays there is an emerging interest in the 3D study of the impact of orthognathic surgery upon PAV, evaluating the impact of each single maxillomandibular movement upon the three dimensions and at each level of the PA in the context of OSA approach [16].

The aim of the present systematic review and meta-analysis was to assess the impact of MMA upon PAV and AHI in the treatment of OSA

MATERIAL AND METHODS

Search strategy

A systematic search was conducted of the PubMed, EMBASE, Cochrane Library and Google Scholar Beta databases on upper airway and polysomnographic changes following MMA for OSA treatment. The study was based on the following PICO question (**population**: OSA patients; **intervention**: MMA; **comparison**: magnitude of MMA; **outcome**: final PA dimensions and final AHI): **How does MMA surgery affect PAV and consequently AHI in OSA patients?**

The PubMed search was conducted with the following Medical Subject Headings (MeSH) entry terms and thesaurus vocabulary for indexing articles:
[("Orthognathic surgery" OR "Orthognathic Surgeries" OR "Surgeries, Orthognathic" OR "Surgery, Orthognathic" OR "Maxillofacial Orthognathic Surgery" OR "Maxillofacial Orthognathic Surgeries" OR "Orthognathic Surgeries, Maxillofacial" OR "Orthognathic Surgery, Maxillofacial" OR "Surgeries, Maxillofacial Orthognathic" OR "Surgery, Maxillofacial Orthognathic" OR "Jaw Surgery" OR "Jaw Surgeries" OR "Surgeries, Jaw" OR "Surgery, Jaw" OR "Orthognathic Surgical Procedures" OR "mandibular setback" OR " mandibular advancement" OR "maxillary setback" OR "maxillary advancement" OR "bimaxillary surgery" OR" maxillomandibular advancement") AND ("Polysomnographies" OR "Monitoring, Sleep" OR "Sleep Monitoring" OR "Somnography" OR "Somnographies" OR "oximetry" OR "Oximetry" OR "Oximetries" OR "Oximetry, Pulse" OR "Oximetries, Pulse" OR "Pulse Oximetries" OR "Pulse Oximetry") AND ("Sleep Disordered Breathing" OR "Apneas, Obstructive Sleep" OR "Obstructive Sleep Apneas" OR "Sleep Apneas, Obstructive" OR "Obstructive Sleep Apnea Syndrome" OR "Obstructive Sleep Apnea" OR "OSAHS" OR "Syndrome, Sleep Apnea, Obstructive" OR "Apnea, Obstructive Sleep" OR "Sleep Apnea Hypopnea Syndrome" OR "Syndrome, Obstructive Sleep Apnea" OR "Upper Airway Resistance Sleep Apnea Syndrome" OR "Syndrome, Upper Airway Resistance, Sleep Apnea" or "Apnea Syndrome, Sleep" OR "Apnea Syndromes, Sleep" OR "Sleep Apnea Syndrome" OR "Apnea, Sleep" OR "Apneas, Sleep" OR "Sleep Apnea" OR "Sleep Apneas" OR "Sleep Hypopnea" OR "Hypopnea, Sleep" OR "Hypopneas, Sleep" OR "Sleep Hypopneas" OR "Sleep-Disordered Breathing" OR "Breathing, Sleep-Disordered" OR "Sleep Disordered Breathing" OR "Sleep Apnea, Mixed Central and Obstructive" OR "Mixed Central and Obstructive Sleep Apnea" OR "Sleep Apnea, Mixed" OR "Mixed Sleep Apnea" OR "Mixed Sleep Apneas" OR "Sleep Apneas, Mixed" OR "Hypersomnia with Periodic Respiration")]. The same strategy was used in the case of the Cochrane Library, since it also employs MeSH terms.

The EMBASE database was searched using the Emtree preferred terms and supplementary data: *“Orthognathic surgery”/exp AND “Obstructive Sleep Apnea”/syn.*

Grey literature from the Google Scholar Beta database was also searched in order to retrieve studies published in journals not indexed in the major databases. All duplicates from the four systematic searches were subsequently removed.

Study selection

The electronic search was conducted by two authors (MGH and AVO) to avoid subjectivity. Those studies that fulfilled the inclusion criteria were retrieved for full-text reading.

The inclusion criteria were: intervention studies; patients > 18 years of age with moderate to severe OSA (AHI ≥ 15 events/hour) eligible for MMA; studies assessing the effect of orthognathic surgery on PA dimensions; studies assessing the impact of orthognathic surgery upon PSG related parameters; a minimum follow-up period of 6 months; and reporting of the magnitude of advancement of the maxilla, mandible and chin. Studies in which patients underwent turbinectomy and/or septoplasty as adjunctive procedures were also included, since these procedures do not modify PA dimensions. The exclusion criteria were: case reports; literature reviews; and studies reporting patients undergoing setback orthognathic surgery or Hs, tonsillectomy, adenoidectomy or uvulo-palato-pharyngoplasty as adjunctive procedures, since these procedures may modify PA dimensions.

In the event of disagreement between the authors, the identified papers were subjected to full-text reading, and eligibility under discussion was then assessed. If any doubts arose, a third reviewer (FHA) screened and read in full the included articles and was then discussed whether one of the authors had rejected it. The level of inter-rater agreement between authors was assessed by Cohen’s kappa coefficient (k).

Data extraction

Demographic, surgical and methodological data were compiled from the included studies. Any discrepancies were resolved by consensus between the authors (MGH and AVO).

Outcome measures

The following outcome measures were evaluated: AHI, PA dimensions and success and cure rates (SR and CR, respectively). Regarding the AHI assessment, it was established as the final postoperative score (final AHI) and the pre- versus post-surgery difference (AHI reduction). Moreover, final AHI was assessed to establish “success” and “cure” rates of surgical treatment of OSA after MMA, as described elsewhere [1,4-6,32-39,50]. A final AHI < 20 events / hour, with a reduction of 50% postoperatively, defines surgical success [1,5,7]. A final AHI < 5 events / hour is regarded as a surgical cure criterion [1,4-6,32-39,50].

As to PA enlargement evaluation, both 3D and 2D measures assessed by CBCT and cephalometric analysis, respectively were included as primary indicators of the anatomical changes as follows: PAV and PA space (PAS) gain (in cm3 and mm, respectively). Finally, as key independent variables, the magnitude of maxillary and mandibular (in mm) advancement, as well as the ratio between maxillary and mandibular advancement, were extracted from the included studies.

Statistical analysis

The statistical analysis included a demographic study (mean, standard deviation [SD], range and median for continuous variables, and absolute and relative frequencies for categorical variables). Paired t-tests were used to compare pre- and postoperative mean values. Statistically significant differences were considered for $p < 0.05$. The R 3.0.2 statistical package was used throughout.

Study of heterogeneity and risk of bias

The Preferred Reported Items for Systematic Reviews and Meta-Analyses (PRISMA) [17] statements were used as a basis to ensure transparency of the systematic review, comprising 27 checklist items (referred to title, abstract, introduction, methods, results, discussion and funding) and a four-phase flowchart (identification, screening, eligibility and inclusion) [17,18]. Heterogeneity among the included items was assessed using the I2 statistics and corresponding statistical null test. Galbraith plots were used to visualize the degree of heterogeneity. In situations of significant heterogeneity, the source was explored through sensitivity analysis.

Subgroup analyses were made to examine the different surgical techniques of the studies since genioplasty (Gp), the surgical correction of the projection of the chin, can add an increase in the PA. Thus, two surgical factors were considered for the two group analyses: a) “MMA group” (n = 108), which excluded studies with Gp [32,35,37,39] and b) “MMA ± Gp” group (n = 159), including all articles regardless of Gp [32-39]. Forests plots were used to show the effects. A meta-regression model was developed to assess the association between the largest number of studies regarding maxillary and/or mandibular advancement. These random effects were supported by the inverse variance method of DerSimonian and Laird [19]. A 95% confidence interval (CI) was pooled.

The quality of the papers was assessed using the adaptation of the bias analysis used by Haas Jr, Becker and Oliveira 2015 [16,20]. The criteria based on sample selection, blinding of the authors, comparison between treatments, statistical analysis and outcome validation measured the degree of bias, definition of inclusion and exclusion criteria, and postoperative follow-up. They were categorized as low risk if all the criteria were met, uncertain risk when only one criterion was missing, and high risk if two or more criteria were missing according to the analysis of Haas Jr 2015 et al 16. With respect to publication bias, funnel plots and the Egger test were used.

RESULTS

Search strategy and study selection

The strategies of the main search and grey literature search were applied up to December 2017. A four-phase flowchart (identification, screening, eligibility and inclusion) is provided of each step of the systematic search, confirming the thoroughness of the screening process. The aim of this diagram is to help the authors improve the reporting of systematic reviews (Fig. 1) [17-18].

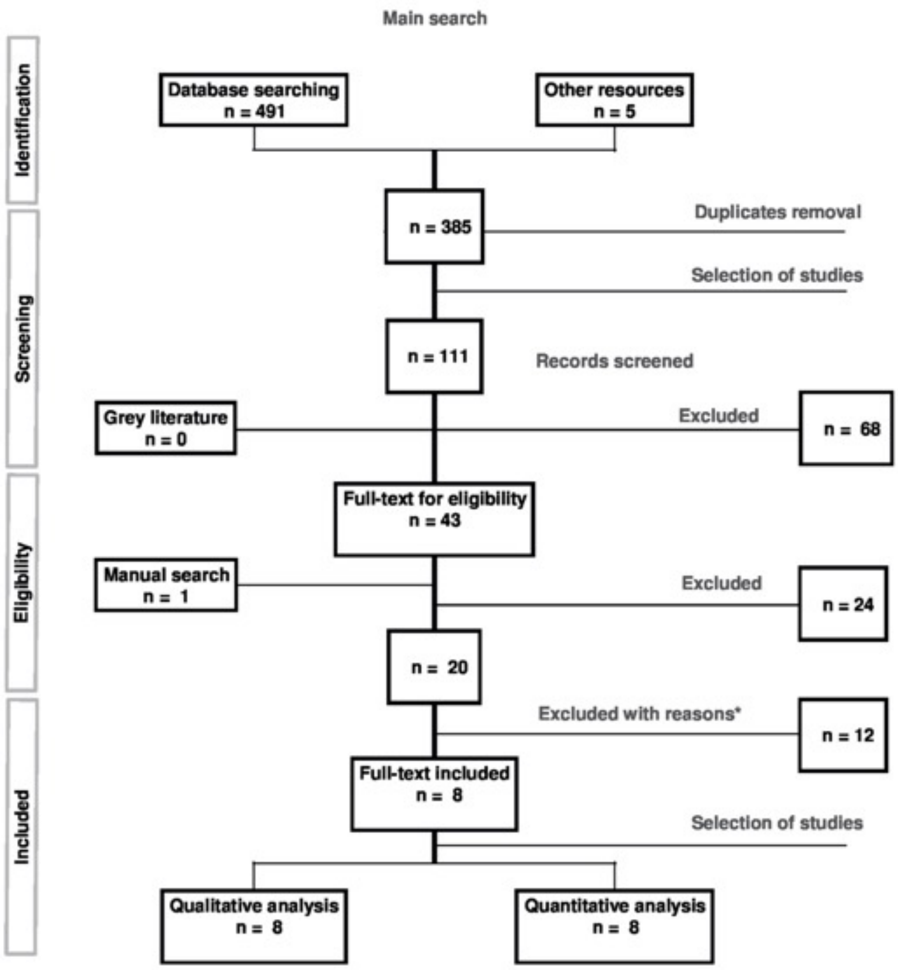


Figure. 1. Systematic PRISMA flow chart.
** No response or inappropriate data were received from the authors of the excluded studies.*

The main electronic search yielded a total of 496 articles. Of these, 491 were found in PubMed and 5 in the Cochrane Library and EMBASE databases. The titles and abstracts of 111 articles were scrutinized independently by the two investigators (MGH and AVO), after the removal of duplicates. Of these studies, 43 were subjected to full-text reading. The inter-rater agreement coefficient was k = 0.856 (95%CI 0.773 to 1) for study selection.

Study eligibility

The same two authors independently evaluated the 43 articles subjected to full-text reading. Of these, 20 met the criteria for inclusion. The authors of four studies [13,21-23] were contacted by e-mail for further information, since some doubts arose during the selection process. A period of four weeks was allowed for their reply in providing the missing data but no reply for further information was obtained from any of the authors [13,21-23].

Twelve articles [11,13,30,31,21,22,24–29] were excluded from the systematic review. Of the excluded studies, one 26 failed to report the magnitude of movement during orthognathic surgery, 8 studies [11,21,22,24–27,29] did not report PA measurements and three studies [27,30,31] reported setback procedures.

Eight studies [32-39] were therefore included in the quantitative analysis. The inter-rater agreement regarding study eligibility was considered excellent, with k = 0.813 (95%CI 0.663 to 1).

Data extraction

Data from the included studies are shown in Table 1.

The included studies were mainly retrospective [32–36,39], and only two involved a prospective design [37,38]. The meta-analysis sample consisted of a total of 159 patients from the 8 included studies. Of these, four articles assessed the efficacy of MMA alone (n = 108) [32,35,37,39], while four trials [33,34,36,38] evaluated the effectiveness of MMA + Gp as an adjunctive procedure, though not necessarily in all the patients (n = 51) [33,34,36,38]. Since Gp may add an increase in PA, subgroup analyses were made to examine the different surgical techniques used in the studies: a) “MMA group” (n = 108), which excludes studies with Gp [32,35,37,39] and b) “MMA ± Gp” group (n = 159), which includes all articles regardless of Gp [32-39] (Tables 1 and 2).

Table 1. Demographic data of the included studies.

Author, year	Country, place of study + years of intervention	Study design	Sample a	Gender	Age (years) Mean ± SD	Dental Class I,II,III	Type of OSA: moderate or severe	Evaluation: 3D or 2D	Type of surgery: MMA or MMA+Gp
Fairburn et al. 2007	University of Alabama at Birmingham, Birmingham, AL, USA. 2000-2003	R	n = 20	m:13 f:7	47.6 ± 10.0	NA	Severe	3D	MMA
Jones et al. 2010	University of Adelaide, Australia, 2002-2004.	R	n = 20	NA	NA	NA	Severe	2D	MMA ± Gp
Ronchi et al. 2013	Sant'Anna Hospital Como, Italy San Raffaele Hospital in Milan	R	n = 15	m:11 f:4	42.3 ± 9.5	I: 5 II: 9 III: 1	Severe	2D	MMA ± Gp
Bianchi et al. 2014	S. Orsola Malpighi University Hospital, Bologna, Italy. 2008-2011	R	n = 10	m:10 f:0	45 ± 14	NA	Severe	3D	MMA
Schendel et al. 2014	Stanford University, Stanford, California, USA.	R	n = 10	m: 8 f:2	46.4 ± 9.7	I: 2 II: 8	Severe	3D	MMA ± Gp
Hsieh et al. 2014	Chang Gung Memorial Hospital, Taoyuan, Taiwan.	P	n = 16	m:12 f:4	33 ± 7.9	I: 1 II: 15	Severe	3D	MMA
Veys et al. 2017	Bruges, Belgium. January to December 2015.	P	n = 11 (only 6 assessed: pt. 1,2,3,5, 7,11	m: 8 f: 3	44.7 ± 9.5	NA	Moderate-to-severe	3D	MMA ± Gp
De Ruiter et al. 2017	Academic Medical Centre of the University of Amsterdam. 2011-2015.	R	n = 62	m: 54 f: 8	54 (47–61)	NA	Severe	2D	MMA

F: female; M: male; R: retrospective; P: prospective; NA: not assessed by the authors; pt: patients; SD: standard deviation; MMA: maxillomandibular advancement; Gp: genioplasty.
a: In the sample of Veys et al. 2017, only 6 patients were assessed out of 11.

No gender differences were identified in any study, though the male sample was larger in all the included studies (total of 116 males and 28 females) [32–39]. The mean age was 39 years (range 33 - 61) [32-39].

All of the studies [32-39] included moderate to severe OSA patients assessed by PSG. In relation to the PSG parameters, most of the studies used the AHI index [32,34,39]. However, one publication 33 used the Respiratory Disturbance Index (consisting of the apneas + hypopneas and arousals). Both metrics were considered equivalent when assessing OSA severity [5]. In particular, the patients eligible for MMA included in this systematic review were not able to adhere to CPAP therapy (defined as > 4 hours of night use of CPAP during 70% of nights) [6] or failed previous adjunctive surgery such as UPPP, Hs or adenoidectomy, among others [32-39].

Regarding the imaging techniques used, the majority of the studies [32,35-38] assessed the PA measurements with 3D methods (CBCT). In all studies, patients were scanned sitting in an upright position in the Frankfort horizontal plane. This position is closer to the natural head position (NHP), and is recommended for the baseline assessment of upper airway dimensions 8-14. Of these publications, 5 reported 3D PA measurements (PAV) [32,35-38], and three reported 2D PA measurements 33,34,39 in the sagittal plane (PAS), consisting of the minimum distance between the base of the tongue and the posterior pharyngeal wall [33,34,39] (Table 3).

Table 2. Data referred to outcome measures of the included studies.

Author, year	Samp le*	BMI pre- (Kg/m²)	BMI post- (Kg/m²)	Type of surgery: MMA or MMA ± Gp	AHI pre- mean SD (Events/h our)	AHI post- mean SD (Events/h our)	Success rate	Cure rate
Fairburn et al. 2007	n = 20	32.24 ± 4.7	31.74 ± 5.0 (p 0.61)	MMA	69.2 ± 35.8	18.6 ± 6.3	90%	50%
Jones et al. 2010	n = 20	33.9 ± 8.5 (p 0.61)	34.7 ± 9.2 (p 0.61)	MMA ± Gp	61.41 ± 19.6 (p > 0.01)	29.4 ± 19.4 (p > 0.01)	65%	NA
Ronchi et al. 2013	n = 15	NA	NA	MMA ± Gp	58.7 ± 16 (p < 0.001)	8.1 ± 7.8 (p < 0.001)	100%	NA
Bianchi et al 2014	n = 10	NA	NA	MMA	56.8 ± 16.6 (p < 0.005)	12.3 ± 5.5 (p < 0.005)	100%	NA
Schendel et al. 2014	n = 10	28.6	NA	MMA ± Gp	42.9 ± 21.2	5.2 ± 8.3	100%	NA
Hsieh et al. 2014	n = 16	22 ± 3.3	NA	MMA	35.7 ± 18.0 (p < 0.001)	4.8 ± 4.4 (p < 0.001)	100%	NA
Veys et al. 2017 *	n = 11	NA	NA	MMA ± Gp	27.7 ± 14.7 (p 0.005)	8.5 ± 10 (p 0.005)	70%	40%
De Ruiter et al. 2017	n = 62	29 (27–33) (p 0.609)	NA	MMA	52 ± 10 (p 0.515)	16 ± 10 (p 0.515)	71%	NA

NA: not assessed by the authors; pt: patients; SD: standard deviation; MMA: maxillomandibular advancement; GP: genioplasty; BMI: body mass index; AHI: apnea-hypopnea index.
** In the sample of Veys et al. 2017, only 6 patients were assessed out of 11. (Only 6 pt assessed: pt 1,2,3,5,7,11).*
*** p – values < 0.05 were accepted as significant (95%CI)*

Table 3. Analyses of the included studies regarding PA, MMA and PAS.

Author, year	Point PA	PA pre- mean SD (cm³)	PA post- mean SD (cm³)	Max ADV (mm)	Mand ADV (mm)	Mx/md ADV ratio	PAS pre- mean SD (mm)	PAS post- mean SD (mm)	Change in PAS mean SD
Fairburn et al. 2007	PAS	NA	NA	NA	10	NA	11.125	16.96	5.8 ± 3
Jones et al. 2010	PAS	NA	NA	12.05 ± 2.7	16.23 ± 5.72	NA	9.5 ± 3.66	13.28 ± 5.72	2.55 ± 3.18 (p > 0.01)
Ronchi et al. 2013	PAS	NA	NA	5.2 ± 4.5	9.5 ± 8.7	1.83	5 ± 2.2	9.5 ± 3.3	4.5 ± 2.75 (p 0.74)
Bianchi et al 2014	PAS	12.9 ± 4.0 (p < 0.005)	20.7 ± 3.5 (p < 0.005)	10	10	1.00	NA	NA	NA
Schendel et al. 2014	PAS	74.1	176.9	9.4	9.5	1.01	6.07 ± 2.3	9.60 ± 4.1	3.53 ± 3.2
Hsieh et al. 2014	PAS	17.1 ± 7.0 (p < 0.001)	23.2 ± 8.6 (p < 0.001)	NA	NA	NA	NA	NA	NA
Veys et al. 2017	PAS	28.78 ± 8.4 (p 0.002)	38.97 ± 15.07 (p 0.002)	8.0 ± 2.1	9.8 ± 1.8	1.23	NA	NA	NA
De Ruiter et al. 2017	PAS	NA	NA	7 ± 2.2 (p 0.164)	7 ± 3.7 (p 0.248)	1.00	7 ± 3.7	14 ± 4.4	7 ± 4.05

NA: not assessed by the authors; pt: patients; SD: standard deviation; MMA: maxillomandibular advancement; Max: maxillary; Mand: mandibular; ADV: advancement; PAS: Pharyngeal airway space; PA: pharyngeal airway; ADV: advancement.
** In the sample of Veys et al. 2017, only 6 patients were assessed out of 11. (Only 6 pt assessed: pt 1,2,3,5,7,11).*
*** p – values < 0.005 were accepted as significant (95%CI)*

Quantitative analysis

The meta-analysis estimated the effects of the PSG parameters (final AHI, AHI reduction, SR and CR), and PA measurements (3D PAV gain or 2D PAS gain) in relation to the maxillary and mandibular advancement achieved in the 8 studies regardless of Gp ("MMA ± Gp" group) [32-39]. In a second stage, the analyses were replicated for the studies only reporting MMA ("MMA" group) [32,35,37,39] in order to evaluate the sole effect of the MMA, without Gp. Meta-regression was estimated at the time of assessment of the effects in terms of the magnitude of maxillary and mandibular advancement and the maxillary/mandibular ratio related to AHI as independent variables [40].

Effect of MMA upon AHI
Data on the outcomes assessed in this meta-analysis can be extracted from Tables 2 and 3.

Regarding the final AHI in both groups:

a) *"MMA ± Gp"* group [32-39]: The mean postoperative AHI scores for the global sample of 159 patients ranged from 4.8 [37] to 29.4 events / hour [33], with a mean final AHI of 12.4 events/hour (95%CI 7.18 to 17.6; $p < 0.001$) (Fig. 2a). The results suggest that the treatment ensures a final AHI value below the threshold of 20 on average. Specifically, the p-values for meta-regression of the maxillary, mandibular and maxillary/mandibular ratio were 0.073, 0.747 and 0.316, respectively. A strong tendency was seen, though no significant effects were detected for any of them separately.

b) *"MMA" group [32,35,37,39]:* A global sample of 108 patients who did not undergo Gp yielded a mean postoperative AHI score of 4.8 [37] to 18.6 [32] events/hour. The mean final AHI score was 12.9 events/hour (95%CI 6.94 to 18.85; $p < 0.001$), which suggests that the treatment ensures a final AHI value below the threshold of 20 [32,35,37,39]. Individually, no significant effect was shown for maxillary advancement ($p = 0.200$), though a statistically significant effect was detected for both mandibular advancement and the maxillary/mandibular ratio ($p = 0.025$ and 0.002, respectively). For every additional 1 mm of mandibular advancement the final AHI score was reduced by an average of 1.45 events/hour [32,35,37,39] and for every additional unit of maxillary/mandibular ratio the final AHI score was reduced by an average of 0.81 events/hour [32,35,37,39], respectively.

On the other hand, results regarding AHI reduction were as follows:

a) *"MMA ± Gp"* group [32-39]: The average reduction values ranged between 30.9 [32] and 50.6 events/hour [34]. The mean estimated overall effect for AHI reduction was 38.0 events/hour (95%CI 31.7 to 44.3) ($p < 0.001$) (Fig. 2b). Meta-regression analysis referred to the magnitude of maxillary and mandibular advancement and the maxillary/mandibular ratio yielded no statistically significant results for any of the groups ($p = 0.977$, 0.263 and 0.520, respectively).

b) *"MMA" group* [32,35,37,39]*:* The average reduction values ranged between 30.9 [37] - 50.6 events/hour [32] for the sample of 108 patients. A statistically significant mean decrease in AHI of 39.0 events/hour (95%CI 31.5 to 46.6; $p < 0.001$) was obtained. In particular, the maxillary advancement had a significant effect on the reduction of AHI ($p = 0.044$). Hence, for each additional 1 mm of maxillary advancement, the AHI further decreased by 1.34 events/hour. However, no significant effect was shown for mandibular advancement ($p = 0.544$) or maxillary/mandibular ratio ($p = 0.258$).

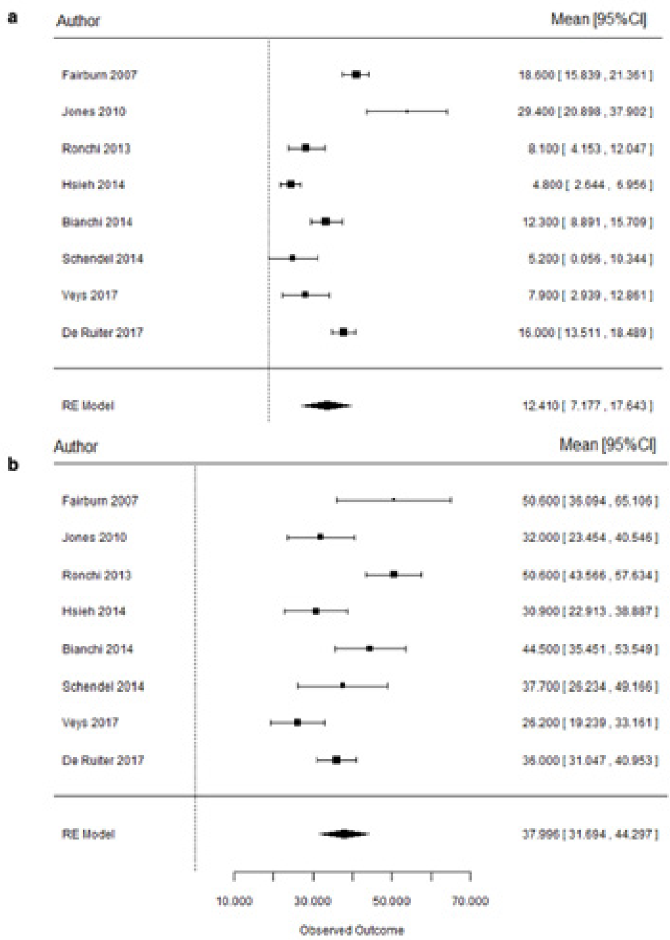


Figure 2. Forest plots representing the final mean AHI (a) and AHI reduction (b) in both groups.

Finally, in relation to SR, both groups achieved high surgical success rates. An overall SR of 87.5% (95%CI 76.8 to 98.2%) and 90.3% (95%CI > 76.8%) was obtained for the “MMA ± Gp” and “MMA” groups, respectively (Fig. 3). However, no statistically significant associations were found between maxillary, mandibular advancement and maxillary / mandibular ratio (p = 0.289, p = 0.901, p = 0.394) in any group.

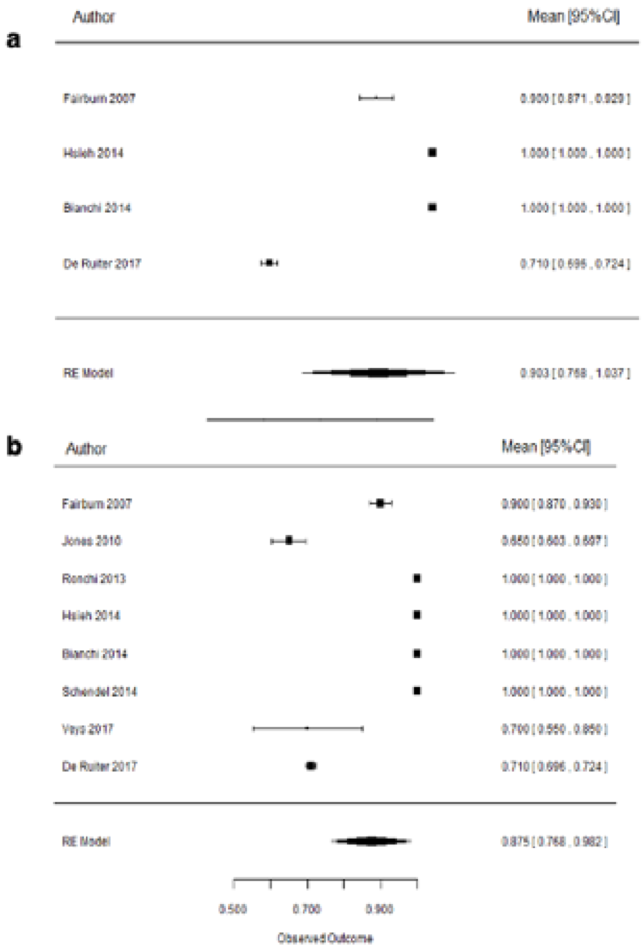


Figure 3. Forest plots corresponding to success rate for both groups, (a) “MMA” and (b) “MMA ± Gp”.

Effect of MMA upon PAS and PAV

With regard to the 2D PAS increase, the following results were found in each group:

a) “MMA ± Gp” group [32–34,36,39]: 5 studies comprising a sample of 127 patients, reported 2D PA measurements. The overall mean PAS gain was 4.75 mm (95%CI 3.15 to 6.35), and proved statistically significant ($p < 0.001$) (Fig. 4). Meta-regression analysis yielded no statistically significant results for maxillary advancement or the maxillary/mandibular ratio ($p = 0.211$ and 0.560, respectively). However, mandibular advancement was found to be statistically significant in terms of PAS gain ($p < 0.001$). Our results suggest that the greater the mandibular advancement, the greater the PAS gain: each additional 1 mm of mandibular advancement implied a 0.5 mm gain in PAS.

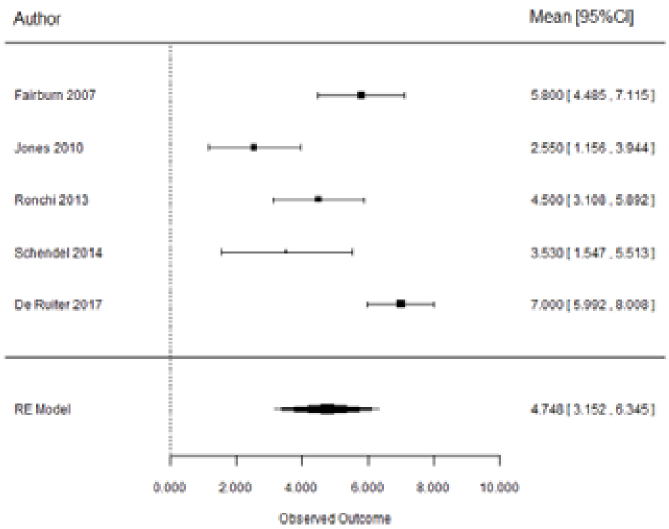


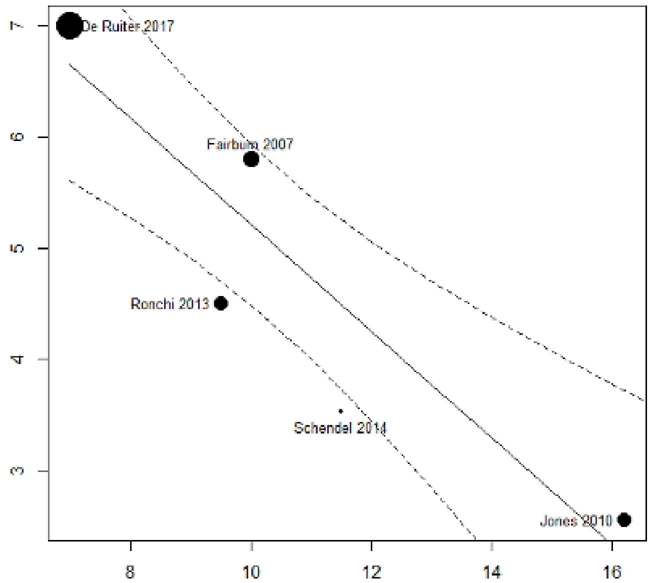
Figure 4. Forest plots representing PAS gain for both the “MMA” and “MMA ± Gp” groups.

b) “MMA” group: only two studies [32,39] comprising a total of 82 patients reported 2D PA measurements with a mean PAS gain of 6.48 mm (95%CI 5.31 to 7.64; $p < 0.001$). Since only two papers are included in this group, a reliable meta-regression analysis was not possible.

On the other hand, only two studies [35,37], included within both groups (“MMA ± Gp” and “MMA”), reported data on absolute 3D PAV gain. The mean PAV gain was 7.35 cm3 (95%CI 5.35 to 9.34), and proved statistically significant ($p < 0.001$). Since only two papers are included in this group, a reliable meta-regression analysis was not possible.

Correlation between PAS/PAV gain and AHI

Regarding 2D PA measurements, only 4 studies corresponding to the "MMA ± Gp" group (comprising a sample of 107 patients) reported information on PAS gain and final AHI/ AHI reduction [32,34,36,39]. A statistically significant association was found between PAS gain and final AHI (r = 0.41, p = 0.023), meaning that for each 1 mm of PAS gain, AHI was reduced in 3.58 events/hour (95%CI 0.49 to 6.68). Therefore, a greater change in PAS would result in a lower final AHI [32,34,36,39] (Suppl. Fig. S1).



Supplementary Figure S1. Meta-regression corresponding to PAS gain and final AHI ("MMA ± Gp" group).

With regard to the 3D PA measurements, two papers [35,37], included within both groups (*"MMA ± Gp" and "MMA"*), provided correlations between PAV and AHI reduction in a sample of 72 patients. Both studies obtained positive correlations (Pearson correlation coefficient (r) 0.576 according to Bianchi [35] and 0.76 according to De Ruiter [39]). The global effect estimated for the correlation was 0.75 (95%CI 0.65 to 0.85), reflecting a strong relationship between changes in both variables. Therefore, the greater the volume gain, the greater the corresponding AHI reduction.

Analysis of publication bias

Data reporting the risk of bias are shown in Table 4. The risk of bias of the papers included in this systematic review was classified as high for 5 studies [32-34,36,39] and as medium / unclear for three studies [35,37,38]. None of the studies reported blind assessment.

Quality criteria	Fairburn et al. 2007	Jones et al. 2010	Ronchi et al. 2013	Schendel et al. 2014	Bianchi et al. 2014	Hsieh et al. 2014	Veys et al. 2017	De Ruiter et al. 2017
Sample randomization	No	No	No	No	No	No	No	No
Comparison between treatments	No	No	No	Yes	No	No	No	No
Blind assessment	No	No	No	No	No	Yes	Yes	No
Description of measurements	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Statistical analysis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Defined inclusion/exclusi on criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Report of follow-up	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Risk of bias[a]	High	High	High	Unclear	High	Unclear	Unclear	High

Table 4. Results of the quality analysis of the included studies.

a. Risk of bias assessment: high = 0-4 'Yes'; unclear = 5-6 'Yes'; low = 7 'Yes'.

Funnel plots were used to depict the risk of publication bias. No publication bias was detected for final AHI (Egger test p = 0.547 for "MMA" and p = 0.297 for "MMA ± Gp") or PAS gain (Egger test p = 0.156 for "MMA" and p = 0.109 for "MMA ± Gp"). Sensitivity analysis of the estimates identified two publications [32,33] as potentially being responsible for most of the heterogeneity between studies. Disparity between data was due to the patient sample regarding OSA severity. In terms of final AHI, heterogeneity accounted for 94.6% of the total variability, with Q = 102.9 ($p < 0.001$). The problem seemed to point primarily to one study [33], with a fairly high value in comparison to the other studies. No publication bias was likewise suggested with respect to PAS gain.

However, regarding AHI reduction, sensitivity analysis suggested that all the aforementioned heterogeneity could be due to maxillary advancement in the "MMA" group, given the adjustment found (I^2 = 0.0%, Q = 0.85, p = 0.357). This could be due to studies [32] that reported large reductions in AHI. The Egger test yielded a low p-value (p = 0.144), taking into account its limited power in application to these sample sizes. In contrast, homogeneity between studies was found on assessing PA (I^2 = 0%, Q = 0.64, p = 0.422).

DISCUSSION

The aim of the present systematic review with meta-regression analysis was to assess the impact of MMA upon PA dimensions and AHI in the treatment of OSA, as there is limited evidence regarding their exact correlations [32–39]. Indeed, it has been widely reported that MMA increases PA and decreases AHI in the context of OSA, but additional multidisciplinary studies assessing aspects other than PA and AHI are needed to determine which types of maxillary, mandibular and chin movements (e.g., advancement, rotation, impaction, descent) are best for enlarging the PA in its specific compromised levels and for finally reducing AHI, as well as patient characterization in terms of OSA severity, comorbidities and facial profile, among other factors [5, 41-43].

With regard to MMA surgery according to the analyzed articles [32-39], the positive effect of the intervention was clearly evidenced by the surgical success rate obtained (87.5%). However, while most of the included studies [34,35,37] obtained SR values of 100%, Jones et al. [33] recorded the lowest rate (65%). Specifically, a mean final AHI of 12.4 events/hour (95%CI 7.18 to 17.6; $p < 0.01$) [32–39] was achieved in all of the literature reviewed. Hence, orthognathic surgery in application to OSA ensures surgical success with a final AHI < 20 events/hour and an AHI reduction of at least 50% according to the criteria defined by Riley et al. [25]. But some patients would still require ongoing CPAP treatment after MMA, since OSA may not be cured (AHI < 5 events / hour) 5,25, and would eventually have more difficulty in adhering to CPAP after surgery [44]. None of the included studies reported the number of patients requiring ongoing CPAP after MMA [32-39].

However, the surgical success criterion remains subject to controversy [5, 44]. In this regard, some authors suggest that surgical success in OSA should be assessed on the basis of improvement or resolution of the clinical signs and symptoms of OSA, the normalization of sleep, AHI reduction (AHI < 20), and quality of life [44]. On the other hand, surgical cure rates (AHI < 5 events/hour) were only assessed by two studies (Fairburn et al. [32] and Veys et al. [38]) with cure rates of 50% and 40%, respectively (Table 2) [32,38]. Thus, we were not able to draw definitive conclusions on the impact of MMA on cure rates [32,38].

Scarce data is available on the required MMA advancement to benefit the patient with OSA [5,42]. In terms of the amount of surgical movement achieved, to date a MMA of 10 mm has been considered the gold standard orthognathic surgery treatment in OSA patients [25]. Nevertheless, the combination of MMA with counterclockwise (CCW) rotation has proven to be the movement with the strongest impact upon PA [1,7,8,13,25,32-39,41-43].

However, there is not enough evidence to establish the magnitude and direction of maxillary or mandibular movement required in order to cure OSA [5]. Our results in this meta-analysis showed that for each additional 1 mm of mandibular advance, the final AHI is reduced by 1.45 events / hour on average [32,37], but further in-depht investigations would be helpful to carry out patient tailored surgeries depending on their skeletal facial profile, PA shape, OSA characteristics and patients' comorbidities [45,46].

The surgical treatment of OSA through MMA is occasionally performed in combination with additional procedures such as septoplasty, turbinectomy, tonsillectomy, adenoidectomy, UPPP or genial tubercle advancement (GTA) [5, 26, 41,42]. As specified by the inclusion criteria, studies where patients underwent turbinectomy and/or septoplasty as adjunctive procedures were included, since it is considered that these procedures do not modify PA dimensions [33,34,36,38]. Hs, tonsillectomy, adenoidectomy or UPPP as adjunctive procedures were excluded, since they may alter PA dimensions [33,34,36,38]. Regarding GTA and Gp, these procedures were included provided that the magnitude of advancement was reported [33,34,36,38].

However, in order to discard any independent effect or impact of Gp in MMA in terms of AHI reduction, variation in PAS and PAV gain of two group analyses assessing MMA alone and MMA with Gp were carried out [32 - 39]. In the last decades, the effectiveness of MMA in modifying PAS and PA has been evaluated using 2D or 3D methods, respectively [14]. All of the studies [32-39] assessed PAV by means of CBCT or cephalometry – both techniques (2D and 3D) being considered a safe and predictable way to measure PA, though the former lacks the option of evaluating the transverse dimension [32–39]. The PA was assessed two-dimensionally in three of the included studies [33,34,39] taking the minimum distance between the base of the tongue and the posterior pharyngeal wall - though not all of them indicated the exact landmarks / reference points used [33,34,39]. A significant difference between pre- and postoperative PAS of 4.75 mm (95%CI 3.15 to 6.35) was found. Particularly, mandibular advancement was seen to be statistically significant when considering PAS gain ($p < 0.001$): 1 mm of mandibular advancement implied 0.5 mm gain in PAS [32–34,36,39]. But only Hsieh et al. [37] and Veys et al. [38] reported 3D airway measurements and were evaluated at three different levels with respect to the limits of the PA subregions: nasopharynx, oropharynx and hypopharynx [14]. Taking into account that orthognathic surgery impacts three-dimensionally and in different subregions of the PA [14], further studies reporting volumetric data with different PA levels of measurement are needed, in addition to those included in our review [32,37,38,41,43] Thus, it is important to standardize the PA measurements for homogeneity purposes and thus be able to draw relevant conclusions [14,45].

Regarding the correlations between changes in PAS/PAV and AHI reduction in terms of MMA, a statistically significant association between PAS gain and final AHI was found in four of the studies included in the meta-analysis (p = 0.023) [32,34,36,39]. For each 1 mm PAS gain, AHI was reduced by 3.58 events/hour [32,34,36,39]. With regard to the 3D studies, PAV gain and AHI reduction were positively correlated (r = 0.75; 95%CI 0.65 to 0.85) [35,39], reflecting a strong relationship between changes in both dimensions. Thus, the greater the volume gain, the greater the AHI reduction.

OSA severity and its clinical signs and symptoms, as well as special patient features such as comorbidities and facial profile, among others, should be considered when dealing with OSA patients [5]. Regarding OSA severity, to date MMA is only indicated in moderate to severe cases and not in mild OSA cases (AHI < 5) [5]. All of the included articles established the type of OSA as moderate to severe in their inclusion criteria [32–39] (Table 1). However, it should be noted that two studies [32,37] reported AHI values at baseline that moved further away from the average (mean 57.9 events/hour, range 35.7 ± 18.0 32 to 69.2 ± 35.8 37). Thus, further studies are needed in order to evaluate the impact of MMA in mild OSA patients. Another relevant issue is the importance of a comprehensive assessment of the global OSA symptoms of the patient for diagnostic and disease monitoring purposes [4]. Excessive daytime sleepiness and quality of life can be subjectively evaluated through the use of multiple clinical tools and questionnaires such as the Epworth sleepiness scale (ESS) or the OSA Functional Outcomes of Sleep Questionnaire, respectively [3,5,38]. Improvement of daytime sleepiness assessed by ESS was reported by one of the included studies [38]. A significant decrease in EES from 14 (10-18) to 6 (4-7), pre- and postoperatively, was observed (p = 0.0014) [38].

Moreover, anatomical factors such as body mass index (BMI) are relevant factors that compromise OSA [5,47]. In our review, only two studies [32,33] addressed pre- and postoperative BMI. In this context, a 10% of weight loss has been associated to a 26% decrease in final AHI [47]. Nonetheless, untreated obesity is also considered a major risk factor for the progression of OSA [5,47]. Another crucial factor is the patient facial profile, since the maxillo-mandibular complex sustains the PA soft tissues. Facial analysis of many patients with OSA evidences maxillary or mandibular hypoplasia, which generally can be corrected by orthognathic surgery [48]. Accordingly, mandibular advancement devices - apart from being an option for treating mild to moderate OSA - are also useful in deciding which patients may benefit from surgical mandibular advancement in the context of OSA. Unfortunately, no similar maxillary devices for predicting the impact of maxillary advancement upon OSA are available [5].

The importance of non-anatomical factors in relation to sleep disturbance surgery outcomes has been underscored, including neuromuscular tone, rostral fluid shift, airway collapsibility and loop gain [46,49]. Li et al. [49] attributed an average of 61% of the recorded variation in postoperative AHI to these parameters ($r = 0.47$, $p < 0.01$) [49]. Therefore, anatomical and non-anatomical factors are of great value in the diagnosis and treatment of OSA patients [45-47]. Hence, the current literature suggests that a multidisciplinary strategy is strongly advisable, taking into account all the related factors in order to ensure the long-lasting success of surgical treatment [5,45,49].

Finally, our study has a number of significant limitations: 1) The main limitation is the fact that none of the included studies were randomized controlled clinical trials (RCTs) [50]; 2) Few articles were included in the meta-analysis; 3) Definitive generalizations cannot be made, given that of the eight studies included [32-39], only two were prospective. The remainder were retrospective and therefore subjected to the usual biases and limitations of retrospective studies [40]; 4) There was a lack of homogeneity among the studies regarding the PA measurements (2D or 3D); 5) Some of the studies did not directly provide mean values or standard deviations – such data being calculated directly from the tables reporting individual patient values; 6) Regarding the PSG parameters, most of the studies used the AHI index [32,34,39]. However, one publication [33] used the Respiratory Disturbance Index; 7) No firm conclusions on the impact of MMA on surgical cure rate can be stated since only two studies reported cure rates.

CONCLUSIONS

There is a lack of homogeneous and detailed data in the current literature regarding AHI reduction and PAS/PAV gain after MMA in patients with a retrusive facial profile. However, within the limitations of this systematic review, there is sufficient evidence to conclude that MMA significantly increases PA dimensions and ensures a final AHI score below the threshold of 20 events/hour, obtaining a mean SR of 87.5%. However, further studies are needed to individualize the required magnitude and direction of surgery-induced movements for each patient.

REFERENCES

1. Knudsen TB, Laulund AS, Ingerslev J, Homøe P, Pinholt EM. Improved apnea-hypopnea index and lowest oxygen saturation after maxillomandibular advancement with or without counterclockwise rotation in patients with obstructive sleep apnea: A meta-analysis. J Oral Maxillofac Surg. 2015;73(4):719–26.

2. Lloberes P, Duran-Cantolla J, Martinez-Garcia MA, Marin JM, Ferrer A, Corral J, et al. Diagnosis and treatment of sleep apnea-hypopnea syndrome. Spanish Society of Pulmonology and Thoracic Surgery. Arch Bronconeumol. 2011 Mar;47(3):143–56.

3. Durán J, Esnaola S, Rubio R, Iztueta A. Obstructive sleep apnoea-hypopnoea and related clinical features in a population-based sample of subjects aged 30 to 70 years. Am J Respir Crit Care Med. 2001;163(3):685–9.

4. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea : An American Academy of Sleep Medicine Clinical Practice Guideline. 2017;13(3):479–504.

5. Dicus Brookes CC, Boyd SB. Controversies in Obstructive Sleep Apnea Surgery. Oral Maxillofac Surg Clin North Am. 2017;29(4):503–13.

6. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. Proc Am Thorac Soc. 2008;5: 173–178.

7. Guilleminault C, Tilkian A, Dement WC. The Sleep Apnea Syndromes. Annu Rev Med 1976;27(1):465–84.

8. Holty JE, Guilleminault C. Maxillomandibular advancement for the treatment of obstructive sleep apnea: a systematic review and meta-analysis. Sleep Med Rev 2010;14:287–97.

9. Hernandez-Alfaro F, Guijarro-Martinez R, Mareque-Bueno J. Effect of mono- and bimaxillary advancement on pharyngeal airway volume: cone-beam computed tomography evaluation. J Oral Maxillofac Surg. 2011 Nov;69(11):e395-400.

10. Guijarro-Martínez R, Swennen GRJ. Cone-beam computerized tomography imaging and analysis of the upper airway: A systematic review of the literature. Int J Oral Maxillofac Surg. 2011;40(11):1227–37.

11. Prinsell JR. Obstructive Sleep Apnea—Surgical Treatment. In: Current Therapy In Oral and Maxillofacial Surgery. Elsevier; 2012. p. 1048–63.

12. Prinsell JR. Maxillomandibular advancement surgery in a site-specific treatment approach for obstructive sleep apnea in 50 consecutive patients. Chest. 1999;116(6):1519–29.

13. Butterfield KJ, Marks PLG, McLean L, Newton J. Linear and volumetric airway changes after maxillomandibular advancement for obstructive sleep apnea. J Oral Maxillofac Surg. 2015 Jun;73(6):1133–42.

14. Guijarro-Martínez R, Swennen GRJ. Three-dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: A validation study. Int J Oral Maxillofac Surg. 2013;42(9):1140–9.

15. Christovam IO, Lisboa CO, Ferreira DMTP, Cury-Saramago AA, Mattos CT. Upper airway dimensions in patients undergoing orthognathic surgery: a systematic review and meta-analysis. Int J Oral Maxillofac Surg. 2016;45(4):460–71.

16. Haas OL, Becker OE, De Oliveira RB. Computer-aided planning in orthognathic surgery - Systematic review. Int J Oral Maxillofac Surg. 2015;44(3):329–42.

17. Moher, D; Liberati, A; Tetzlaff J, Altman D. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Preferred Reporting Items for Systematic reviews and Meta-Analyses. BMJ Br Med J 2010;8:b2535.

18. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, et al. The PRISMA Statement for Reporting Systematic Reviews and Meta-Analyses of Studies That Evaluate Health Care Interventions: Explanation and Elaboration. PLoS Med. 2009 Jul 21 [cited 2017 Sep 3];6(7):e1000100.

19. Dersimonian R, Laird N. Meta-Analysis in Clinical Trials. Stat Med. 1986;188:177–88.

20. Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343(7829):1–9.

21. Susarla SM, Abramson ZR, Dodson TB, Kaban LB. Upper airway length decreases after maxillomandibular advancement in patients with obstructive sleep apnea. J Oral Maxillofac Surg. 2011 Nov;69(11):2872–8.

22. Giarda M, Brucoli M, Arcuri F, Benech R, Braghiroli A, Benech A. Efficacy and safety of maxillomandibular advancement in treatment of obstructive sleep apnoea syndrome. Acta Otorhinolaryngol Ital. 2013 Feb;33(1):43–6.

23. Abramson Z. Three-Dimensional Computed Tomographic Airway Analysis of Patients With Obstructive Sleep Apnea Treated by Maxillomandibular Advancement. 2011;677–86.

24. Waite P., Wooten V, Lachner J, Guyette R. Maxillomandibular advancement surgery in 23 patients with obstructive sleep apnea syndrome. J Oral Maxillofac Surg. 1989;47(12):1256–61.

25. Riley RW, Powell NB, Li KK, Troell RJ, Guilleminault C. Surgery and obstructive sleep apnea: long-term clinical outcomes. Otolaryngol Head Neck Surg. 2000 Mar;122(3):415–21.

26. Santos Junior JF dos, Abrahao M, Gregorio LC, Zonato AI, Gumieiro EH. Genioplasty for genioglossus muscle advancement in patients with obstructive sleep apnea-hypopnea syndrome and mandibular retrognathia. Braz J Otorhinolaryngol. 2007;73(4):480–6.

27. Hasebe D, Kobayashi T, Hasegawa M, Iwamoto T, Kato K, Izumi N, et al. Changes in oropharyngeal airway and respiratory function during sleep after orthognathic surgery in patients with mandibular prognathism. Int J Oral Maxillofac Surg. 2011 Jun;40(6):584–92.

28. Abramson Z, Susarla SM, Lawler M, Bouchard C, Troulis M, Kaban LB. Three-dimensional computed tomographic airway analysis of patients with obstructive sleep apnea treated by maxillomandibular advancement. J Oral Maxillofac Surg. 2011;69(3):677–86.

29. Barrera JE. Virtual surgical planning improves surgical outcome measures in obstructive sleep apnea surgery. Laryngoscope. 2014 May;124(5):1259–66.

30. Gokce SM, Gorgulu S, Gokce HS, Bengi AO, Karacayli U, Ors F. Evaluation of pharyngeal airway space changes after bimaxillary orthognathic surgery with a 3-dimensional simulation and modeling program. Am J Orthod Dentofacial Orthop. 2014 Oct;146(4):477–92.

31. Uesugi T, Kobayashi T, Hasebe D, Tanaka R, Ike M, Saito C. Effects of orthognathic surgery on pharyngeal airway and respiratory function during sleep in patients with mandibular prognathism. Int J Oral Maxillofac Surg. 2014 Sep;43(9):1082–90.

32. Fairburn SC, Waite PD, Vilos G, Harding SM, Bernreuter W, Cure J, et al. Three-Dimensional Changes in Upper Airways of Patients With Obstructive Sleep Apnea Following Maxillomandibular Advancement. J Oral Maxillofac Surg. 2007;65(1):6–12.

33. Jones R, Badlani J, Jones C. Maxillary , mandibular and chin advancement surgery for the treatment of obstructive sleep apnoea. 2010;55(3):314–21.

34. Ronchi P, Cinquini V, Ambrosoli A, Caprioglio A. Maxillomandibular advancement in obstructive sleep apnea syndrome patients: a restrospective study on the sagittal cephalometric variables. J oral Maxillofac Res. 2013;4(2):e5.

35. Bianchi A, Betti E, Tarsitano A, Morselli-Labate AM, Lancellotti L, Marchetti C. Volumetric three-dimensional computed tomographic evaluation of the upper airway in patients with obstructive sleep apnoea syndrome treated by maxillomandibular advancement. Br J Oral Maxillofac Surg. 2014 Nov;52(9):831–7.

36. Schendel SA, Broujerdi JA, Jacobson RL. Three-dimensional upper-airway changes with maxillomandibular advancement for obstructive sleep apnea treatment. Am J Orthod Dentofacial Orthop. 2014 Sep;146(3):385–93.

37. Hsieh Y-J, Liao Y-F, Chen N-H, Chen Y-R. Changes in the calibre of the upper airway and the surrounding structures after maxillomandibular advancement for obstructive sleep apnoea. Br J Oral Maxillofac Surg. 2014 May;52(5):445–51.

38. Veys B, Pottel L, Mollemans W, Abeloos J, Swennen G, Neyt N. Three-dimensional volumetric changes in the upper airway after maxillomandibular advancement in obstructive sleep apnoea patients and the impact on quality of life. Int J Oral Maxillofac Surg. 2017;46(12):1525–32.

39. de Ruiter MHT, Apperloo RC, Milstein DMJ, de Lange J. Assessment of obstructive sleep apnoea treatment success or failure after maxillomandibular advancement. Int J Oral Maxillofac Surg. 2017;46(11):1357–62.

40. Thompson SG, Higgins JPT. How should meta-regression analyses be undertaken and interpreted? Stat Med. 2002;21(11):1559–73.

41. Tan SK, Leung WK, Tang ATH, Zwahlen RA. How does mandibular advancement with or without maxillary procedures affect pharyngeal airways? An overview of systematic reviews. PLoS One. 2017;12(7):1–20.

42. Bartolucci ML, Bortolotti F, Raffaelli E et al. The effectiveness of different mandibular advancement amounts in OSA patients: a systematic review and meta-regression

43. Sher AE, Schechtman KB, Piccirillo JF. The efficacy of surgical modifications of the upper airway in adults. Sleep 1976;19:156.

44. Hobson JC, Robinson S, Antic NA et al. What is ''Success'' Following Surgery for Obstructive Sleep Apnea?: The Effect of Different Polysomnographic Scoring Systems. Laryngoscope, 2012;122:1878–1881.

45. Dedhia RC. Time for surgeons to think outside the anatomical box. J Clin Sleep Med .2017;13(9):1023–1024.

46. Sin DD, Fitzgerald F, Parker JD, Newton G, Floras JS, Bradley TD. Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. Am J Respir Crit Care Med. 1999;160(4):1101–6.
47. Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea: Implications for treatment. Chest. 2010;137(3):711–9.
48. Ristow O, Ruckshlo T, Berger T el al. Short and long-term changes of the pharyngeal airway after surgical mandibular advancement in Class II patients a three-dimensional retrospective study. Journal of Cranio-Maxillo-Facial Surgery 2018;46:56-62
49. Li Y, Ye J, Han D, et al. Physiology-based modeling may predict surgical treatment outcome for obstructive sleep apnea. J Clin Sleep Med.2017;13(9):1029–1037.

50. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. Ann Int Med 2010;152. Epub 24 March.

3.2

3.2 Paper two

Variation between natural head orientation and Frankfort horizontal planes in orthognathic surgery patients:

187 consecutive cases

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ABSTRACT

The purpose of this study was to assess the relationship between the Frankfort Horizontal (FH) and natural head orientation (NHO), their correlation between patients' malocclusion, and the impact of counterclockwise rotation (CCW) in the FH-NHO angle variation after orthognathic surgery. An evaluation of 187 consecutive patients was performed at the Maxillofacial Institute (Teknon Medical Center, Barcelona). FH-NHOº was measured pre- and postoperatively at 1- and 12-months, respectively, after 3D superimposition using a software (Dolphin®). Patients were classified as follows: 3.2%, 48.7% and 48.1% class I,II and III, respectively. Baseline FH-NHOº was significantly positive for patients with dentofacial deformities (2.73º ± 4.19 (2.12-3.33º, $p < 0.001$). The impact of orthognathic surgery in FH-NHOº was greater in class II when compared to class III patients, with a variation of 2.04º ± 4.79 ($p < 0.001$) and -1.20º ± 3.03 ($p < 0.001$), respectively. FH-NHOº increased when CCW rotational movements were performed ($p=0.006$). The results of this study suggest that pre- and postoperative NHO differs from FH in orthognathic patients. The angle between FH and NHO is significantly larger in class III than in class II patients at baseline, which converges after orthognathic surgery when CCW rotation is performed. Therefore, NHO should be used as the real horizontal plane when planning for orthognathic surgery.

Keywords: Patient Positioning; Orthognathic surgery; dentofacial deformities; Three-dimensional imaging; Cone-beam computed tomography.

INTRODUCTION

Head orientation is a key factor in cephalometric and facial analysis for orthodontic and orthognathic surgery treatment planning, since it influences the antero-posterior perception of the maxillomandibular complex and may result in an incorrect diagnosis (1).

Various reference planes have been described for head orientation, both extracranial and intracranial (2). One of the most commonly used is the Frankfort horizontal (FH) plane, which was first described in the Frankfort Craniometric Agreement (1882) (3), and was defined as a plane that passes through the upper rim of the external acoustic meatus (porion, Po) and the lowest point of the orbital rim (orbitale, Or) (2,3). However, a potential variability has been observed with the FH plane and similar planes that use only intracranial landmarks, since the anatomical landmarks are influenced by individual biological variability (4). The FH plane has been found to deviate from the true horizontal plane depending on head inclination, especially in patients with dental or facial deformities (5).

Extracranial reference planes, such as the natural head position (NHP) and natural head orientation (NHO) are alternatives to the intracranial reference planes, enabling the use of true vertical and horizontal lines for clinical facial analysis (6). The concept of NHP was introduced in cephalometric analysis in the 1950s and is defined as the physiological position of the head that feels most natural to a living person (6,7). Thus, NHP has been described as the ideal reference in cephalometric analysis due to its reliability and reproducibility, as it focuses on a distant point and therefore is not influenced by cranial base variability (5,8). Although there are different methods for the patient to achieve NHO, the most common is to indicate the individual to look straight ahead at a point in front of them at eye level (e.g. looking into a mirror) (6). However, there is a slight subjectivity in head orientation since it depends on the patient who has to be told how to achieve a natural posture, and it sometimes requires a certain experience of the clinician (9).

Furthermore, NHO is influenced by other factors such as the visual and vestibular apparatus, local proprioceptors, craniocervical posture, facial and neck muscles, temporomandibular joints, maxillo-mandibular relation and dental occlusion (10). Then, since the maxillomandibular relation is one of the defining factors of head positioning, NHO should theoretically change after orthognathic surgery, and even more when counterclockwise (CCW) rotational movements are performed, due to its effect on the accommodation of the head on the cervical column (11,12).

Therefore, the main objectives of this research were to assess the relationship between FH and NHO and its correlation between patients' dental class, and the impact of CCW rotation in the FH-NHO angle variation after orthognathic surgery.

MATERIALS AND METHODS

To address the research purpose, the investigators designed and implemented a retrospective cohort study. The study population was composed of consecutive patients with a dentofacial deformity who underwent orthognathic surgery (either mono- or bimaxilar) during 2019 at the Maxillofacial Institute (Teknon Medical Center in Barcelona, Spain). Clinical data and 3D radiological images were obtained from the Institute's database. Each patient provided written informed consent to access their cone-beam computed tomography data (CBCT). This study was approved by the Teknon Medical Hospital Institutional review board (IRB) (Barcelona, Spain) (Ref.2019/60-CMF-TEK), and was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its subsequent amendments. All participants signed an informed consent agreement.

Patients of any gender, over the age of 18 years old with a completed growth of the maxillofacial complex and who underwent orthognathic surgery (mono- or bimaxillary) were included in the study. Patients with craniofacial syndromes or craniocervical posture pathology, patients with missing follow-up photographs and CBCTs or not willing to sign the informed consent were excluded from the study.

Presurgical three-dimensional (3D) planning protocol, as described elsewhere, was performed with a three-party software and the upper incisor soft-tissue nasion plane (UI-STP) was used an absolute reference to guide the anteroposterior positioning of the maxillomandibular complex (11). Intermediate and final surgical splints were designed and printed in-house. Patients were operated on under general anesthesia by the same surgeon (FHA) following the mandible-first protocol. A mandibular bilateral sagittal split osteotomy (BSSO) was performed using the Dal Pont-Obwegeser method and/or a maxillary LeFort I osteotomy was carried out using the minimally invasive 'Twist technique' described elsewhere (14) Surgical data was collected regarding type of mono- or bimaxillary surgery and whether clockwise or CCW rotation movements were performed.

All included patients had followed the standard pre- and post-operative imaging workflow protocol for orthognathic surgery of the Department, which involves facial and occlusal pictures and CBCT at three time points: preoperatively (T0) and postoperatively at 1- (T1) and 12- (T2) months follow-up. These two postoperative time points were chosen in order to evaluate the short- and long-term effect of orthognathic surgery in NHO.

The CBCT scans were performed using an i-CAT Vision system (iCAT, Imaging Sciences International, Hatfield, PA, USA). For both records (CBCT and photographs), patients were previously instructed by clinical trained personnel in order to achieve a proper head orientation: they were indicated to adopt a standing position and to look straight ahead at a point at eye level located on the wall in front of them (1m) (6). In addition, a 2 mm centric relation wax bite was placed to avoid occlusal interferences.

Each patient had three CBCT datasets (pre-operative (T0), post-operative at one-month (T1) and post-operative at 12 months (T2)). Data were primarily saved in DICOM (Digital Imaging and Communications in Medicine) format using a 3D software (Dolphin Imaging, version 11.95 premium, Chatsworth, CA, USA). Routine photographic records in NHO were used to orientate and match up the CBCT 'virtual patient' ('soft tissue layer') as follows: a true horizontal line was traced on the photograph (lateral view), passing through two points: the lateral canthus of the eye and at some point of the helix (auricular point, which varied depending on each patient) (Fig.1).

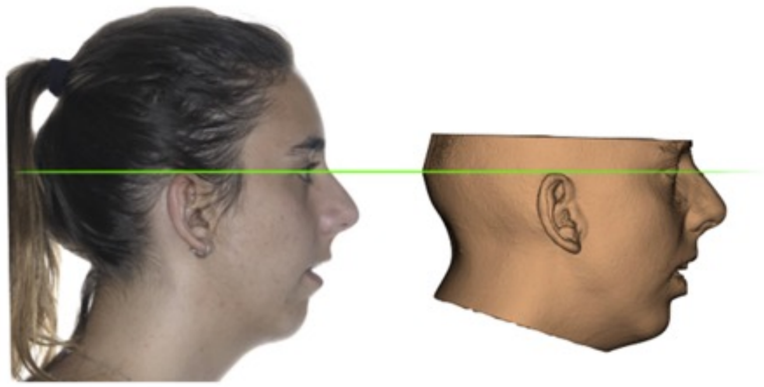

Fig. 1. Extracranial true horizontal line used by the clinicians to orient the cone-beam computed tomography. A true horizontal line was traced on the photograph (lateral view), passing through two points: the lateral canthus of the eye and at a determined point of the helix (auricular point, which varied depending on each patient).

Once external orientation of the virtual patient was performed ('soft tissue layer'), the three CBCTs datasets were superimposed in accordance with the voxel-based superimposition protocol described previously by the authors elsewhere (15) to avoid measurement error. The software orientation calibration tool was used along pitch (x), yaw (y) and roll (z). Orientation of both the 'Base volume' (original DICOM) and '2nd volume' (duplicate DICOM) was undertaken to achieve the same original positions of the CBCTs ('Hard tissue layer'). Then, superimposition of the preoperative CBCTS at T1 and T2 was done using the cranial base, as it remains stable after surgery. The software allows a proper manual adjustment following the superimposition three-step protocol as follows (1): Landmark based superimposition ('side-by-side superimposition), (2): Voxel-based superimposition ('overlay superimposition by volume sub-regions') and (3): Head orientation export ('Export to 2nd volume'). This means that all the three images (T0, T1, and T2) were in the same coordinate position after voxel-based superimposition and orientation were performed. Then, the FH plane was marked as a line connecting the right porion (Po, the upper rim of the external acoustic meatus) and right orbitale (Or, the lowest point of the orbital rim) ('Hard tissue layer') (3).

The angle between FH and NHO (FH-NHOº) was measured by two investigators (MGH and AVO) before the intervention (T0), at 1-month (T1) and 12-months follow-up (T2). Its relationship was considered positive if the FH was located superior to the NHO plane and negative if FH was inferior to it (Fig.2). In order to ensure truly accurate and reproducible measurements, the examiners tagged all virtual models independently on two separate occasions (two weeks apart), thus avoiding inter and intra-observer differences, respectively. Inter and Intra-class correlation analyses (ICC) were used to calculate examiner differences and reliability (16,17).

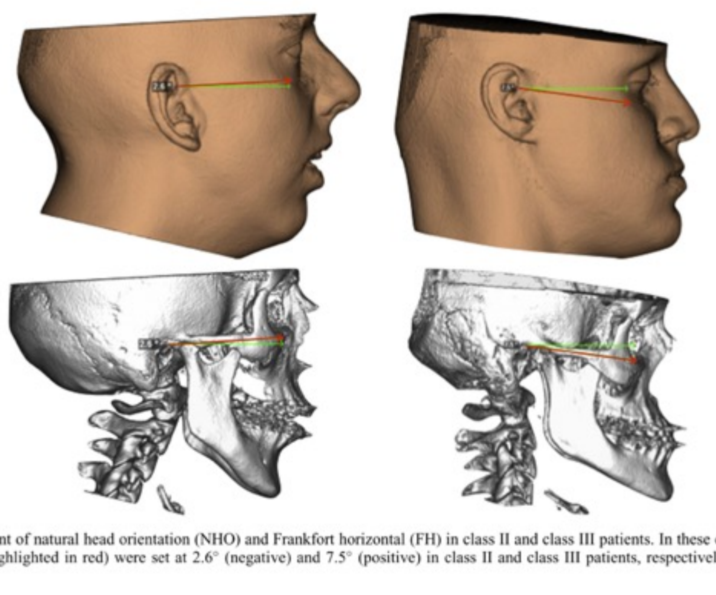

Fig. 2. Assessment of natural head orientation (NHO) and Frankfort horizontal (FH) in class II and class III patients. In these cases, NHO with respect to FH (highlighted in red) were set at 2.6° (negative) and 7.5° (positive) in class II and class III patients, respectively.

Statistical analysis (IBM SPSS Software Version 25) was used to investigate the relationship between FH and NHO before, and 1-month and one-year after surgery. Descriptive analysis evaluated the most relevant statistics for all analyzed variables, and a Kolmogorov-Smirnov test was used to check the normal distribution of FH-NHO dimensions. In order to compare measurements at different time points and their correlation with dental class and surgical procedure, an inferential analysis was performed using the ANOVA test and the Bonferroni correction. Two-sided p-values <0.05 were considered significant for all of the statistical tests. A mixed ANOVA model reached a statistical power of 98% when detecting mean differences in NHO between groups, with a medium effect size (f = 0.25) and a 95% confidence interval. The statistical power was 88% with a small-medium effect size (f = 0.15) for intra-observer variation and differences over time (T0, T1, T2).

RESULTS

A sample of 187 consecutive patients who underwent orthognathic surgery were included in the study. The sample comprised of 124 women (66.3%) and 63 men (33.7%), with a mean age of 33.9 ± 11.2 years (range 15-67). Patients were classified as dental class I (3.2%), class II (48.7%) or class III (48.1%) according to Angle's malocclusion classification (18). All of the selected patients underwent bimaxillary (80%) or monomaxillary (20%) surgery, of whom 55.9% and 43% received a CCW and clockwise rotation of the maxillomandibular complex, respectively. No rotational movements were performed in 1% of the sample (Table 1). The ICC obtained for the angles was < 0.11°.

Table 1. Descriptive characteristics of the studied sample.

	n = 187	%
Gender		
Male	63	33.7
Female	124	66.3
Type of dentofacial deformity		
Class I	6	3.2
Class II	91	48.7
Class III	90	48.1
Type of interventions		
Bimaxillary surgery	149	79.6
Monomaxillary surgery	38	20.4
Rotational movements		
CW	80	43
CCW	104	55.9
No rotation	3	1.1
Age (mean ± SD)	33.9 ± 11.2	

Abbreviations: clockwise rotation; CCW: counterclockwise rotation.

The mean baseline FH-NHO° was 2.73° ± 4.19° (2.12-3.33°, $p < 0.001$). FH-NHO° was significantly positive for the population eligible for orthognathic surgery ($p < 0.001$, t-test). In particular, regarding FH-NHO° related to Angle's dental class, statistically significant differences between class II and III patients in each group were observed ($p < 0.001$, test F) (Fig. 3).

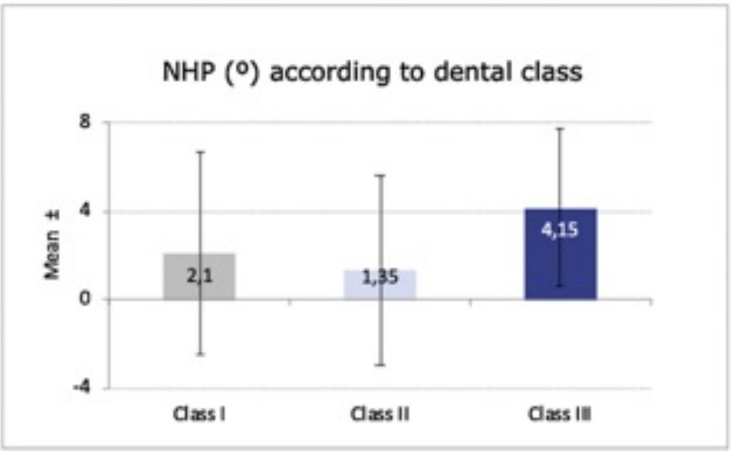

Fig. 3. Mean angle between Frankfort horizontal and natural head orientation (FH-NHO°) for class I, II and III patients. NHP, natural head position.

Regarding FH-NHO° changes after surgery, there were no significant differences for the total sample, neither at 1-month (2.86° ± 3.12) ($p = 1.000$) nor at 12-months follow-up (3.15° ± 3.19) ($p = 0.539$). However, a variation in FH-NHO° was observed between dental class II and III patients ($p < 0.001$) (Fig. 4). A greater impact of surgery was evidenced in class II compared to class III patients, reporting FH-NHO° changes between T0 and T2 as follows: 2.04° ± 4.79 ($p < 0.001$) and -1.20° ± 3.03 ($p < 0.001$), respectively.

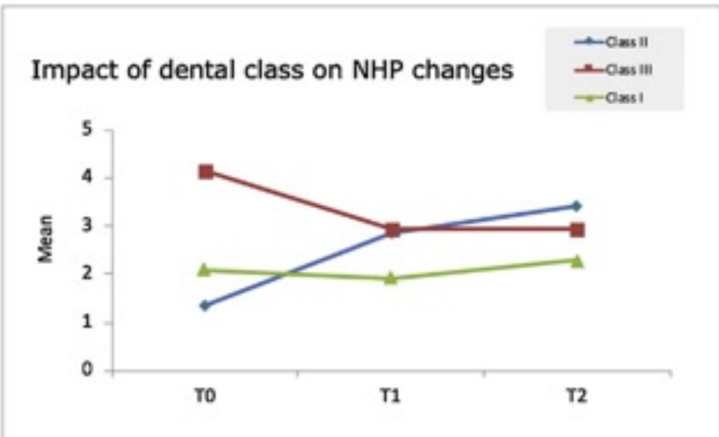

Fig. 4. Impact of dental class (I, II and III) on the angle between Frankfort horizontal and natural head orientation (FH-NHO°) over time (T0, T1 and T2). NHP, natural head position.

No significant changes could be detected based on the type of surgery (mono- and bimaxillary surgery) (p=0.318). Nevertheless, patients who received a CCW rotation in the context of a bimaxillary surgery (compared to those patients with CW or without rotational movement), FH-NHP° increased significantly (p = 0.006) (Fig. 5).

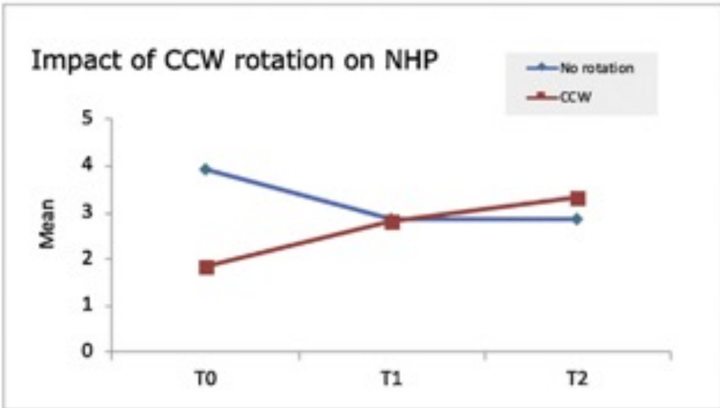

Fig. 5. Impact of counterclockwise (CCW) rotation on Frankfort horizontal and natural head position (FH-NHP°) over time (T0, T1 and T2).

A multivariate model was calculated including each single independent variable in order to rule out eventual bias and confounding factors. Results showed that FH-NHO° changes significantly depends on the dental class of the patient (p < 0.001) and the CCW rotation performed at surgery in the bimaxillary group (p = 0.082) (Fig. 6).

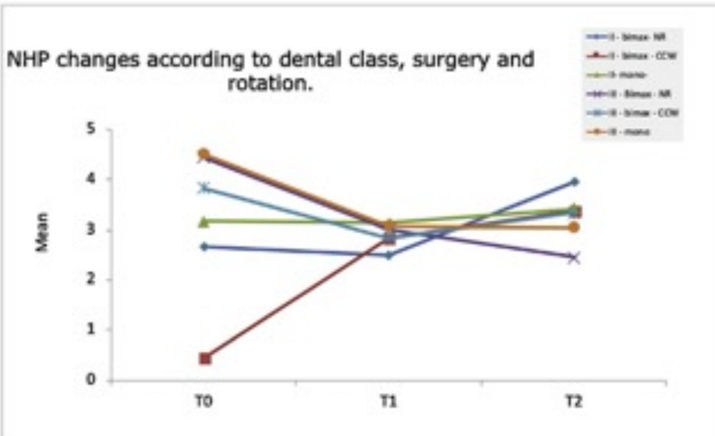

Fig. 6. Multivariate analysis of changes in the angle between Frankfort horizontal and natural head orientation (FH-NHO°) over time according to dental class (I, II or III), type of surgery (mono- or bimaxillary) and rotation [no rotation (NR) or counterclockwise (CCW)], in the short and long term.

DISCUSSION

The head positioning of the CBCT is essential for the virtual planning of orthognathic surgery. The results of the present study show that FH is not equivalent to NHO and that a positive angle between FH-NHO exists (2.73° ± 4.19, $p < 0.001$, t-test). This implies that FH is located superiorly to the NHO plane in most cases, which is in agreement with the published literature (5). However, when grouping patients according to dental class, class II patients showed a smaller FH-NHO angle (1.35° ± 4.29), whereas class III patients presented an increased relationship (4.15° ± 3.60) ($p < 0.001$) (Fig. 3). Emphasis should be placed when adjusting the head position of the patient during NHO registration to avoid diagnostic errors, as Class II and Class III facial types tend to compensate for their head position (19). Class II subjects tilt their head upwards, whereas class III subjects do it downwards, so the FH represents an upward or downward inclination in relation to the true horizontal plane, respectively (19). Thus, it is plausible that NHO should be the 'gold standard' reference plane instead of FH, since a reliable reference plane is necessary for a correct 3D facial analysis, which becomes even more evident in patients with dentofacial deformities (4). Needless to say, both treating orthodontists and surgeons should use the same reference plane in order to use a common terminology for treatment planning, and therefore align treatment goals, increase accuracy and improve final outcomes.

Reproducibility of NHO in the sagittal, coronal and axial planes with 3D imaging has been proven to be as reliable as with cephalometric radiographs (17,20,21). When recording NHO three-dimensionally, a CBCT in an upright position without external immobilizers is recommended, rather than a conventional computed tomography in a supine position (21). Although it would be desirable for patients to undergo the scan with a proper NHO, some unexpected changes in head position during the recording process are unavoidable. For this reason, new tools and softwares have been designed to record, transfer and adjust NHO properly; such as stereophotogrammetry, laser surface scanner, or digital gyroscope, among others (17,22,23). However, the devices themselves may influence the accuracy of re-orientated head position, and in some cases may cause soft tissue distortion (20,24,25). Therefore, surgeons usually use a simple virtual skull re-orientation method according to NHO based on frontal and lateral photographic records (26).

As stated previously, extracranial references such as NHO allow the use of true vertical and horizontal lines as optimal reference planes for surgical planning (27,28). In this context, the authors used a soft tissue vertical line that passes through nasion soft tissue as an absolute reference to guide the anteroposterior positioning of the maxillomandibular complex, further described elsewhere (11).

Besides, when Class I was obtained after surgery, FH-NHO angulation increased in class II patients (3.40° ± 3.41), while it reduced in class III (2.95° ± 3.04). Remarkably, final FH-NHO relationship for both groups converged after treatment yielding to a more similar value, which was close to the overall postsurgical FH-NHO value of the entire sample (3.15° ± 3.19), which can be considered as a close approximation to the standard FH-NHO relationship of class I patients (Fig.4). Therefore, this relationship was still positive, which reaffirms the earlier statement that FH is not equivalent to NHO.

The relationship between the final FH-NHO° and the patients' dentofacial deformity was greater in class II than in class III patients, which reverses the initial situation of the angle (Fig. 4). This is explained by the previous adaptation of the cranio-cervical posture, facial and neck muscles, temporomandibular joints, visual and vestibular apparatus and local proprioceptors which counteract the pre-surgical dental class and pattern of maxillomandibular imbalance (12,29).

To our knowledge, this is the first study to evaluate the impact of CCW rotation in FH-NHO° after orthognathic surgery. Although neck and head posture changes after orthognathic surgery have been widely reported in the literature (30,31), CCW rotation of the maxillomandibular complex was significantly related to FH-NHO° changes ($p = 0.006$) (Fig. 5), which suggests that occlusal plane changes have an impact on the cranio-cervical posture, and these differences increased after surgery (11). This is explained because of patients' tendency to reduce their pre-surgical postural CCW adaptation after orthognathic surgery. Then, once it is surgically corrected, there is no need for this adaptation.

The type of surgery did not induce significant changes in the NHO, but the rotational movements performed. Thus, when CCW rotation was performed in the context of bimaxillary surgery, FH-NHO angulation increased at one-month follow up (from 1.83° to 2.81°) and to a greater extent at 12- follow-up (from 2.81° to 3.32°) (Fig. 5). Similarly, the same pattern was observed in class II patients: FH-NHO° increased immediately after surgery and even further at long-term follow-up (T0-T1-T2: 1.35° - 2.84° - 3.40°, respectively). However, FH-NHO° decreased significantly after surgery and remained stable over time in class III patients (T0-T1=T2, from 4.15° to 2.95°) (Fig. 4). This suggests that the period of adaptability of the abovementioned influencing factors in NHO is longer in class II patients when CCW rotation is performed, than in class III patients.

A potential limitation to this study was on the reliability analysis of NHO determination and measurement assessment. To overcome this problem, emphasis was placed at landmark identifications and angle measurements. In order to ensure truly accurate, reproducible measurements and to avoid landmark errors produced by magnification and distortion, both of the examiners (MGH, AVO) were previously calibrated: both clinicians tagged all virtual models independently on two separate occasions (two weeks apart), thus avoiding inter- and intra-observer differences, respectively. ICC (inter- and intra-) analyses were performed throughout the present study. With regard to NHO re-orientation reliability, 3D imaging techniques do not maintain the previously recorded NHO of the patient, then, subjective re-orientation by expert clinicians of the 3D images is needed (Fig. 1) (17). Given that, some authors (17) have determined a moderate reliability for both intra- and inter-rater reliability for re-orientating 3D images into the estimated natural head position (17). In their study, the authors found a small median ICC difference for roll and yaw, but larger for pitch (17). This means that clinicians tended to position the chin posteriorly (6.3 ± 5.2 mm), reducing the perceived severity of the dentofacial deformity in the antero-posterior direction. Therefore, this data highlights the importance of orientating the 3D images prior to measuring and planning. Both calibration and ICC analyses followed those from Lagravere et al. 2010 (16) and Zhu et al. 2018 (17) previous studies, and measurements were taken in the three axis (x,y,z) as abovementioned. In this study, the ICC obtained by the authors for the angle variability was < 0.11°. Thus, our ICC analyses for this study are in line with those previously accepted in the literature, which demonstrates the accuracy of the followed approach on NHO determination and landmark identification among different examiners (16).

CONCLUSIONS

In conclusion, the results of this study suggest that pre- and postoperative NHO differs from FH in orthognathic patients. The angle between FH and NHO is significantly larger in class III patients than in class II patients at baseline, which converges after orthognathic surgery when CCW rotation is performed. Therefore, NHO should be used as the real horizontal plane when planning for orthognathic surgery.

REFERENCES

1. Barbera AL, Sampson WJ, Townsend GC. Variation in natural head position and establishing corrected head position. HOMO- J Comp Hum Biol. 2014;65(3):187–200.

2. Naini FB. The Frankfort plane and head positioning in facial aesthetic analysis-The perpetuation of a myth. JAMA Facial Plast Surg. 2013;15(5):333–4.

3. J.G. G. The Frankfort Craniometric Agreement , with Critical Remarks Thereon . Author (s): J . G . Garson Source : The Journal of the Anthropological Institute of Great Britain and Ireland , Vol . 14. 1885;14(1885):64–83.

4. Lundström A, Lundström F. The Frankfort horizontal as a basis for cephalometric analysis. Am J Orthod Dentofac Orthop. 1995;107(5):537–40.

5. Bjerin R. A Comparison Between the Frankfort Horizontal and the Sella Turcica - Nasion As Reference Planes in. Acta Odontol Scand. 1957;15(1):1–12.

6. Lundström A, Lundström F, Lebret, Moorrees CFA. Lundstrom.Natural head position and natural head orientation- basic considerations in cephalometric analysis a. European journal of orthodontics..pdf. 1995. p. 111–20.

7. Moorrees CFA, Kean MR. Natural head position, a basic consideration in the interpretation of cephalometric radiographs. Am J Phys Anthropol. 1958;16(2):213–34.

8. Cuccia AM, Carola C. The natural head position. Different techniques of head positioning in the study of craniocervical posture. Minerva Stomatol. 2009;3(58):601–12.

9. Capon T. Standardised anatomical alignment of the head in a clinical photography studio. A comparison between the Frankfort Horizontal and the natural head position. J Vis Commun Med. 2016;39(3–4):105–11.

10. Solow B, Sonnesen L. Head posture and malocclusions. Eur J Orthod. 1998;20(6):685–93.

11. Savjani D, Wertheim D, Edler R. Change in cranio-cervical angulation following orthognathic surgery. Eur J Orthod. 2005;27(3):268–73.

12. Paya-Argoud M, Tardieu C, Cheynet F, Raskin A, Borel L. Impact of orthognathic surgery on the body posture. Gait Posture [Internet]. 2019;67(September 2018):25–30. Available from: https://doi.org/10.1016/j.gaitpost.2018.09.019

13. Hernández-Alfaro F. Upper incisor to Soft Tissue Plane (UI-STP): A new reference for diagnosis and planning in dentofacial deformities. Med Oral Patol Oral Cir Bucal. 2010;15(5):8–10.

14. Hernandez-Alfaro F, Guijarro-Martinez R. “Twist technique” for pterygomaxillary dysjunction in minimally invasive Le Fort I osteotomy. J Oral Maxillofac Surg. 2013 Feb;71(2):389–92.

15. Haas Junior OL, Guijarro-Martínez R, Sousa Gil AP de, Méndez-Manjón I, Valls-Otañón A, de Oliveira RB, et al. Cranial Base Superimposition of Cone-Beam Computed Tomography Images. J Craniofac Surg. 2019;00(00):1.

16. Lagravère MO, Low C, Flores-Mir C, Chung R, Carey JP, Heo G, et al. Intraexaminer and interexaminer reliabilities of landmark identification on digitized lateral cephalograms and formatted 3-dimensional cone-beam computerized tomography images. Am J Orthod Dentofac Orthop. 2010;137(5):598–604.

17. Zhu S, Keeling A, Hsung TC, Yang Y, Khambay B. The difference between registered natural head position and estimated natural head position in three dimensions. Int J Oral Maxillofac Surg [Internet]. 2018;47(2):276–82. Available from: http://dx.doi.org/10.1016/j.ijom.2017.07.016
18. Wolford LM, Chemello PD, Hilliard F. Occlusal plane alteration in orthognathic surgery-part I: Effects on function and esthetics. Am J Orthod Dentofac Orthop. 1994;106(3):304–16.
19. Arnett GW, Gunson MJ. Facial planning for orthodontists and oral surgeons. Am J Orthod Dentofac Orthop. 2004;126(3):290–5.
20. Weber DW, Fallis DW, Packer MD. Three-dimensional reproducibility of natural head position. Am J Orthod Dentofac Orthop [Internet]. 2013;143(5):738–44. Available from: http://dx.doi.org/10.1016/j.ajodo.2012.11.026
21. Cassi D, De Biase C, Tonni I, Gandolfini M, Di Blasio A, Piancino MG. Natural position of the head: Review of two-dimensional and three-dimensional methods of recording. Br J Oral Maxillofac Surg [Internet]. 2016;54(3):233–40. Available from: http://dx.doi.org/10.1016/j.bjoms.2016.01.025
22. Hsung TC, Lo J, Li TS, Cheung LK. Recording of natural head position using stereophotogrammetry: A new technique and reliability study. J Oral Maxillofac Surg [Internet]. 2014;72(11):2256–61. Available from: http://dx.doi.org/10.1016/j.joms.2014.03.025
23. Yang HJ, Han JJ, Hwang SJ. Accuracy of 3D reproduction of natural head position using three different manual reorientation methods compared to 3D software. J Cranio-Maxillofacial Surg [Internet]. 2018;46(9):1625–30. Available from: https://doi.org/10.1016/j.jcms.2018.06.013
24. Damstra J, Fourie Z, Ren Y. Simple technique to achieve a natural position of the head for cone beam computed tomography. Br J Oral Maxillofac Surg [Internet]. 2010;48(3):236–8. Available from: http://dx.doi.org/10.1016/j.bjoms.2009.10.001
25. Manders PJD, Wolke JGC, Jansen JA. Bone response adjacent to calcium phosphate electrostatic spray deposition coated implants: An experimental study in goats. Clin Oral Implants Res. 2006;17(5):548–53.
26. Xia JJ, McGrory JK, Gateno J, Teichgraeber JF, Dawson BC, Kennedy KA, et al. A new method to orient 3-dimensional computed tomography models to the natural head position: A clinical feasibility study. J Oral Maxillofac Surg [Internet]. 2011;69(3):584–91. Available from: http://dx.doi.org/10.1016/j.joms.2010.10.034
27. Zebeib AM, Naini FB. Variability of the inclination of anatomic horizontal reference planes of the craniofacial complex in relation to the true horizontal line in orthognathic patients. Am J Orthod Dentofac Orthop. 2014;146(6):740–7.
28. Meiyappan N, Tamizharasi S, Senthilkumar KP, Janardhanan K. Natural head position: An overview. J Pharm Bioallied Sci. 2016;2(2):424–7.
29. Cuccia AM, Carola C. The measurement of craniocervical posture: A simple method to evaluate head position. Int J Pediatr Otorhinolaryngol. 2009;73(12):1732–6.
30. Lin X, Edwards SP. Changes in natural head position in response to mandibular advancement. Br J Oral Maxillofac Surg [Internet]. 2017;55(5):471–5. Available from: http://dx.doi.org/10.1016/j.bjoms.2017.01.007
31. Cho D, Choi DS, Jang I, Cha BK. Changes in natural head position after orthognathic surgery in skeletal Class III patients. Am J Orthod Dentofac Orthop [Internet]. 2015;147(6):747–54. Available from: http://dx.doi.org/10.1016/j.ajodo.2015.01.026

3.3

3.3 Paper three

What are the surgical movements in orthognathic surgery that most affect the upper airways?

A three-dimensional analysis

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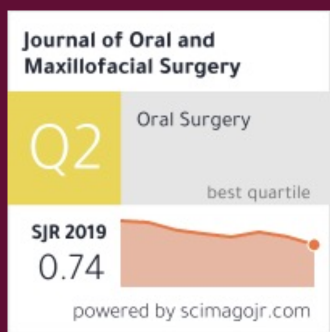

ABSTRACT

Purpose: Most studies have focused on airway changes after maxillomandibular advancement (MMA), however airway size will change depending on the type, direction and magnitude of each skeletal movement. The aim of this study was to assess the effect of the maxillary and/or mandibular movements upon the pharyngeal airway volume (PAV) and the minimum cross-sectional area (mCSA) using three-dimensional cone-beam computed tomography voxel-based superimposition.

Patients and methods: The investigators designed and implemented a retrospective cohort study composed of patients with dentofacial deformity subjected to orthognathic surgery. The predictor variable were the surgical movements performed at surgery. The primary outcome variables were the PAV and mCSA measured preoperatively, at 1 and at 12-month follow-up. Skeletal and volumetric relapse and stability were recorded as secondary outcomes at 1 and 12 months, respectively. Descriptive, bivariate and correlation analyses were computed. Significance was set at P< .05.

Results: The sample was composed of 103 patients grouped as follows: bimaxillary (BimaxS = 53) maxillary (MaxS = 25) or isolated mandible (MandS = 25). All of the surgical treatments resulted in a significant linear pattern of initial-immediate increase of 33.4% (95% CI: 28.2 – 38.7%; p<.001) in volumetric (naso- (28.7%, CI: 22.7 34.9%; p<.001) , oro- (36.2%, CI: 29.0 – 43.5%; p<.001) and hypopharynx (31.5%, CI:25.7 – 37.3%; p<.001)); and mCSA parameters (BimaxS = 104%, (CI: 87.1 – 122.1%; p<.001), MaxS = 39.5%, (CI: 18.4 – 60.7%; p<.05) and MandS = 65.8%, (CI:48.1 – 83.6%; p<.05), respectively), followed by a slight downward trend (stabilization) at 12 months follow-up. Airway increase was favored by mandibular advancement (p<.05) and mandibular occlusal plane (MOP) changes by counterclockwise rotation (CCW) (p<.05).

Conclusion: The results of this study suggest that there is a favorable effect of orthognathic surgery in the upper airway regardless of the surgical approach, with bimaxillary advancement and MOP changes by CCW rotation being the most significant contributors.

Keywords: Orthognathic surgery; dentofacial deformities; Three-dimensional analysis; Upper airway; Cone-beam computed tomography.

INTRODUCTION

The combination of orthognathic surgery and orthodontic treatment aims to re-establish facial aesthetics and optimize dental occlusion while moving the jaws. Although orthognathic surgery corrects bone discrepancies by means of osteotomies and jaw repositioning, it also implies soft tissue changes of the facial envelope (1). Similarly, repositioning of the muscles attached to jaws and pharyngeal walls creates significant volumetric changes in the pharyngeal airway: in general terms, the pharyngeal airway walls are expanded or diminished when the facial skeletal framework is repositioned either forwards or backwards, respectively (1). Thus, pharyngeal airway dimensions will change depending on the type, direction and magnitude of the skeletal movements (2). As widely reported, a mean 10 mm maxillomandibular advancement (MMA) results in a mean increase in the pharyngeal airway space (PAS) of 4.75 mm (range 3.15 - 6.35) and a mean pharyngeal airway volume (PAV) gain of 7.35 cm3 (range 5.35 - 9.34) over the long term (3). Conversely, there is evidence to support a significant narrowing of the PAS after sole mandibular setback procedures (mean decrease of 4.46 mm in males and 3.20 mm in females) for treating mandibular prognathism (4). However, no studies have evaluated the impact of the type, direction and magnitude of the different skeletal movements upon upper airway size changes at long term.

Therefore, we have designed the current study considering the following gaps that exist in the current literature which require more in-depth evaluation: 1) Orthognathic surgery involves repositioning of both the maxillary and mandibular bones, and each individual repositioning is related to specific pharyngeal airway changes. Separate study is therefore required of the impact of isolated maxillary, mandibular (and chin) movements, as well as study of the maxillomandibular complex jointly; 2) Orthognathic surgery is a procedure that implies three-dimensional (3D) movements (counterclockwise (CCW) / clockwise (CW) rotation, advancement / setback, impaction / descent, leveling and constriction / segmentation procedures), which behave differently at the pharyngeal level and should be evaluated separately; 3) There are not clear guidelines or references to determine where the maxilla and mandible should be repositioned to simultaneously maximize airway volume, still not compromising facial aesthetics; 4) Orthognathic surgery impacts three-dimensionally upon PAV (sagittal, vertical and transversal planes), so linear, volumetric and cross-sectional measurements of the pharyngeal airway are required, 5) Orthognathic surgery induces changes in all three levels of the pharyngeal airway (naso-, oro- and hypopharynx), so all of them need to be assessed; and finally, 6) Pharyngeal airway changes induced by orthognathic surgery may relapse over time, so long-term trials (12-months of follow-up) are compulsory.

The purpose of this study was to assess the effect of maxillary and mandibular movements (isolated or jointly) upon the pharyngeal airway (naso-, oro- and hypo-pharynx) and the minimum cross-sectional area (mCSA) on a three-dimensional basis. The authors hypothesize that each surgical movement during orthognathic impacts differently to increase the upper airway size. Thus, the specific aims of this study were to correlate the magnitude, type and direction of these skeletal movements with the airway dimension gain or impairment and their stability or relapse at 12 months follow-up.

MATERIALS AND METHODS

Study design/sample

To address the research purpose, the investigators designed and implemented a retrospective cohort study. The study population was composed of consecutive patients with a dentofacial deformity who underwent orthognathic surgery between January 2018 and January 2019 at the Maxillofacial Institute (Teknon Medical Center in Barcelona, Spain). Clinical data and 3D radiological images were obtained from the Institute's database.

To be included in the study sample, patients were included as study subjects if they met the following criteria: (1) age ≥ 18 years, (2) good systemic health (ASA score I or II), (3) completed growth of the maxillofacial complex, (4) patients subjected to orthognathic surgery due to occlusal, skeletal or aesthetic problems and (5) signed informed consent. Patients were excluded from the study if they presented: 1) any systemic/disease background capable of compromising bone healing, 2) congenital anomalies, 3) incomplete postoperative follow-up; and 4) missing radiological tests.

This study followed the STROBE statement guidelines (5) (www.strobe-statement.org), including a checklist of 22 items considered essential to report analytical observational studies, and Dodson 2015 (6) updated guidelines on how to report a patient-oriented manuscript. This study was approved by the Teknon Medical Hospital Institutional review board (IRB) (Barcelona, Spain), and all participants signed an informed consent agreement (Ref. 3D-OS-VAS). The study was carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Surgical protocol

All patients were operated upon under general anesthesia and controlled hypotension by the same surgeon (FHA). A mandible first protocol was followed in all cases. Mandibular sagittal osteotomy was performed following the Dal Pont-Obwegeser technique and settled with a hybrid technique (one miniplate fixed with 4 monocortical screws and a retromolar bicortical screw) (7). Maxillary procedures included Le Fort I osteotomy with or without segmental maxillary osteotomies, and always through a minimally invasive approach using the Twist technique described elsewhere (8,9). All patients were extubated in the operating room, maintaining a dynamic maxillomandibular fixation with guiding elastics. Antibiotics, antiinflammatory drugs and a closed-circuit cold mask at 17ºC were prescribed during admission. Patient were discharged 24 hours after surgery. Functional training with light guiding elastics was prescribed for one month, with a soft diet during the same period of time.

Study variables

Demographic characteristics of the sample were included: age (years), gender and type of dentofacial deformity (I, II or III). The primary outcomes measured were PAV (mm3) and mCSA (mm2), the secondary outcomes measured were surgical movements (mm) and skeletal relapse (%), pre- and postoperatively at 1 (T1) at 12 months (T2) after surgery. Patients were divided according to the orthognathic surgery procedure involved as follows: 1) BimaxS: combined surgery involving segmented or non-segmented Le Fort I maxillary osteotomy and mandibular bilateral sagittal split osteotomy (BSSO) with or without genioplasty; 2) MaxS: isolated segmented or non-segmented Le Fort I maxillary osteotomy; and 3) MandS: isolated BSSO with or without genioplasty. All these surgical techniques were evaluated in linear and angular measurements - advancement, setback, upward, downward, centering, non-centering, clockwise rotation (CW), counterclockwise rotation (CCW) and mandibular occlusal plane (MOP).

Data collection

All patients followed the standard pre- and post-operative imaging workflow for orthognathic surgery of the Department, which involves cone-beam computed tomography (CBCT) at three time points: preoperatively (T0) and postoperatively at one (T1) and at 12 (T2) months of follow-up. The CBCT scans were performed using an i-CAT Vision system (iCAT, Imaging Sciences International, Hatfield, PA, USA) and patients were previously instructed by trained personnel in order to achieve the standard key-points for orthognathic surgery diagnosis and planning: the patient breathing quietly without swallowing, sitting upright in the natural head position (NHP) with the Frankfort and bipupilar planes parallel to the floor; indicating the patient to look straight ahead at a point in front of them at eye level (looking into a mirror), the tongue in a relaxed position and the mandible in centric relation with a 2 mm wax bite in place in order to avoid direct contact between teeth. An expert clinician paid special attention during the pre- and postoperative CBCT to minimize posture influence in the airway evaluation.

Presurgical 3D planning was performed with Dolphin software and the soft tissue – nasion plane was used as an absolute reference to guide anteroposterior positioning of the maxillomandibular complex (10). Intermediate and final surgical splints were printed in-house (11).

Each patient had three CBCT datasets (T0, T1 and T2) that were superimposed in accordance to the voxel-based superimposition protocol described previously by the authors (12). All CBCT scans were evaluated by the same researcher (MGH). Data were primarily saved in DICOM (Digital Imaging and Communications in Medicine) format using a 3D software (Dolphin Imaging, version 11.0, Chatsworth, CA, USA). The software orientation calibration tool was used along pitch (x), yaw (y) and roll (z). Orientation of both the 'Base volume' (original DICOM) and '2nd volume' (duplicate DICOM) was undertaken to achieve the same original positions of the CBCTs. Then, superimposition of the preoperative CBCTS at T1 and T2 was done using the cranial base, as it remains stable after surgery. The software allows a proper manual adjustment following the superimposition three-step protocol: (1): Landmark based superimposition ('side-by-side superimposition), (2): Voxel-based superimposition ('overlay superimposition by volume sub-regions') and (3): Head orientation export ('Export to 2nd volume') (12). This means that all the three images (T0, T1, and T2) were in the same coordinate position after the voxel-based superimposition (Fig. 1). This position is recommended for the baseline assessment of upper airway dimensions (13–15).

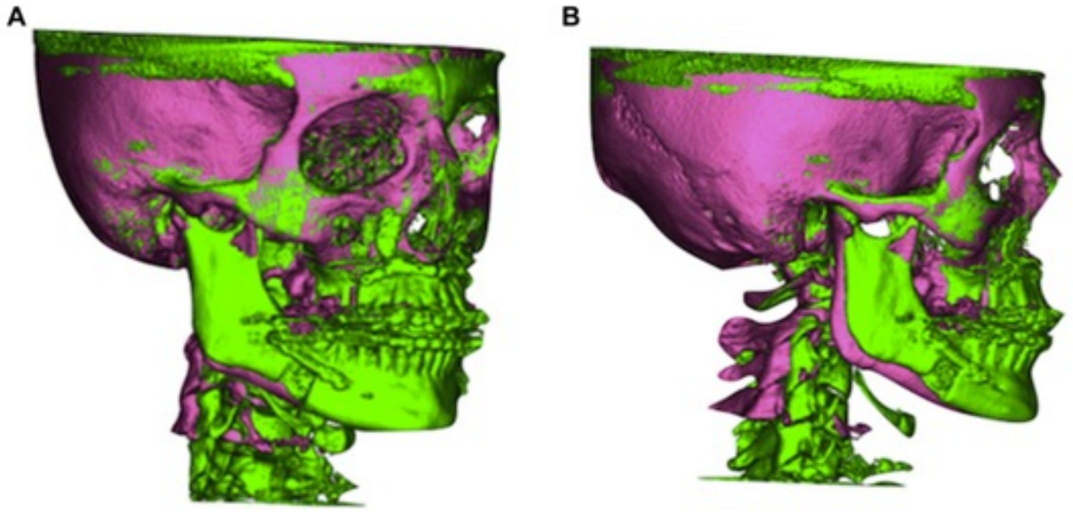

FIGURE 1. *A*, Preoperative and postoperative color map superimposition—front view. Color legend as follows: Pink, preoperative CBCT (T0); Green, postoperative CBCT (T1 or T2). *B*, Preoperative and postoperative color map superimposition—lateral view. Color legend as follows: Pink, preoperative CBCT (T0); Green, postoperative CBCT (T1 or T2).

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Data analyses

Skeletal surgical movements were assessed from angular (º) and linear measurements (mm). Upper airway data were evaluated in terms of volumetric (mm3) and cross-sectional areas (mm2).

Surgical movements

The following measurements were assessed in each patient: 1) angular: SNA, SNB, SNPg and MOP; and 2) linear: posterior nasal spine (PNS), Point A, Point B, pogonion (Pg), most anterior point of the hyoid body, superior incisor (Sup I), inferior incisor (Inf I) and transversal maxilla in frontal view. The root mean square displacement of all the parameters in the reference space or system was calculated according to the following formulas:

$$\Delta\,(T1 - T0) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

$$\Delta\,(T1 - T2) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

$$\Delta\,(T2 - T0) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

Upper airway analysis

Manual segmentation was performed to delimit the anatomical and technical boundaries of the upper airway at the anterior, posterior, upper and lower limits respectively, as reported by Swennen and Guijarro-Martínez (16). In relation to the upper airway dimensions, three regions of interest were defined for this purpose, measuring the naso -, oro - and hypopharynx. The nasopharynx was delimited by the Frankfort horizontal (FH) - posterior nasal spine (PNS) - sphenoid bone, extended to the soft tissue pharyngeal wall contour. The oropharynx was defined beyond the FH/PNS extended to FH – most anterior point of the body of C3 – soft tissue pharyngeal wall contour. Finally, the hypopharynx was assessed at FH/PNS parallel – most anterior point of the body of C3 – soft tissue pharyngeal wall contour to FH/PNS parallel – most anterior pole of the body of C4. An automatic threshold value of 60 was set manually to obtain the pharyngeal airway dimension (mm3) and mCSA (mm2) (Fig. 2).

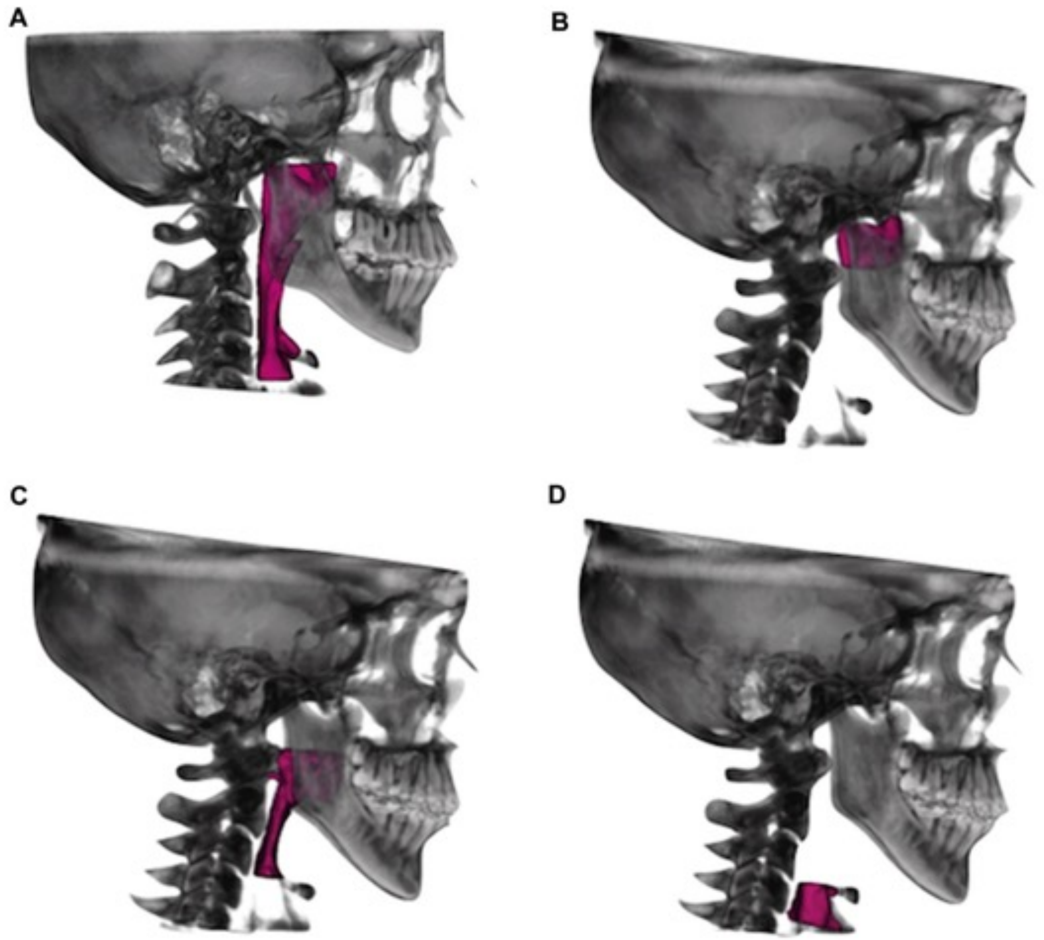

FIGURE 2. *A*, 3-dimensional total PAV assessment according to *Guijarro and Swenen, 2013* (16) PAV boundaries. *B*, 3-dimensional PAV boundaries—Delimitation of the nasopharynx PAV boundary (16).*C*, 3-dimensional PAV boundaries—Delimitation of the oropharynx PAV boundary (16).*D*, 3-dimensional PAV boundaries—Delimitation of the hypopharynx PAV boundary (16). Abbreviation: PAV, pharyngeal airway volume

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Statistical analyses

The data analysis was performed using SPSS for Windows, version 25.0.0 software (SPSS Inc, Chicago, IL). Power analysis was conducted from results of a pilot study carried out in n=15 patients. It was concluded that a minimum sample size of 50 patients for the global sample should be included to reach 80% power in order to detect volumetric changes, assuming a medium effect size (d=0.5) and 95% of confidence. The descriptive analysis included the most relevant statistics for all analyzed variables: mean, standard deviation (SD), minimum, maximum and median for continuous variables and absolute and relative frequencies (percentages) for qualitative variables. The comparative analysis included the assessment of normal distribution of the measurements using the Kolmogorov-Smirnov test. The inferential analysis included the following statistical methods: (1) The analysis of variance (ANOVA) general linear model for repeated measures was used to compare the evolution of the skeletal and volumetric parameters over follow-up. Multiple comparisons were made with Bonferroni correction to avoid type I error, and allowed the evaluation at short term (T1-T0), stability (T2-T1) and long term (T2-T0) effects; (2) Pearson's linear correlation coefficient (r) was used to estimate the degree of association between volumetric and skeletal changes, likewise in different periods; (3) Student t-test for independent samples (t) , with use of the nonparametric Mann-Whitney U-test (MW) and Kruskal-Wallis test (KW) to assess differences in volumetric changes according to aspects of the patient profile and type of surgery; and (4) Exploratory factor analysis of main components (PCA) was performed to identify the underlying dimensions or common movement patterns of both skeletal and airway parameters between T0 and T2. For all analyses, the level of statistical significance was set at .05.

RESULTS

The study sample comprised a total of 103 patients, 36 males (35%) and 67 females (65%), with a mean age of 31.9 ± 10.9 years (range 18-60). Preoperatively, 52.4% of the sample presented dentofacial deformity class II, 45.6% class III and 2% class I dentofacial deformities. Descriptive and demographic data with regard to the surgical characteristics involved in each group (Bimax, MaxS or MandS) are presented in Table 1. The analysis regarding the linear and angular skeletal changes in the three groups are presented in Table 2. In turn, Table 3 displays the pre-, postoperative (short and long term), and final percentages of variations (long-term gain and relapse) in the volumetric and mCSA measurements. Overall, an immediate positive effect (T1-T0) of orthognathic surgery upon the skeletal, volumetric and cross-sectional parameters was observed, followed by a slight downward trend and stabilization over time (T2) in all the three groups.

Bimaxillary orthognathic surgery

Although there was a small skeletal relapse at long term (T1-T2), with statistical significance being reached only for SNA° (-0.6 ± 1.0°; $p < .001$) (Table 2), no significant changes were observed for PAV and for mCSA. On average, the final PAV and mCSA gains were 41.9%, (95% CI: 33.6 – 50.2%; $p < .001$) and 104% (95% CI: 87.1-122.1%; $p < .001$), respectively (Table 3).

Correlation analysis showed volume gain (total or subregional) at T2 to be favored by certain surgical movements (versus (vs) the absence of them): maxillary CCW rotation – downward displacement of PNS at nasopharynx (7,456.5 vs 4,121.5 mm3, $r = 0.045$, $p < .05$); mandibular CCW rotation at oropharynx (9,837.7 vs 5,845.6 mm3, $t = 0.013$, $p < .05$); centering of the maxilla at oropharynx (8,922.2 vs 5,736.3 mm3, $t = 0.041$, $p < .05$) and sagittal mandibular advancement at hypopharynx (2,500 vs 523 mm3, MW = 0.012, $p < .05$). The total PAV was mainly influenced by maxillary CCW rotation (18,652.5 vs 9,757 mm3, KW = 0.032, $p < .05$), centering of the mandible (13,313.3 vs 9,853.6 mm3, $t = 0.049$, $p < .05$) and MOP increase ($r = 0.272$, $p = .049$). Therefore, when quantifying major volumetric variations based on skeletal changes, hypopharynx volume gain was increased by 61.4 mm3 for every 1 mm of mandibular advancement ($p < .001$), and by 102.4 mm3 for every 1 mm of downward movement of the posterior maxilla in terms of PNS displacement ($r = 0.304$, $p < .05$). In relation to cross-sectional parameters, changes in mCSA were directly correlated with a further increment in size of the upper airway ($r^2 = 0.421$, $p < .001$). In particular, for every 1 mm2 of mCSA increase, a mean gain of 31.88 mm3 in total PAV was observed ($r^2 = 0.177$, $p < .001$).

Single-jaw orthognathic surgery (MaxS or MandS)

Regarding skeletal relapse rates, the MaxS group presented significant relapse of final PAV when vertical movement of the maxilla without rotation was performed (23%, mean relapse of 6,850.5 mm3 KW = 0.020, p<.05), but this proved irrelevant compared to the total volume gain at T2 (mean 38,909.3 ± 7,421.9 mm3). In the case of the MandS group, the greater the setback movement (Pg reduction), the greater the observed PAV relapse at hypopharynx level (mean reduction of 1,789 mm3, r2 = 0.367, p<.001) (Table 2).

Total PAV gain for single jaw surgeries was smaller when compared to the BimaxS group, with a 26% increase for MaxS (95% CI: 15.7 – 35.5; p< .001) and 25% for MandS (95% CI: 15.4 – 34.1; p< .001). In the same line as for PAV, the cross-sectional parameters increased significantly by 39.5% (95% CI: 18.4-60.7%; p<.05) and 65.8% (95% CI: 48.1-83.6%; p<.05) in the MaxS and MandS groups, respectively.

According to Angle's classification, the total volume gain was greater in class II compared to class III malocclusion (12,958 vs 3,054 mm3; p< .05) (Table 3).

Correlations between beneficial surgical movements (versus the absence of them) in terms of PAV and mCSA gains were identified for both groups: 1) MaxS: segmentation at nasopharynx level (2,370 vs 1,594 mm3, MW = 0.032, p< .05) and displacement of the PNS at oropharynx level – maxilla CCW rotation with posterior downward displacement (6,324 vs 3,712 mm3, r=0.571, p= .003). The total PAV gain was positively influenced by maxillary advancement (9,107 vs 6,724.5 mm3, r=0.605, p= .001) and by centering of the maxilla (8,156.2 vs 6,990.8 mm3, MW=0.075, p< .05); 2) MandS: mandibular advancement at hypopharynx level (1,457.1 vs -613.5 mm3, MW=0.013, p< .05), CCW rotation (5,139.77 vs 3,457.33 mm3, MW 0.027, p< .05) and sagittal chin advancement (with genioplasty) (6,791.3 vs 4,585.1 mm3, MW=0.046, p< .05) at oropharynx level. The total PAV was enlarged by mandibular advancement (7,981.1 vs 1,009 mm3, r=0.494, p= .012). Finally, vertical upwards (2.27 ± 5.99 mm) and sagittal forwards displacements (2.58 ± 5.44 mm) of the hyoid bone were correlated to mandibular advancement and greater PAV gain at long term (r=0.435, p= .030). Then, quantification analyses of relevant PAV and cross-sectional changes were as follows: 1) MaxS: 1 mm of maxillary advancement, implied 373.3 mm3 total volume gain (p= .020); 1 mm of PNS displacement implied an average total PAV gain of 556.9 mm3 (p= .002); 1° of SNA increase by CCW rotation of the maxilla implied a mean nasopharynx gain of 151.6 mm3 (p= .011) and 2) MandS: 1° of MOP CCW resulted in 605.4 mm3 total PAV gain (r2=0.628, p= .003). No correlations between mCSA and one-jaw surgeries were found in our study.

Table 1. Descriptive statistics for study population for the three groups (Bimax, MaxS and MandS) (n =103).

	Bimax (n = 53)		MaxS (n=25)		MandS (n=25)	
	n	%	n	%	n	%
Gender						
Male	15	28.3	12	48	16	64
Female	38	71.7	13	52	9	36
Type of dentofacial deformity						
Class I	0	0	2	8	0	0
Class II	32	60.4	0	0	22	88
Class III	21	39.6	23	92	3	12
Maxilla						
Segmented LeFort I	28	52.8	9	36	-	-
Non-segmented LeFort I	25	47.2	16	64	-	-
Advancement	53	100	25	100	-	-
setback	0	0	0	0	-	-
Upwards (impaction)	16	30.2	4	16	-	-
Downwards (descend)	11	20.8	12	48	-	-
No vertical movement	26	49.1	9	3.6	-	-
Centering	21	39.6	5	20	-	-
No centering	32	60.4	20	80	-	-
Mandible						
BSSO	43	81.1	-	-	23	92
Setback	2	3.8	-	-	2	8
Centering	27	50.9	-	-	17	68
No centering	26	49.1	-	-	8	32
Chin						
Advancement genioplasty	26	49.1	-	-	3	12
No sagittal genioplasty	27	50.9	-	-	22	88
Downwards (descend)	5	9.4	-	-	2	8
No vertical genioplasty	48	90.6	-	-	23	92
Rotational movements						
CW	4	7.5	0	0	0	0
CCW	49	92.5	25	100	3	12
No rotation	0	0	0	0	22	88
Age (mean ± SD)	29.6 ± 9.4		39.7 ± 9.2		29.1 ± 12	

Abbreviations: BimaxS: bimaxillary surgery; MaxS: maxillary surgery; MandS: mandibullary surgery; CW: clockwise rotation; CCW: counterclockwise rotation; BSSO: bilateral sagittal split osteotomy.

Table 2. Linear and angular skeletal changes at 1- and 12-months follow-up in the three groups (Bimax, MaxS and MandS).

Angles and skeletal movements*	BimaxS T1-T0	BimaxS T1-T2	BimaxS T2-T0	MaxS T1-T0	MaxS T1-T2	MaxS T2-T0	MandS T1-T0	MandS T1-T2	MandS T2-T0
Max adv	**5.9 ± 4.9**	**1.2 ± 0.6**	**5.6 ± 4.8**	**14.4 ± 9.5**	**0.1 ± 0.1**	**14.4 ± 9.5**	0.03 ± 0.14	0.0 ± 0.0	0.03 ± 0.14
Mand adv	**14.2 ± 11.4**	**2.9 ± 10.8**	**12.7 ± 8.1**	**0.5 ± 1.9**	**0.01 ± 0.03**	**0.5± 1.9**	**5.1 ± 3.5**	**0.5 ± 0.3**	**5.2 ± 3.6**
Chin adv	**16.8 ± 10.3**	**1.4 ± 1.1**	**16.6 ± 10.2**	0.6 ± 2.3	0.00 ± 0.02	0.5 ± 2.3	**6.4 ± 4.1**	**0.4 ± 0.3**	**6.4 ± 4.2**
SNA	**4.4 ± 2.8**	**-0.7 ± 1.0**	**3.7 ± 2.9**	**4.3 ± 3.5**	-0.07 ± 0.15	**4.2 ± 3.5**	-0.01 ± 0.12	0.01 ± 0.09	0.0 ± 0.1
SNB	**6.2 ± 4.1**	-0.1 ± 0.9	**6.1 ± 4.2**	02 ± 1.6	-0.02 ± 0.08	0.1 ± 1.6	**2.9 ± 3.3**	-0.2 ± 0.7	**2.7 ± 3.0**
SNPg	**7.4 ± 5.1**	-0.2 ± 1.6	**7.2 ± 5.2**	-0.2 ± 1.5	-0.01 ± 0.04	-0.2 ± 1.2	**2.6 ± 3.1**	-0.02 ± 1.58	**2.6 ± 2.6**
PNS	**5.7 ± 3.9**	**1.2 ± 1.1**	**5.9 ± 3.7**	**12.4 ± 9.0**	**0.1 ± 0.1**	**12.4 ± 9.03**	0.06 ± 0.22	0.01 ± 0.04	0.07 ± 0.22
Hyoid	**18.0 ± 13.3**	**2.5 ± 6.8**	**17.1 ± 11.7**	1.5 ± 3.8	0.01 ± 0.03	1.5 ± 3.8	**9.9 ± 5.6**	**0.4 ± 0.4**	**9.9 ± 5.7**
Max Exp.	**4.0 ± 4.4**	-0.05 ± 0.4	**3.9 ± 4.3**	**2.2 ± 3.5**	0.0 ± 0.0	**2.2 ± 3.5**	0.07 ± 3.83	0.1 ± 0.4	0.2 ± 3.6
MOP	**5.3 ± 4.6**	0.4 ± 1.8	**5.7 ± 4.9**	-0.5 ± 6.0	0.2 ± 0.4	-0.3 ± 62	1.5 ± 5.3	-0.3 ± 1.0	1.2 ± 5.6

Note: Statistically significant parameters are presented in bold: $p<0.05$. Mean ± SD and t test from ANOVA and Bonferroni correction.
Mean ± SD (standard deviation).
*Angles, skeletal movements and planes are given in ° and mm, respectively.
Abbreviations: Maxillary adv (mm): maxillary advancement (A point); Mandibular adv (mm): mandibular advancement (B point); Chin adv (mm): pogonion advancement (pogonion); Angular SNA, SNB and SNPg measurements are given in terms of rotation: SNA (°): sella – nasion - point A; SNB (°): sella – nasion - point B; SNPg (°): sella -nasion pogonion; Max Exp (mm): maxillary transversal expansion and MOP (°): mandibular occlusal plane (MOP reduction in terms of rotation)

Table 3. Volumetric and cross-sectional measurements and percentage variation in the three groups pre- and postoperatively at 1 (T1) and 12-months follow-up (T2).

		T0	T1	T2	Long term gain (%)	95% CI	p-value
BimaxS	Nasopharynx	7,397.9 ± 1973.4	11,426.3 ± 3219.9	10,475.7 ± 2883.3	41.6	30.9 – 52.3	p<0.001***
	Oropharynx	16,200.6 ± 5,397.6	26,850.0 ± 7,539.5	23,199.2 ± 6,510.7	43.2	32.1 – 54.3	p<0.001***
	Hypopharynx	4,111.5 ± 1,274.2	6,703.8 ± 1,471.3	5,692.0 ± 1,310.7	38.4	29.7 – 47.2	p<0.001***
	Total PAV	27,720.6 ± 6,534.3	44,905.8 ± 9,881.0	39,336.8 ± 8,338.1	41.9	33.6 – 50.2	p<0.001***
	mCSA	120.9 ± 59.3	290.9 ± 96.5	247.4 ± 76.9	104	87.1-122.1	p<0.001***
MaxS	Nasopharynx	8,980.3 ± 1,545.9	11,745.1 ± 2,637.2	11,000.2 ± 1,928.9	22.5	13.6 – 31.4	p<0.001***
	Oropharynx	17,649.2 ± 4,662.1	23,988.4 ± 6,632.8	22,755.3 ± 6,039.0	28.9	14.8 – 43.1	p<0.001***
	Hypopharynx	4,356.6 ± 844.9	5,153.7 ± 971.6	5,049.5 ± 1,040.3	18.3	9.1 – 27.5	p=0.001**
	Total PAV	30,986.2 ± 6,010.3	41,143.0 ± 8,689.7	38,909.3 ± 7,421.9	26	15.7 – 35.5	p<0.001***
	mCSA	168.2 ± 67.1	239.8 ± 89.2	234.7 ± 86.2	39.5	18.4-60.7	p<0.05*
MandS	Nasopharynx	8,602.6 ± 1,612.1	10,210.0 ± 2,463.8	9,635.2 ± 2,048.2	12	2.2 – 21.8	p<0.001***
	Oropharynx	16,603.6 ± 4,157.9	24,666.7 ± 6,355.1	21,541.5 ± 5,494.4	29.7	16.1 – 43.4	p<0.001***
	Hypopharynx	4,174.8 ± 948.7	6,208.5 ± 1613.1	5,466.2 ± 1,297.1	30.9	18.1 – 43.8	p<0.001***
	Total PAV	29,381.1 ± 5,803.1	41,085. 3 ± 8,689.7	36,643.0 ± 6,656.5	25	15.4 – 34.1	p<0.001***
	mCSA	136.5 ± 54.4	231 ± 56.9	226.5 ± 58.9	65.8	48.1 - 83.6	p<0.05*

Note: *p<0.05; **p<0.01; ***p<0.001: mean ± SD (standard deviation).
Abbreviations: PAV: pharyngeal airway volume; BimaxS: bimaxillary group; MaxS: monomaxillary group; MandS: isolated mandibular group; mCSA: minimum cross-sectional area; CI: confidence interval.
*volumes are given in mm^3 and areas in mm^2.

DISCUSSION

The purpose of this study was to assess the effect of maxillary and mandibular movements upon the pharyngeal airway on a three-dimensional basis in patients subjected to orthognathic surgery, either bimaxillary or monomandibular. The authors hypothesized that each surgical movement during orthognathic impacted differently to increase or decrease the upper airway dimension. Thus, to address this hypothesis, the authors identified three groups of patients who underwent bimaxillary or mono mandibular surgery (Bimax, MaxS and MandS, respectively) to evaluated the PAV and mCSA changes at 1- and 12-months follow-up.

Overall, the positive effect of either mono- or bimaxillary surgery was proven in all aspects (linear, cross-sectional and volumetric analysis): an immediate increase in PAV and mCSA, with bimaxillary advancement and MOP changes by CCW rotation were the most significant contributors. Our results show that forward surgical procedures in both the maxilla and the mandible were carried out in almost the entire sample, regardless of the initial dentofacial deformity involved (class I, II or III). In fact, only four patients (2 BimaxS and 2 isolated MandS cases) received mandibular setback surgery. This is consistent with the upper incisor-to-soft tissue plane (UI-STP) surgical 3D planning protocol used by the authors and previously described elsewhere (10), and which is used as an absolute reference to guide the anteroposterior positioning of the maxillo-mandibular complex, irrespective of the previous occlusal problems (class II or III). Once in class I, the complex is displaced and rotated so both the upper incisor and soft tissue pogonion lie (1 to 5 mm) in front of this plane (10). However, the PAV gain was greater in class II than in class III patients (class II presenting 12% (95% CI: 10.1-22.1) more PAV gain than class III patients, (MW: 0.020, $p < .05$). This is explained because this population in general requires greater mandibular advancement, which is considered to be the main factor for increasing PAV.

Our results are in line with those of many authors who have found that MMA increases PAV, and that the effect remains stable at one-year of follow-up (17–19). A linear mean maxillary advancement of 6.41 ± 7.72 mm, mandibular advancement of 9.92 ± 8.05 mm and a global chin advancement of 10.22 ± 10.27 mm (isolated chin 3.85 ± 2.06) were achieved, with a subsequent mean total PAV increase of 33.4% (95% CI: 28.2 – 38.7%; $p<.001$) for the global sample - the results being more significant in the BimaxS group 42% (95% CI: 33.6 – 50.2%; $p< .001$) (naso-, oro- and hypopharynx increments of 41.6%, 43.2% and 38.4%, respectively). When isolated maxillary or mandibular surgeries were performed, volume gain was obtained but to a lesser extent compared to the BimaxS group, with an average PAV increase of 26% (95% CI: 15.7 – 35.5; $p< .001$) in the MaxS group (naso-, oro- and hypopharynx 22.5%, 28.9% and 18.3%, respectively) and

25% (95% CI: 15.4 – 34.1; $p < .001$) in the MandS group (naso-, oro- and hypopharynx 12%, 29.7% and 30%, respectively) (Table 3). It thus can be affirmed that both maxillary and mandibular movements impact on the three levels of the PAV, although maxillary forward movements further widen the oro- > naso- > hypopharynx, while mandibular forward movements further widen the hypo- > oro- > nasopharynx, in these orders. Obviously, bimaxillary surgeries that move the entire maxillomandibular complex increase total PAV and cross-sectional parameters even further (Fig. 3). In this regard, it is important to underscore that one-jaw surgeries (MaxS and MandS) yielded similar volumetric gains in our study – only the MandS group achieving less volume compared to the MaxS group, which is explained because most isolated mandibular surgeries involved only mandibular centering without any advancement or CCW rotation.

As previously stated, some movements significantly favored PAV gain, while some jeopardized it. With regard to two-jaw surgeries, mandibular advancement ($p < .05$) and CCW rotation of the mandible ($p < .05$) favored PAV gain at oro- and hypopharynx level. Hypopharynx airway volume was increased by 61.4 mm3 for every 1 mm of mandibular advancement. Our results suggest that 55% of the PAV changes after orthognathic surgery are explained by mandibular surgical movements ($r2= 0.547$, $p < .001$). This is in line with the literature (2,3), which suggests that the influence of the mandible plays a major role in widening both mCSA and PAV at long term. In the same way as for mandibular advancement, a mean 5.74 ± 4.90° reduction of the MOP ($r2 = 0.272$, $p= .049$) in terms of CCW rotation significantly incremented both total PAV ($p < .05$) and nasopharynx volume ($p < .05$), with a 68.2% (95% CI: 42.8 – 88.3%, $p < .05$) more of total PAV gain when compared to the absence of rotation. Thus, our results support that MOP stabilization ($p < .05$) by CCW rotation determines the final volume gain. This is due to the advancement of the suprahyoid muscles by both the mandibular advancement and the correction of the MOP at the time of surgery, allowing further expansion of airway size, with a subsequent volume gain (17). Previous studies focused on the normalization of the MOP to achieve an increment in the upper airway. Our findings are in agreement with those published by Rubio et al. (17), who associated a 6 to 10 mm mandibular advancement with concomitant correction of MOP by CCW rotation to be essential for incrementing mCSA and PAV.

A positive effect of the downward movement of the posterior maxilla in terms of PNS displacement was observed in relation to total PAV and hypopharynx for BimaxS and MaxS ($p < .05$ and $p < .001$), respectively. One millimeter of downward movement of the posterior maxilla (PNS) resulted in 102.4 mm3 of hypopharynx gain. The descent of the posterior part of the maxilla (PNS) together with a CCW rotation enlarges the pharynx, because the muscles of the soft palate are pulled to an anterior and downward position, which favors the upper airway space. In addition, segmentation / expansion and sagittal advancement of the maxilla incremented naso- and total PAV gain ($p < .05$).

Greater oropharyngeal and total volume were achieved when centering of the maxilla was performed compared to non-centering (8,922.2 mm3 vs 5,736.3 mm3; p< .05). This occurs because maxillary asymmetry may trigger muscular constriction on one side of the upper airway. To our knowledge, the present study is the first to describe a potential relationship between maxillary asymmetries and constriction of the upper airway.

On the other hand, concomitant chin advancement during mandibular advancement significantly improved the airway at oropharynx level (p< .05). Chin advancement involves forward movement of the genial tubercles, which together with the hyoid movements, potentially leads to more airway flow (20). Also, a recent meta-analysis has evidenced that MMA together with genioplasty significantly increase PAV (p< .001) (3). In this same line, there was a clear relationship between mandibular advancement and hyoid advancement and ascent, with a subsequent PAV increase (p< .05). The hyoid bone is a mobile structure anchored to both the pharyngeal wall and to mandibular anatomical structures, exerting a pulley function between them. Thus, this structure assumes a major role in widening the upper airway when hyoid-mandibular muscles are straightened or tensed (21).

Finally, mention must be made of the relationship between mCSA increase and final PAV gain. Our results showed that for each square millimeter of mCSA increase, there was a 32 mm3 of total PAV gain after bimaxillary surgery (p< .001). Thus, minimal CSA increase is extremely important in terms of maximizing airflow through the oropharynx and minimizing friction and resistance of air penetration to the respiratory region. It should be noted that the mCSA increase doubled in size (104%, (95% CI: 87.1 – 122.1%; p<.001)) in the Bimax group compared to the effect of isolated maxillary procedures (39.5% (95% CI: 18.4 – 60.7%; p<.05)) or sole mandibular surgery (65.8%, (95% CI:48.1 – 83.6%; p<.05)). An explanation for this is that the pharyngeal walls are complex structures mainly composed of muscles (superior, middle and inferior constrictors muscles among others) that delimit upper airway flow. However, although monomaxillary procedures increased mCSA and increased the pharyngeal volume, bimaxillary procedures, by moving the whole maxillomandibular complex together, allow further widening of the airway and constriction areas. Therefore, bimaxillary surgery should be contemplated to secure further increase in terms of mCSA and PAV. In addition, other studies associated the differences in constriction areas between class II and class III patients with tongue position as well as adenoid and tonsillar hypertrophy (22) - though constriction areas are mainly found in the oro- and hypopharynx regions, owing to severe systemic consequences like obstructive sleep apnea (OSA) (23).

In this same line, Schendel et al. (24) observed a relationship between OSA and constriction areas, reporting a high probability of developing OSA when mCSA was < 52 mm2; an intermediate probability when 52-110 mm2; and a low probability when > 110 mm2. Hence, 3D surgical planning in individuals potentially at risk of suffering from or developing OSA should be patient-tailored and considered in all future primary studies (3).

In contrast, other surgical movements penalized volume gain: total vertical downward movement of the maxilla without rotation reduced nasopharynx volume (MaxS; p< .05), and isolated setback procedures in the mandible reduced hypopharynx volume gain (BimaxS and MandS; p< .05 and p< .01, respectively). Our results are also consistent with the data found in the literature (25,26), where mandibular setback procedures were found to result in higher upper airway constriction (p< .05) and became a risk factor for developing OSA when exceeding 4-8 mm of setback movement of the mandible (26). Likewise, as reported by Lee et al. (27), isolated either maxillary (maxillary setback LeFort I osteotomy) or mandibular setback surgery decreased both oro- and hypopharynx volumes and significantly reduced mCSA (p< .05). However, no cases of isolated maxillary setback were reported in our study.

Overall, a linear pattern of initial-immediate increase in pharyngeal airway volumetric parameters followed by a slight downward trend related to skeletal relapse was observed during the study in all the three groups (Fig. 3). Global relapse was 10%, which was insufficient to offset the total PAV and mCSA gains, regardless of the surgical approach involved. Greater PAV relapse occurred mainly at oropharynx level (-2,936.41 mm3), compared to > naso- (-809.45 mm3) and > hypopharynx (-762.85 mm3), though statistical significance was not reached. The oropharynx was probably the most relapse-prone area, due to the impact of both maxillary and mandibular bones relapses, apart from being the most enlarged area after surgery. In our study, skeletal relapses referred to the different groups only proved significant for maxillary procedures: SNA in terms of rotation (p< .001) and downward vertical movement of the maxilla without rotation (p< .05). This is consistent with the observations of Haas Junior et al. (28), who together with our team proposed a hierarchical pyramid to assess the stability of orthognathic surgery according to surgical movements. The authors found surgical movements in the maxilla to be more relapse-prone ('unstable') than mandibular procedures ('highly stable') (28,29). Hence, we highlight this pyramid as an additional tool for helping surgeons to choose the technique with the best surgical outcomes, and for reducing (but not avoiding) skeletal and volumetric relapse to a certain degree.

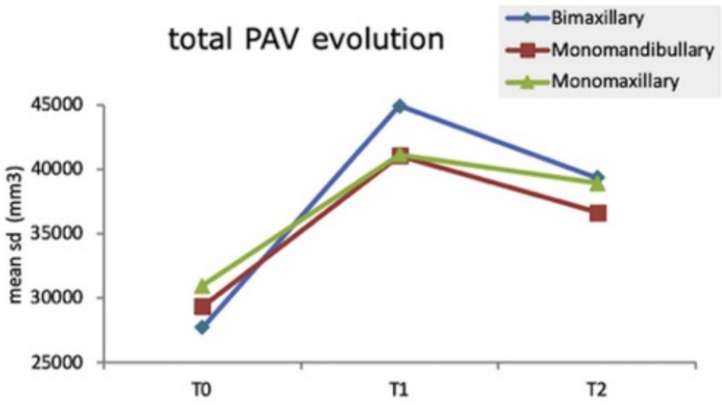

FIGURE 3. Total upper airway evolution as per type of surgery at long-term (T2-T0) in the 3 groups. Abbreviation: PAV, pharyngeal airway volume

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To avoid measurement error, emphasis was placed on the 3D voxel-based superimposition protocol in measurement assessment throughout the study. This protocol was chosen because it enables unbiased analysis of surgical outcomes based on a software application that affords accuracy and precision, and avoids complex, technically demanding and time-consuming measurements (12). This study exemplifies the recommended method. The results of this study, however, should be interpreted with caution. Although many authors fail to give information on the protocol used for 3D skeletal and volumetric measurements in their primary studies, it is important to standardize these factors for homogeneity purposes and thus to be able to draw relevant conclusions from our studies.

A limitation to this study was that it is a retrospective study and therefore, subjected to the usual biases of its nature. Then, the improvement of the clinical symptoms of OSA were not assessed. In particular, although our results confirm the use of MMA as a stable procedure to enlarge the upper airway dimensions, the relationship between our results and patient sleep parameters could not be evaluated by polysomnography pre- and postoperatively (at T1 and T2). As a result, we were unable to establish which surgical movement is more effective in terms of treating OSA, as well as to equate skeletal and volumetric changes with the changes in clinical symptoms of OSA. An ongoing prospective study (clinicalTrials.gov ID NCT03796078 registration) regarding sleep and patient-centered parameters will determine whether there are any correlations between the direction, magnitude and type of surgical movement and the increase in PAV and cross-sectional areas with definitive curing of OSA, and whether orthognathic surgery should be considered part of the first-line armamentarium for OSA treatment in selected patients.

To summarize, taking into account the different variables analyzed, the surgical movements and upper airway gain correlated beyond the sample size with short and long-term relapse, we suggest a basic surgical protocol when the main concern is the upper airway. We believe that all the surgical planning should begin with the idea that bimaxillary advancement with CCW rotation is necessary, and whenever possible, chin advancement and CCW rotation with posterior maxillary downward displacement must be considered to allow further airway improvement (Fig. 4).

Proposed surgical protocol for maximizing the upper airway

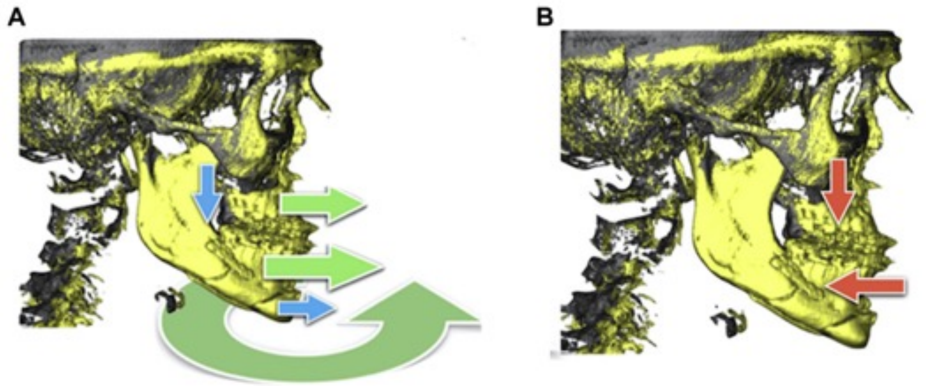

FIGURE 4. *A*, Surgical planning protocol for maximizing the upper airway. Hierarchical graphic representation of the increase/decrease in upper airway as per surgical movements in orthognathic surgery. Illustration of the favoring surgical movements to increase upper airway (CCW rotation, mandibular and maxillary advancements [*green arrows*]); movements to further increase PAV for chin advancements and posterior maxillary displacement of the PNS (*blue arrows*).*B*, Nonfavorable surgical movements (total maxillary downward and setback mandibular movements) which jeopardize the upper airway (*red arrows*). Abbreviations: CCW, counterclockwise; PAV, pharyngeal airway volume.

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CONCLUSIONS

In conclusion, the results of this study suggest that orthognathic surgery, when planned and executed using soft tissue – nasion plane as an absolute reference, induces 3D increments at all levels of the pharyngeal airway at long term, regardless the surgical technique involved, with bimaxillary advancement and MOP changes by CCW rotation being the most significant contributors. Conversely, total maxillary downward displacement without rotation and mandibular setback movements penalized PAV gain in the different groups ($p < .05$, $p < .01$). however, a 10% skeletal and volumetric relapse should be expected at 12 months-follow-up. A continued research effort into the study of the diverse anatomical and non-anatomical factors which affect skeletal and airway size relapse after orthognathic surgery will allow a better match between personalized surgery-induced movements and a defined protocol to achieve a long-lasting success of the surgical treatment.

REFERENCES

1. Christovam IO, Lisboa CO, Ferreira DMTP, Cury-Saramago AA, Mattos CT. Upper airway dimensions in patients undergoing orthognathic surgery: a systematic review and meta-analysis. Int J Oral Maxillofac Surg [Internet]. 2016;45(4):460–71. Available from: http://dx.doi.org/10.1016/j.ijom.2015.10.018

2. Hernandez-Alfaro F, Guijarro-Martinez R, Mareque-Bueno J. Effect of mono- and bimaxillary advancement on pharyngeal airway volume: cone-beam computed tomography evaluation. J Oral Maxillofac Surg. 2011 Nov;69(11):e395-400.

3. Giralt-Hernando M, Valls-Ontañón A, Guijarro-Martínez R, Masià-Gridilla J, Hernández-Alfaro F. Impact of surgical maxillomandibular advancement upon pharyngeal airway volume and the apnoea-hypopnoea index in the treatment of obstructive sleep apnoea: Systematic review and meta-analysis. BMJ Open Respir Res. 2019;6(1):1–13.

4. Mattos CT, Vilani GNL, Sant'Anna EF, Ruellas ACO, Maia LC. Effects of orthognathic surgery on oropharyngeal airway: A meta-analysis. Int J Oral Maxillofac Surg [Internet]. 2011;40(12):1347–56. Available from: http://dx.doi.org/10.1016/j.ijom.2011.06.020

5. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg. 2014;12(12):1495–9.

6. Dodson TB. Writing a Scientific Paper Is Not Rocket Science! J Oral Maxillofac Surg. 2015;73(12):S160–9.

7. Obwegeser H. The indications for surgical correction of mandibular deformity by the sagittal splitting technique. Br J Oral Surg. 1963;1(C):157–71.

8. Hernandez-Alfaro F, Guijarro-Martinez R. "Twist technique" for pterygomaxillary dysjunction in minimally invasive Le Fort I osteotomy. J Oral Maxillofac Surg. 2013 Feb;71(2):389–92.

9. Raffaini M, Hern F, Paredes-de-sousa-gil A, Magri S, Guijarro-martı R. Three-Dimensional Analysis of Long-Term Stability After Bilateral Sagittal Split Ramus Osteotomy Fixed With a Single Miniplate With 4 Monocortical Screws and 1 Bicortical Screw : A Retrospective 2-Center Study. 2017;1036–45.

10. Hernández-Alfaro F. Upper incisor to Soft Tissue Plane (UI-STP): A new reference for diagnosis and planning in dentofacial deformities. Med Oral Patol Oral Cir Bucal. 2010;15(5):8–

11. Aboul-Hosn Centenero S, Hernandez-Alfaro F. 3D planning in orthognathic surgery: CAD/CAM surgical splints and prediction of the soft and hard tissues results - our experience in 16 cases. J Craniomaxillofac Surg. 2012 Feb;40(2):162–8.

12. Haas Junior OL, Guijarro-Martínez R, Sousa Gil AP de, Méndez-Manjón I, Valls-Otañón A, de Oliveira RB, et al. Cranial Base Superimposition of Cone-Beam Computed Tomography Images. J Craniofac Surg. 2019;00(00):1.

13. Solow B, Sandham A. Cranio-cervical posture: A factor in the development and function of the dentofacial structures. Eur J Orthod. 2002;24(5):447–56.

14. Lin X, Edwards SP. Changes in natural head position in response to mandibular advancement. Br J Oral Maxillofac Surg [Internet]. 2017;55(5):471–5. Available from: http://dx.doi.org/10.1016/j.bjoms.2017.01.007

15. dos Santos RMG, De Martino JM, Haiter Neto F, Passeri LA. Influence of different setups of the Frankfort horizontal plane on 3-dimensional cephalometric measurements. Am J Orthod Dentofac Orthop. 2017;152(2):242–9.

16. Guijarro-Martínez R, Swennen GRJ. Three-dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: A validation study. Int J Oral Maxillofac Surg. 2013;42(9):1140–9.

17. Rubio-Bueno P, Landete P, Ardanza B, Vázquez L, Soriano JB, Wix R, et al. Maxillomandibular advancement as the initial treatment of obstructive sleep apnoea: Is the mandibular occlusal plane the key? Int J Oral Maxillofac Surg. 2017;46(11):1363–71.

18. Veys B, Pottel L, Mollemans W, Abeloos J, Swennen G, Neyt N. Three-dimensional volumetric changes in the upper airway after maxillomandibular advancement in obstructive sleep apnoea patients and the impact on quality of life. Int J Oral Maxillofac Surg. 2017;46(12):1525–32.

19. Camacho M, Noller MW, Del Do M, Wei JM, Gouveia CJ, Zaghi S, et al. Long-term Results for Maxillomandibular Advancement to Treat Obstructive Sleep Apnea: A Meta-analysis. Otolaryngol Neck Surg [Internet]. 2019;019459981881515. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30598047%0Ahttp://journals.sagepub.com/doi/10.1177/0194599818815158

20. Dicus Brookes CC, Boyd SB. Controversies in Obstructive Sleep Apnea Surgery. Oral Maxillofac Surg Clin North Am [Internet]. 2017;29(4):503–13. Available from: https://doi.org/10.1016/j.coms.2017.07.005

21. Ayappa I, Rapoport DM. The upper airway in sleep: Physiology of the pharynx. Sleep Med Rev. 2003;7(1):9–33.

22. Iwasaki T, Sato H, Suga H, Takemoto Y, Inada E, Saitoh I, et al. Relationships among nasal resistance, adenoids, tonsils, and tongue posture and maxillofacial form in Class II and Class III children. Am J Orthod Dentofac Orthop. 2017;151(5):929–40.

23. Prinsell JR. Primary and secondary telegnathic maxillomandibular advancement, with or without adjunctive procedures, for obstructive sleep apnea in adults: A literature review and treatment recommendations. J Oral Maxillofac Surg [Internet]. 2012;70(7):1659–77. Available from: http://dx.doi.org/10.1016/j.joms.2011.03.064

24. Schendel SA, Jacobson R, Khalessi S. Airway growth and development: A computerized 3-dimensional analysis. J Oral Maxillofac Surg [Internet]. 2012;70(9):2174–83. Available from: http://dx.doi.org/10.1016/j.joms.2011.10.013

25. Yang Y, Yang K, Zhao Y. Three-Dimensional Changes in the Upper Airway of Skeletal Class III Patients After Different Orthognathic Surgical Procedures. J Oral Maxillofac Surg [Internet]. 2018;76(1):155–64. Available from: https://doi.org/10.1016/j.joms.2017.06.025

26. Gandedkar NH, Chng CK, Por YC, Yeow VKL, Ow ATC, Seah TE. Influence of Bimaxillary Surgery on Pharyngeal Airway in Class III Deformities and Effect on Sleep Apnea: A STOP-BANG Questionnaire and Cone-Beam Computed Tomography Study. J Oral Maxillofac Surg [Internet]. 2017;75(11):2411–21. Available from: https://doi.org/10.1016/j.joms.2017.05.028

27. Lee JY, Kim Y Il, Hwang DS, Park SB. Effect of maxillary setback movement on upper airway in patients with class III skeletal deformities: Cone beam computed tomographic evaluation. J Craniofac Surg. 2013;24(2):387–91.

28. Haas Junior OL, Guijarro-Martínez R, de Sousa Gil AP, da Silva Meirelles L, Scolari N, Muñoz-Pereira ME, et al. Hierarchy of surgical stability in orthognathic surgery: overview of systematic reviews. Int J Oral Maxillofac Surg. 2019;

29. Haas Junior OL, Guijarro-Martínez R, de Sousa Gil AP, da Silva Meirelles L, de Oliveira RB, Hernández-Alfaro F. Stability and surgical complications in segmental Le Fort I osteotomy: a systematic review [Internet]. Vol. 46, International Journal of Oral and Maxillofacial Surgery. Elsevier; 2017 [cited 2017 Jul 2]. p. 1071–87. Available from: http://www.ncbi.nlm.nih.gov/pubmed/28601432

3.4

3.4 Paper four

Airway volume changes after orthognathic surgery in patients with down syndrome:

A diagnostic-therapeutic algorithm

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ABSTRACT

Purpose: To describe a protocol for the surgical management of dento-facial deformities in Down syndrome (DS) patients. The present study describes a protocol for the surgical management of orodental and facial deformities in DS patients based on a series of three cases and a review of the literature. All patients presented with midface retrusion due to underlying severe maxillary hypoplasia and dental crowding. A mean maxillary advancement of 4.53 mm and a mean maxillary descent of 3.6 mm were obtained. A mean pharyngeal airway volume gain of 10,954.33 mm3 (50%) was recorded at the one-month follow-up visit. Non-relevant skeletal and airway relapses were noted. Stable occlusion was achieved in all cases after postoperative orthodontic treatment, with proper chewing function, and the parents referred decreased snoring. The results of this study suggest that in selected DS patients with specific dysmorphic orofacial features, orthodontics and orthognathic surgery constitute the management of choice for the occlusion disorders and associated feeding, respiratory and related problems, and moreover contribute to resolve obstructive sleep apnea.

Keywords: Down syndrome; Orthognathic surgery; Obstructive sleep apnoea; Pharyngeal airway volume.

INTRODUCTION

Down syndrome (DS) is the most frequent chromosomal disorder, occurring in one out of every 700 births 1. Since 1866, when the British physician John Langdon Down first described the disorder, trisomy 21 has gained scientific relevance and is currently one of the most extensively studied genetic alterations. Apart from intellectual disabilities of varying degrees, these patients may suffer a broad range of organic defects 2.

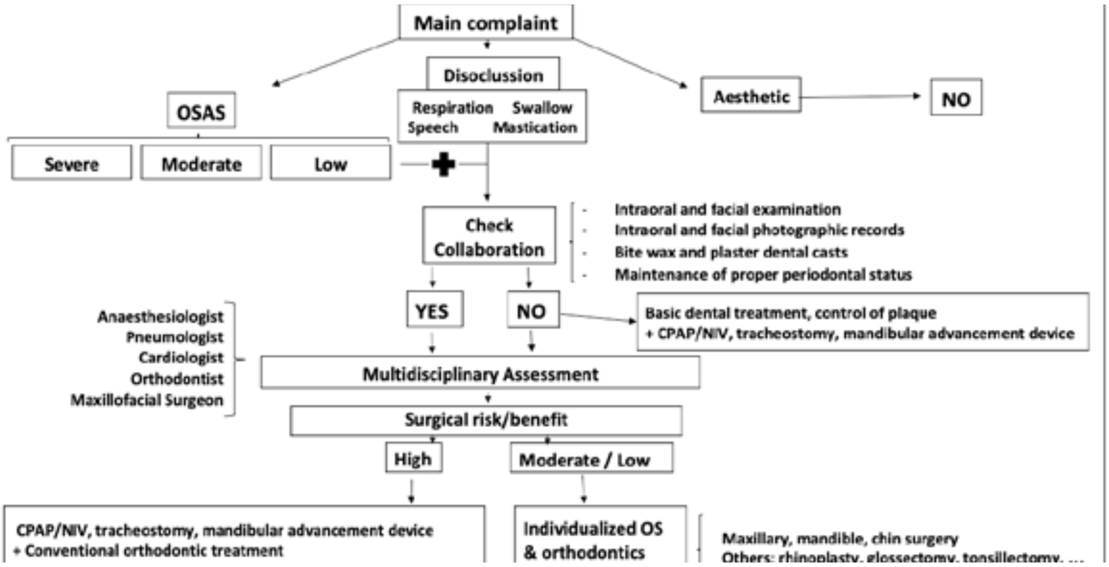
Dysmorphic cranial and orofacial features have also been widely described in DS patients, particularly a small cranium, a flat nose and flat malar bones with slanted eyes, severe maxillary hypoplasia with a high-arched and constricted palate, and mandibular hypoplasia although seemingly prognathic mandible because of the previous issue, hypodontia, relative macroglossia because of the small maxillo-mandibular framework with the tongue resting inactively between the lips due to muscle hypotonia in the orofacial region and, ultimately, a flattened face with anterior open bite and Class III dental and skeletal relationships 3. These anatomical features may lead to speech, swallowing and masticatory functional impairments, as well as to an increased predisposition to obstructive sleep apnoea (OSA) and mouth breathing 4.

Medical advances and the multidisciplinary management of DS patients have doubled the life expectancy of these patients in the last decade, from 30-40 to 60-70 years, with increased quality of life and more community-involved and productive lives 5. This in turn opens new horizons for improvement of their oral, dental and facial functions, among others.

The present study describes a protocol for the surgical management of dento-facial deformities in DS patients based on a series of three cases and a review of the literature.

PATIENTS AND METHODS

Three consecutive patients with DS were referred to our Department for dentofacial deformity treatment with orthognathic surgery (OS). A retrospective evaluation was made of the treatment applied in all three cases, and a review of the literature was carried out in order to validate the proposed management algorithm (Fig. 1)



The guidelines of the Declaration of Helsinki were followed in all the treatment phases. Consent was requested from the legal guardians of the patients. As this was a retrospective analysis, Institutional Review Board approval of the study was not considered necessary.

Diagnostic work-up

The diagnostic work-up comprised three phases, which were also used to concomitantly evaluate patient and parent collaboration: a) physical intraoral and facial examination, with intraoral and facial photographic records and the study of plaster dental casts and wax bites; b) periodontal evaluation and a follow-up visit to check patient and parent capacity to maintain proper periodontal health; and c) cone-beam computed tomography (CBCT) (i-CAT, Imaging Sciences International, Inc., Hatfield, USA) study to complete the facial analysis.

Obstructive sleep apnoea diagnosis and follow-up

A thorough anamnesis is required, with quality of life evaluation in children with OSA 6,7. When OSA is suspected, polysomnography (PSG) should be requested. In addition, three-dimensional (3D) pharyngeal airway volume (PAV) was assessed by CBCT at one and twelve-months follow-up, respectively.

Pre-admission medical and anaesthesia evaluation

The anaesthetic management of patients with DS constitutes a challenge for the anaesthetist, due to the difficulty of the airway, the possible associated comorbidities they may present, and behavioural and communication problems [8].

The airway may prove difficulty in intubation due to the following DS-related issues: a) small airway size secondary to maxillary hypoplasia, micrognathia, macroglossia, tonsillar hypertrophy, short neck, glottic and subglottic stenosis and tracheomalacia; b) atlanto-axial / atlanto-occipital instability with a high risk of spinal cord injury; and c) OSA secondary to central apnoea, low muscle tone in the mouth and upper airway, poor coordination of airway movements, and the abovementioned small airway size [4,9,10]. Thus, potential disease conditions require in depth evaluation, as well as the management of potential complications planned beforehand, in order to ensure a safe anaesthetic procedure [8,11].

Perioperative management

The patients were operated upon under general anaesthesia and with endotracheal intubation, as in conventional orthognathic surgery procedures. However, a smaller tube than expected for the age of the patient was chosen in all cases in order to reduce the incidence of subglottic oedema and post-intubation stridor.

Surgery

All patients received pre- and postoperative orthodontic treatment and were operated upon under general anaesthesia by the same surgeon (FHA). A bilateral mandibular sagittal split osteotomy was performed using the Dal Pont-Obwegeser technique, with a maxillary LeFort I osteotomy using the ‘twist technique’ described elsewhere [14]. All patients were extubated in the operating room, and all wore a closed-circuit cold mask (17ºC) during hospital admission. Standard antibiotic and anti-inflammatory medication for OS was prescribed. Functional training with light guiding elastics was followed for one month, together with a soft diet during the same period of time.

Postoperative evaluation

Eventual surgical complications were recorded at one week and 1, 6 and 12 months of follow-up. In addition, two control CBCT scans were performed at one month (T1) and one year of follow-up (T2) in order to assess both airway and bony surgical enlargement (T1-baseline [T0]) and its long-term stability after surgery (T2-T1). CBCT scans were obtained in DICOM (Dental Imaging Communication) format and processed with specific third-party software (Dolphin® 3D Orthognathic Surgery Planning Software Version 11.8). A 3D volume was created with hard tissue reconstruction for the T0, T1 and T2 databases. Three-dimensional superimposition and dimensional comparisons were performed by means of surface matching between different datasets [15].
In order to evaluate surgical bony enlargement and stability, the following linear measurements were obtained at the maxillary midline in all three spatial planes:

- Sagittal plane: projected distance from A-point to nasion perpendicular (A-Nper) for the maxilla; and projected distance from B-point to nasion perpendicular (B-Nper) for the mandible.

- Transverse plane: distance between both greater palatine foramina (PFR-PFL) for the maxilla; and distance between both gonions (GoR-GoL) for the mandible.

- Vertical plane: perpendicular distance from A-point to the Frankfort horizontal plane through the nasion (A-FHN) for the maxilla; and distance from B-point to the Frankfort horizontal plane through the nasion (B-FHN) for the mandible.

Lastly, PAV enlargement and its stability were assessed by measuring enlargement three-dimensionally (3D) at three different levels with respect to the limits of the pharyngeal airway subregions: nasopharynx, oropharynx and hypopharynx, following a previously validated protocol described in detail elsewhere [16].

Statistical analysis

A descriptive analysis was made of the study variables, with calculation of the mean, standard deviation (SD), minimum and maximum values, and median for continuous variables. Absolute and relative frequencies (percentages) were reported in the case of qualitative variables. The statistical analysis was carried out using the SPSS version 15.0.1 statistical package (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used for quantitative analysis. Percentage variation referred to maxillary or mandibular surgical movements (relapse) for each patient was calculated as follows: one-year postoperative A/B-point position · 100 / one-month postoperative A/B-point position. Similarly, percentage variation referred to PAV (relapse) for each patient was calculated as follows: one-year postoperative PAV · 100 / one-month postoperative PAV.

RESULTS

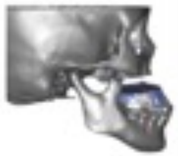
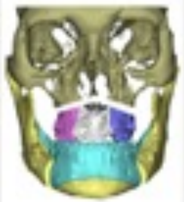
The clinical cases are summarized in Table 1. The study sample comprised two men and a woman with a median age of 26.7 years (range 20-37). The main reason for consultation was the presence of patient chewing difficulties, though thorough anamnesis also evidenced snoring and excessive daytime sleepiness (EDS) in all patients. None of them were diagnosed of OSA or used night time continuous positive airway pressure (CPAP). No multiorgan alterations were observed at the pre-admission medical evaluation.

Table 1. Preoperative facial, occlusal and airway features and images.

PATIENT	SEX	AGE	MAIN COMPLAINT	OTHER PATHOLOGIES	FACIAL PROFILE	OCCLUSION	OSA	PRE-OPERATIVE PAV (mm^3)	ANTERIOR VIEW	LATERAL VIEW	PA 3D	OCCLUSAL VIEW	PROFILE
1	F	37	• Difficulty in chewing • Snoring	• Maxillary hypoplasia • Anteroposterior mandibular hyperplasia • Hypoplasic nasal bone • Hypothyroidism • Scoliosis	• Concave • Brachycephalic	• Class III • Anterior open bite • Superior and inferior dental crowding	Symptoms but not diagnosed	15681					
2 (JL)	M	20	• Difficulty in chewing	• Sagittal maxillary hypoplasia • Sagittal mandibular hypoplasia • Right mandibular deviation • Macroglossia • Nasal hypoplasia	• Concave • Dolichofacial	• Class III • Anterior open bite • Superior and inferior dental crowding • Bilateral crossbite • Microdontia • Supernumeray tooth	Symptoms but not diagnosed	42204					
3	M	23	• Difficulty in chewing • Snoring	• Anteroposterior maxillary hypoplasia • Right mandibular deviation	• Concave • Brachycephalic	• Class III • Anterior Crossbite • Superior dental crowding	Symptoms but not diagnosed	19467					

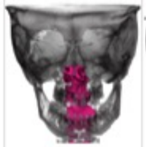
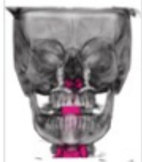
a F: female; M: male; OSA: obstructive sleep apnea; PAV: pharyngeal airway volume; PA: pharyngeal airway

Table 2. Surgical virtual plan, procedures and complications. Postoperative PAV gain and skeletal movement through CBCT superimposition after one month of follow-up

PATIENT	SURGERY				VIRTUAL SURGICAL PLAN ANTERIOR VIEW	VIRTUAL SURGICAL PLAN LATERAL VIEW	INTRAOPERATIVE COMPLICATIONS	1-MONTH PAV (mm^3)	PAV GAIN (%) (T1-T0)	CBCT SUPERIMPOSITION (T1-T0) ANTERIOR VIEW	CBCT SUPERIMPOSITION (T1-T0) LATERAL VIEW
	Maxillary	Mandible	Chin	Others							
1	Lefort I • Forward (5 mm)	None	Genioplasty • Forward (6 mm) • Downward (4 mm)	• Rhinoplasty (pyramid augmentation) • Septoplasty			None	27420	74%		
2	Segmented Lefort I • Forward (5mm) • Downward (3mm) • Expansion (5mm)	Mandibular retrusion (4.2 mm)	None	• Rhinoplasty • Septoplasty			None	54143	28%		
3	Lefort I • Forward (3.6 mm) • Downward (3.8 mm)	None	None	None			None	28652	47%		

a PAV: pharyngeal airway volume; PA: pharyngeal airway.

Table 3. Final outcome after one year of follow-up: skeletal and airway stability and degree of satisfaction with the overall procedure.

PATIENT	POSTOPERATIVE COMPLICATIONS	SKELETAL RELAPSE	1-YEAR PAV (mm^3)	PAV GAIN (%) (T2-T0)	SATISFACTION PATIENT-FAMILY-SURGEON-ORTHODONTIST	ANTERIOR VIEW	LATERALVIEW	PA 3D	FOLLOW UP
1	Osteosynthesis plate removal due to repetitive inflammation	None	25859	64%	10-10-10-10				10 years
2	None	None	52992	25%	10-10-10-10				24 months
3	None	None	28652	47%	10-10-10-10				18 months

a PAV: pharyngeal airway volume; PA: pharyngeal airway.

Mean basal PAV was 25.784 mm3 (range 15.681-42.204). Cases 1 and 3 presented an underlying constricted upper airway (15.681 mm3 and 19.467 mm3, respectively). Specifically, narrowing was observed in all airway subregions: naso-, oro- and hypopharynx (Table 1). Case 2 presented a normal initial PAV (42.204 mm3).

All patients underwent maxillary surgery, but only case 2 was subjected to mandibular surgery for backward movement. A mean maxillary advancement of 4.53 mm and a mean maxillary descent of 3.6 mm were obtained. Consequently, a mean PAV gain of 10.954.33 mm3 (50%) was recorded at the one-month follow-up visit (Table 2).

Stable occlusion was achieved in all cases after postoperative orthodontic treatment, with proper chewing function and decreased snoring as reported by the parents. Regarding skeletal stability, a non-relevant relapse was observed in maxillary bone: a mean relapse of 1.2 mm in the sagittal dimension, 0.6 mm vertically, and none in the transverse dimension. On the other hand, in relation to PAV stability, we recorded a mild mean relapse at one year of follow-up of -2.712 mm3 (5%), though the final mean PAV gain was notorious 35.834 mm3 (45%) (Table 3).

DISCUSSION

The main reasons why patients seek OS and related surgical orthodontic treatments are occlusal, aesthetic problems and OSA. Although DS is associated to altered facial dimensions, and some authors[17] advocate cosmetic facial surgery to avoid stigmatization and ensure better social acceptance, in our opinion aesthetics should not be the sole indication of OS in DS patients, in view of its unfavorable benefit/risk balance (Fig. 1).

On one hand, occlusal disharmonies with anterior open bite, dental Class III and a lack of inter-arch contacts are common in patients with DS, due to their abovementioned skeletal cranial and orofacial dysmorphic features [3,18]. In the attempt to create more dental contacts these individuals protrude the mandible, which in the end can jeopardize temporomandibular joint function [19]. Besides, such malocclusion involves speech and feeding problems, which are aggravated by their inherent neuro-motor disability for articulation and chewing/swallowing, respectively. This severe malocclusion may have respiratory consequences such as OSA or the aspiration of food or fluids into the lungs [20]. Thus, it is evident that DS patients are in need of treatment for their malocclusions.

On the other hand, persons with DS are prone to develop OSA due to a series of associated anatomical and physiological features [21]: a) a small airway size because of underlying maxillary hypoplasia, micrognathia, relative macroglossia, adeno- and lingual-tonsillar hypertrophy, fat deposits in the lateral wall of the pharynx, glottic and subglottic stenosis and tracheomalacia; and b) low muscle tone in the mouth and upper airway, poor coordination of airway movements, and gastroesophageal reflux disease that leads to inflammation and obstruction of the upper airway[4,9]. Some studies suggest that the prevalence of OSA in children with DS is 30-50%, and that approximately 90% of the adults will develop OSA, which in such cases moreover tends to be severe [9,11,22]. Apart from the typical comorbidities associated to OSA, such as arterial hypertension, altered blood glucose homeostasis, cardiovascular and cerebrovascular diseases, pulmonary hypertension, cognitive deficits and even death, individuals with DS specifically suffer worsening of overall cognitive function - starting with weakening of neurocognitive development in early ages, and followed later on by deteriorated communication ability, behavior, functional outcomes and quality of life [23]. In this regard, several management strategies have been described: a) positive airway support in the form of noninvasive ventilation (NIV) or CPAP, though this is associated to high dropout and non-adherence rates [24]; b) weight loss, which does not cure OSA, but is recommended in addition to other therapies in patients who are overweight [25]; c) airway soft tissue surgery, such as adeno- and lingual-tonsillectomy, which are associated to high OSA persistence rates [4] (adeno- and lingual-tonsillectomy therefore should be indicated only when hypertrophy is clearly evidenced) [4,26]; d) partial glossectomy, which should only be indicated when true excessive enlargement of the tongue results in insufficient space for the organ [27]; e) hypoglossal nerve stimulation, which is a promising and minimally invasive technique, though further studies are needed to optimize patient selection and better assess the long-term efficacy of the technique [28]; and f) tracheostomy, which is linked to severe short and long-term complications and may be required only in cases of severe OSA not amenable to other forms of treatment.

These poor outcomes point to OS as the first line treatment option, considering the characteristic orofacial dysmorphic features of individuals with DS and that contribute to airway narrowing, such as retrusion or shortening of the mandible and maxillary hypoplasia [29]. Although recommending OS in this population is controversial, it has been demonstrated that OS procedures can be carried out with success rates (predictability, complications during and after the operation, and overall treatment stability) as high as in mentally healthy individuals [30].

Once the patient reports for maxillofacial consultation due to occlusal problems or OSA, a number of aspects must be taken into account. Firstly, regarding the craniofacial features, patients with DS have reduced head and facial dimensions with a brachiocephalic cranium, a shorter and flatter cranial base, reduced or absent frontal sinus and nasal bone, small ears, and hypertelorism with slanted eyes. Thus, cephalometric landmarks such as the nasion or porion for facial analysis and head orientation purposes may be altered, making it difficult to properly classify the underlying dentofacial anomaly [31]. For this reason, it is highly advisable to use 3D CBCT for facial analysis instead of 2D X-rays. On the other hand, the diagnosis of OSA in children is based on an association of PSG parameters [32,33], and on clinical symptoms based on a specific OSA quality of life test for children (the OSA-18 survey) [6,7,34]. Apart from the cardinal manifestations of OSA, such as snoring, fatigue and restless sleep, children with DS specifically may also present with failure to thrive, hyperactivity, behavioral disruptions and poor school performance, whereas adults with DS may present with mood dysregulation and depression [22]. Although the cases in our study did not undergo PSG, because their main complaint was malocclusion, it is advisable to systematically perform PSG in all patients presenting OSA symptoms. Besides, diagnostic CBCT for facial analysis may also be used to detect upper airway constrictions. In our study, cases 1 and 3 showed basal upper airway constriction (15,681 mm3 and 19,467 mm3, respectively, compared to reference normal PAV values of 23,400 mm3 [35,36]. Specifically, a narrowed airway was observed in all upper airway subregions: naso-, oro- and hypopharynx. Conversely, mandibular advancement devices, apart from being an option for treating mild to moderate OSA with better patient compliance than when CPAP is used [22], are also useful in deciding which patients may benefit from surgical mandibular advancement in the context of OSA. Unfortunately, similar maxillary devices for predicting the impact of maxillary advancement upon OSA are not available. On the other hand, it is essential to detect as far as possible central origin OSA cases through PSG, since OS would not be worthwhile in such situations.

Correct screening referred to patient eligibility for orthodontic-surgical treatment is essential. We thus propose the above-described diagnostic work-up in order to evaluate patient and parent collaboration (examination - periodontal status and maintenance - CBCT) regardless of the patient intelligence quotient and thus to refine the selection of suitable candidates for OS (Fig. 1). Equally important is the establishment of a good and trusting professional-patient relationship. In this regard it is useful to explain the planned procedures in depth and indicate the expected results and eventual complications to the patient and his/her relatives. Keeping close contact through telephone support and more frequent follow-up visits is also useful.

Surgical planning differs from the regular scenario where aesthetics constitute a key element, and instead priority is placed on minimal surgery in terms of mono- rather than bimaxillary operations, with reduction of the amount of skeletal movements, while always ensuring proper occlusion and sufficient PAV enlargement. Thus, in general, in the presence of a typical midface deficiency with high palate, reduction of its length, together with a narrowed oropharynx, usually imply advancement, widening and antero-posterior levelling/upward maxillary movements. Then, the mandible may be adjusted to maxillary positioning. Regarding the specific surgical management of OSA, a maxilla-mandibular advancement of 1 cm is considered the gold standard in OS [37], but it should be individualized for each patient. Our sample of patients underwent a mean maxillary advancement of 4.53 mm, which was enough to correct both occlusal and narrowed airway problems. Although one patient required mandibular setback for occlusal purposes, it did not adversely affect overall PAV enlargement.

Although it has been widely demonstrated that OS is the most consistent and predictable surgical treatment option for adult patients diagnosed with moderate to severe OSA [38,39], its outcomes are less predictable in the DS population because, as previously mentioned, the causes of OSA in these patients are multiple and additive. Thus, a systematic sleep study based on PSG is strongly recommended prior to and after OS in order to check surgical effectiveness and determine whether further treatments are necessary. In cases where OSA persists after upper airway surgery, CPAP or NIV in the case of alveolar hypoventilation are indicated [4].

Postoperative discomfort should be reduced as far as possible, adopting minimally invasive approaches such as the 'twist technique' [14], the shortening of surgery time, the use of a piezoelectric saw when possible [40], the prescription of standard anti-inflammatory medication, manual lymphatic drainage for OS [41], and the wearing of a closed-circuit cold mask during the postoperative period [42]. Furthermore, whenever possible, light guiding elastics for functional training should be used instead of rigid intermaxillary fixation [30].

Regarding patient age at surgery, the standards advise waiting until cessation of mandibular growth. In the meantime, a two-phase or multiphase orthodontic treatment program is beneficial to assist correction of misalignment and maxillary transverse deficiency by means of palatal expansion or surgically assisted rapid palatal expansion, before and after closure of the palatal suture, respectively [19,43]. Similarly, myofunctional therapy or orofacial rehabilitation should be started during the growth period in order to favor proper maxilla-mandibular growth, establish an adequate resting position of the tongue behind the upper incisors, reinforce orofacial tonicity, encourage nasal respiration and improve swallowing and speech functionality [44].

Besides, it also may reduce the inherent muscular imbalance that predisposes to an increased prevalence of relapse after OS [30]. Likewise, dentofacial harmonization by means of orthodontic treatment and OS have shown significant improvement in oral motor function, including mouth closure, inactive protrusion and positioning of the tongue in DS patients.

CONCLUSIONS

In conclusion, in selected patients with DS presenting specific orofacial dysmorphic features, orthodontics and OS are the management options of choice to address both occlusion (and its consequent feeding- respiratory- and communication-related problems) and OSA. The implementation of improved medical measures, minimally invasive surgery and cutting-edge technologies allows OS to be safely performed in patients with DS.

REFERENCES

1. Sherman SL, Allen EG, Bean LH, Freeman SB. Epidemiology of Down syndrome. Ment Retard Dev Disabil Res Rev. 2007;13(3):221-227.

2. Potter H. Beyond Trisomy 21: Phenotypic Variability in People with Down Syndrome Explained by Further Chromosome Mis-segregation and Mosaic Aneuploidy. Journal of Down Syndrome & Chromosome Abnormalities. 2016;2(1).

3. Bauer D, Evans CA, Begole EA, Salzmann L. Severity of occlusal disharmonies in down syndrome. Int J Dent. 2012;2012:872367.

4. Dudoignon B, Amaddeo A, Frapin A, et al. Obstructive sleep apnea in Down syndrome: Benefits of surgery and noninvasive respiratory support. American Journal of Medical Genetics Part A. 2017;173(8):2074-2080.

5. Agarwal Gupta N, Kabra M. Diagnosis and Management of Down Syndrome. The Indian Journal of Pediatrics. 2014;81(6):560-567.

6. Chiner E, Landete P, Sancho-Chust JN, et al. Adaptation and Validation of the Spanish Version of OSA-18, a Quality of Life Questionnaire for Evaluation of Children with Sleep Apnea-Hypopnea Syndrome. Arch Bronconeumol. 2016;52(11):553-559.

7. Franco RA, Rosenfeld RM, Rao M. First place--resident clinical science award 1999. Quality of life for children with obstructive sleep apnea. Otolaryngol Head Neck Surg. 2000;123(1 Pt 1):9-16. doi:10.1067/mhn.2000.105254

8. Borland LM, Colligan J, Brandom BW. Frequency of anesthesia-related complications in children with Down syndrome under general anesthesia for noncardiac procedures. Paediatr Anaesth. 2004;14(9):733-738.

9. Bassell JL, Phan H, Leu R, Kronk R, Visootsak J. Sleep profiles in children with Down syndrome. Am J Med Genet A. 2015;167A(8):1830-1835.

10. Waage NS, Baker S, Sedano HO. Pediatric conditions associated with compromised airway: part I--congenital. Pediatr Dent. 2009;31(3):236-248.

11. Alexander M, Petri H, Ding Y, Wandel C, Khwaja O, Foskett N. Morbidity and medication in a large population of individuals with Down syndrome compared to the general population. Dev Med Child Neurol. 2016;58(3):246-254.

12. Aboul-Hosn Centenero S, Hernández-Alfaro F. 3D planning in orthognathic surgery: CAD/CAM surgical splints and prediction of the soft and hard tissues results - our experience in 16 cases. J Craniomaxillofac Surg. 2012;40(2):162-168.

13. Hernández-Alfaro F, Guijarro-Martínez R. New protocol for three-dimensional surgical planning and CAD/CAM splint generation in orthognathic surgery: an in vitro and in vivo study. Int J Oral Maxillofac Surg. 2013;42(12):1547-1556.

14. Hernández-Alfaro F, Guijarro-Martínez R. “Twist Technique” for Pterygomaxillary Dysjunction in Minimally Invasive Le Fort I Osteotomy. Journal of Oral and Maxillofacial Surgery. 2013;71(2):389-392. doi:10.1016/j.joms.2012.04.032

15. Haas Junior OL, Guijarro-Martínez R, de Sousa Gil AP, da Silva Meirelles L, de Oliveira RB, Hernández-Alfaro F. Stability and surgical complications in segmental Le Fort I osteotomy: a systematic review. International Journal of Oral and Maxillofacial Surgery. 2017;46(9):1071-1087.

16. Guijarro-Martínez R, Swennen GRJ. Three-dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: a validation study. Int J Oral Maxillofac Surg. 2013;42(9):1140-1149.

17. Olbrisch R-R. Plastic surgical management of children with Down's syndrome: indications and results. British Journal of Plastic Surgery. 1982;35(2):195-200.

18. Mayoral-Trias MA, Llopis-Perez J, Puigdollers Pérez A. Comparative study of dental anomalies assessed with panoramic radiographs of Down syndrome and non-Down syndrome patients. Eur J Paediatr Dent. 2016;17(1):65-69.

19. Javed F, Akram Z, Barillas AP, et al. Outcome of orthodontic palatal plate therapy for orofacial dysfunction in children with Down syndrome: A systematic review. Orthodontics & Craniofacial Research. 2018;21(1):20-26.

20. Hennequin M, Faulks D, Veyrune J-L, Bourdiol P. Significance of oral health in persons with Down syndrome: a literature review. Developmental Medicine & Child Neurology. 2007;41(4):275-283.

21. Fung E, Witmans M, Ghosh M, Cave D, El-Hakim H. Upper airway findings in children with Down syndrome on sleep nasopharyngoscopy: case-control study. J Otolaryngol Head Neck Surg. 2012;41(2):138-144.

22. Lal C, White DR, Joseph JE, van Bakergem K, LaRosa A. Sleep-disordered breathing in Down syndrome. Chest. 2015;147(2):570-579.

23. Skotko BG, Macklin EA, Muselli M, et al. A predictive model for obstructive sleep apnea and Down syndrome. Am J Med Genet A. 2017;173(4):889-896.

24. Brooks LJ, Olsen MN, Bacevice AM, Beebe A, Konstantinopoulou S, Taylor HG. Relationship between sleep, sleep apnea, and neuropsychological function in children with Down syndrome. Sleep Breath. 2015;19(1):197-204.

25. Romero-Corral A, Caples SM, Lopez-Jimenez F, Somers VK. Interactions between obesity and obstructive sleep apnea: implications for treatment. Chest. 2010;137(3):711-719.

26. Prosser JD, Shott SR, Rodriguez O, Simakajornboon N, Meinzen-Derr J, Ishman SL. Polysomnographic outcomes following lingual tonsillectomy for persistent obstructive sleep apnea in down syndrome: PSG Outcomes of Lingual Tonsillectomy in DS. The Laryngoscope. 2017;127(2):520-524.

27. Salmen F, Dedivitis R. Partial glossectomy as an auxiliary method to orthodontic treatment of dentofacial deformity. International Archives of Otorhinolaryngology. 2013;16(03):414-417.

28. Diercks GR, Wentland C, Keamy D, et al. Hypoglossal Nerve Stimulation in Adolescents With Down Syndrome and Obstructive Sleep Apnea. JAMA Otolaryngol Head Neck Surg. 2018;144(1):37-42.

29. Lee RWW, Chan ASL, Grunstein RR, Cistulli PA. Craniofacial phenotyping in obstructive sleep apnea--a novel quantitative photographic approach. Sleep. 2009;32(1):37-45.

30. Bock JJ, Maurer P, Otto C, Fuhrmann RAW, Schubert J. Complications of orthodontic–orthognathic surgery treatment in mentally handicapped patients. Journal of Cranio-Maxillofacial Surgery. 2006;34(3):156-161.

31. Suri S, Tompson BD, Cornfoot L. Cranial base, maxillary and mandibular morphology in Down syndrome. The Angle Orthodontist. 2010;80(5):861-869.

32. Bull MJ, Committee on Genetics. Health supervision for children with Down syndrome. Pediatrics. 2011;128(2):393-406.

33. Amaddeo A, Frapin A, Fauroux B. Long-term non-invasive ventilation in children. Lancet Respir Med. 2016;4(12):999-1008. 5

34. Marcus CL, Brooks LJ, Draper KA, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics. 2012;130(3):e714-755.

35. Shahidi S, Momeni Danaie S, Omidi M. Comparison of the Pharyngeal Airway Volume between Non-Syndromic Unilateral Cleft Palate and Normal Individuals Using Cone Beam Computed Tomography. J Dent (Shiraz). 2016;17(3 Suppl):268-275.

36. Chousangsuntorn K, Bhongmakapat T, Apirakkittikul N, Sungkarat W, Supakul N, Laothamatas J. Upper Airway Areas, Volumes, and Linear Measurements Determined on Computed Tomography During Different Phases of Respiration Predict the Presence of Severe Obstructive Sleep Apnea. J Oral Maxillofac Surg. 2018;76(7):1524-1531.

37. Bartolucci ML, Bortolotti F, Raffaelli E, D'Antò V, Michelotti A, Alessandri Bonetti G. The effectiveness of different mandibular advancement amounts in OSA patients: a systematic review and meta-regression analysis. Sleep Breath. 2016;20(3):911-919.

38. Zaghi S, Holty J-EC, Certal V, et al. Maxillomandibular Advancement for Treatment of Obstructive Sleep Apnea: A Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2016;142(1):58-66.

39. Caples SM, Rowley JA, Prinsell JR, et al. Surgical modifications of the upper airway for obstructive sleep apnea in adults: a systematic review and meta-analysis. Sleep. 2010;33(10):1396-1407.

40. Thereza-Bussolaro C, Galván Galván J, Pachêco-Pereira C, Flores-Mir C. Maxillary osteotomy complications in piezoelectric surgery compared to conventional surgical techniques: a systematic review. Int J Oral Maxillofac Surg. 2019;48(6):720-731.

41. Yaedú RYF, Mello M de AB, Tucunduva RA, da Silveira JSZ, Takahashi MPMS, Valente ACB. Postoperative Orthognathic Surgery Edema Assessment With and Without Manual Lymphatic Drainage. J Craniofac Surg. 2017;28(7):1816-1820.

42. Lateef TA, Al-Anee AM, Agha MTF. Evaluation the Efficacy of Hilotherm Cooling System in Reducing Postoperative Pain and Edema in Maxillofacial Traumatized Patients and Orthognathic Surgeries. J Craniofac Surg. 2018;29(7):e697-e706.

43. Musich DR. Orthodontic intervention and patients with Down syndrome. Angle Orthod. 2006;76(4):734-735.

44. Faulks D, Mazille M-N, Collado V, Veyrune J-L, Hennequin M. Masticatory dysfunction in persons with Down's syndrome. Part 2: management. Journal of Oral Rehabilitation. 2008;35(11):863-869.

3.5

3.5 Paper five

Orthognathic surgery as first line treatment to cure obstructive sleep apnea (OSA):

A Pilot study

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ABSTRACT

The purpose of this study was to assess the success predictors and to correlate the effects of orthognathic surgery as the first line treatment to cure obstructive sleep apnea (OSA) in patients with dentofacial deformity. A prospective evaluation of 23 consecutive patients diagnosed with OSA (mild, moderate or severe) who underwent orthognathic surgery at the Maxillofacial Institute (Teknon Medical Center in Barcelona, Spain) was carried out. Baseline AHI was 20.05 ± 9.9 events/hour (16.7 -29.3). Preoperatively, 60.9% of the patients were diagnosed with mild and 39% with moderate-to-severe OSA (21.7% and 17.4%, respectively). A significant total AHI reduction of 14.3 ± 2.1 events/hour (71.7%, p < 0.001) was observed after orthognathic surgery, followed by a mean relapse of 0.4 ± 1.6 events/hour (7.4%, p = 1.000) at 12-months follow-up. Then, 74% of the patients improved their severity OSA level (p < 0.001) and 60.9% cured OSA after one year (p < 0.001). The results of this pilot study demonstrate the positive effect of OS over AHI parameters. However, preoperative OSA severity is a noteworthy factor in determining the long-term clinical success to cure OSA after OS. Therefore, OS should be used as the first line treatment armamentarium when planning to cure moderate-to-severe OSA in selected patients with a facial retrusive pattern.

Keywords: Orthognathic surgery; Obstructive sleep apnoea; dentofacial deformities; Three-dimensional imaging; Upper airway; Polysomnography

INTRODUCTION

Orthognathic surgery (OS) combined or not with orthodontics aims to reestablish the facial harmony and to correct dentofacial deformities (DFD) by means of different osteotomies and the maxillomandibular complex repositioning with long-term bone and soft tissue stability (1). DFD patients with maxillary or mandibular hypoplasia are more prone to suffer from a chronic sleep-related breathing disorder; and then, inheriting the systemic consequences of obstructive sleep apnea (OSA) syndrome (2,3).

There are different non-surgical and surgical methods used to treat OSA, each of them with the following related problems: a) Continuous positive airway pressure (CPAP), although it is considered the gold standard treatment, it reports high non-adherence rates of 46-86% (adherence being defined as > 4 hours of night use of CPAP during 70% of night) (4); b) tracheotomy, which is associated with a high morbidity (5); c) tonsillectomy and adenoidectomy are effective but only indicated in cases with a subjacent hypertrophy of tonsils and adenoids, respectively; (5) and d) uvulopalatopharyngoplasty (UPPP), hyoid suspension or hyothyroidopexy, among others, with low success and cure rates (40-80%) (5) (being success defined as final apnea-hypopnea index (AHI) threshold of < 20 events/hour (e/h), and its reduction by 50%; and cure defined as a final AHI of < 5 e/h) (6). However, since 1984 (7), maxillomandibular advancement (MMA) was firstly described by the Stanford group to treat OSA in retrognathic patients as an effective surgical procedure at long term (8).

In this context, bone surgery implying enlargement of the maxillomandibular complex also induce enlargement of the airway, introducing a significant increase of the posterior airway space (PAS) and the total pharyngeal airway volume (PAV) (9): a mean 10 mm of maxillomandibular advancement results in a mean increase in the PAS of 4.75 mm (range 3.15-6.35) and a mean PAV gain of 7.35 cm3 (5.35-9.34) with a success rate of 86% to treat OSA patients (2). However, pharyngeal airway volume and minimal cross-sectional areas (mCSA) dimensions vary three-dimensionally (3D) at all levels (naso-, oro-, and hypopharynx) depending on the type, magnitude and direction of the skeletal movements (maxillary and mandibular), as demonstrated in a recent study of our team (10), being the mandibular advancement and occlusal plane changes by means of counterclockwise rotation (CCW) the most effective for upper airway enlargement at 12 months follow up (10).

However, rigorous data is lacking on the evaluation of OS as the first line treatment to cure OSA and which patient's profile will benefit from the optimization of the upper airway. Thus, as a continued effort into the study of diverse anatomical and non-anatomical features, the purpose of this study was to assess the success predictors and to correlate the effects of OS as the first line treatment to cure OSA (in terms of AHI and sleep patient-centered parameters) on a three-dimensional image basis.

MATERIALS AND METHODS

Study design

To address the research purpose, the investigators designed and implemented a clinical trial (ClinicalTrials.gov ID NCT03796078 registration). These are the pilot study results of an ongoing controlled clinical trial with a total sample of 100 patients eligible for OS and undergoing polysomnography (PSG) or home sleep apnea test (HSAT), which is equated to PSG depending on the OSA severity according to the American Association of Sleep Medicine (AASM) (11). Then, this pilot study reports one-month and 12-months follow-up correlations between improvement of OSA-related parameters and airway volume changes after OS. It was approved by the Teknon Medical Hospital Institutional Review Board (IRB) (Barcelona, Spain) (Ref.OSAS-OS-2017-CMF-TEK), and conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its subsequent amendments. All participants signed an informed consent agreement prior to study enrollment.

The pilot study was conducted over patients who underwent OS during 2018 and 2019 at the Maxillofacial Institute (Teknon Medical Center in Barcelona, Spain). Demographic data, PSG or HSAT tests and 3D radiological images were obtained.

Patients of any gender, over the age of 18 years old with a completed maxillomandibular growth diagnosed with a DFD and suffering from mild, moderate or severe OSA based on PSG or HSAT, and eligible for OS (mono- or bimaxillary) were included in the study. Patients with craniofacial syndromes, missing PSG or HSAT, cone beam computed tomography (CBCT), follow-up visits, or not willing to sign the informed consent were excluded from the study.

Treatment

The standard virtual surgical 3D planning protocol (10) was applied (Dolphin Imaging, version 11.95 premium, Chatsworth, CA, USA) and the upper incisor soft-tissue nasion plane (UI-STP) was used as an absolute reference to guide the anteroposterior positioning of the maxillomandibular complex (11). Intermediate and final surgical splints were designed and printed in-house. Patients were operated on under general anesthesia following the mandible-first protocol. A mandibular bilateral sagittal split osteotomy (BSSO) was performed and/or a maxillary LeFort I osteotomy, which was carried out using the minimally invasive 'twist' technique (13).

Study variables and data analyses

All included patients had followed the standard pre- and post-operative imaging workflow protocol (14) for OS of the Department, which involves facial and occlusal pictures and CBCT at three time points: preoperatively (T0) and postoperatively at 1- (T1) and 12- (T2) months follow-up. These two postoperative time points were chosen in order to evaluate the short- and long-term effect of OS in optimizing both the PAV and improvement of the sleep-related parameters of OSA.

The CBCT scans were performed using an i-CAT Vision system (iCAT, Imaging Sciences International, Hatfield, PA, USA). Moreover, household HSAT and/or PSG tests, treatment outcome assessment and long-term care evaluation after orthognathic sleep surgery were performed as indicated together with a group of neurophysiologists according to the AASM algorithm (15).

The following data were collected at three time points (T0, T1 and T2): a) demographic: sex, age and smoking and alcoholic habits; b) anatomical: initial dental class according to Angle's classification (I, II, III), body mass index (BMI (Kg/cm2)), neck perimeter (NP (cm)); c) polysomnographic: AHI (mild: AHI ≥ 5 e/h; moderate: AHI ≥ 15 e/h or severe: AHI ≥ 30 e/h)), nocturnal oxymetry parameters: oxygen desaturation index (ODI), the percentage of time spent at arterial oxygen saturation (SpO2) below 90% (CT90%) and the lower minimum oxygen desaturation (LSpO2); d) daytime drowsiness: Epworth Sleepiness Scale (ESS) score (normal values 0-10 out of 24 points) (16); e) airway volumetric and cross-sectional parameters: PAV (total, naso-, oro- and hypopharynx) (mm3) and mCSA (mm2), respectively; and f) surgical: mono- or bimaxillary surgery, type, direction and amount of movements, and eventual intra- or postoperative complications. Data were recorded in an anonymized electronic report form (e-CRF), where variables were monitored.

Statistical analysis

The data analysis was performed using SPSS for Windows, version 25.0.0 software (SPSS Inc, Chicago, IL). Demographics and other characteristics were presented in terms of descriptive statistics. Continuous variables were presented by means of number (n), mean, standard deviation (SD), minimum, maximum and median; and relative frequencies (percentages) for qualitative variables. The comparative analysis included the assessment of normal distribution of the measurements using the Kolmogorov-Smirnov test. The inferential analysis included the following statistical methods: a) The analysis of variance (ANOVA) general linear model for repeated measures was used to compare the evolution of the skeletal and volumetric parameters over follow-up. Multiple comparisons were made with Bonferroni correction; b) Wilcoxon test to evaluate changes in the variables resulting from the PSG. This non-parametric test was adequate due to the more asymmetric distribution and frequency of atypical cases of this set of variables. The Bonferroni correction was applied; c) Spearman's nonlinear correlation coefficient to estimate the degree of association between the changes in the different groups of variables. For this same objective, nonparametric Mann-Whitney (MW), Kruskal-Wallis (KW) tests and Chi2 independence test or Fisher's exact test are used if any of the variables involved are expressed in categories. Two-sided p-values <0.05 were considered significant for all of the statistical tests. Through this pilot study, it was determined that a minimum sample size of 48 patients (for the ongoing CCT) is needed to reach a statistical power of 80%, with a medium effect size (d=0.5) and 95% confidence interval (CI) in detecting differences in volumetric and OSA parameters over time (T0, T1, T2).

RESULTS

A sample of 23 consecutive patients with a DFD diagnosed of OSA by PSG or HSAT, and eligible for OS were enrolled in this pilot study. The sample was comprised of 6 females (26.1%) and 17 males (73.9%) with a mean age of 42.1 ± 11.8 years (range 18-65). No smoking and alcoholic habits were reported. Patients were classified as dental class I (8.7%), class II (65.2%) or class III (26.1%) according to Angle's malocclusion classification (17). Baseline AHI was 20.05 e/h (16.7 -29.3). Preoperatively, 60.9% of the patients were diagnosed with mild, 21.7% with moderate and 17.4% with severe OSA (Fig.1) (Table 1).

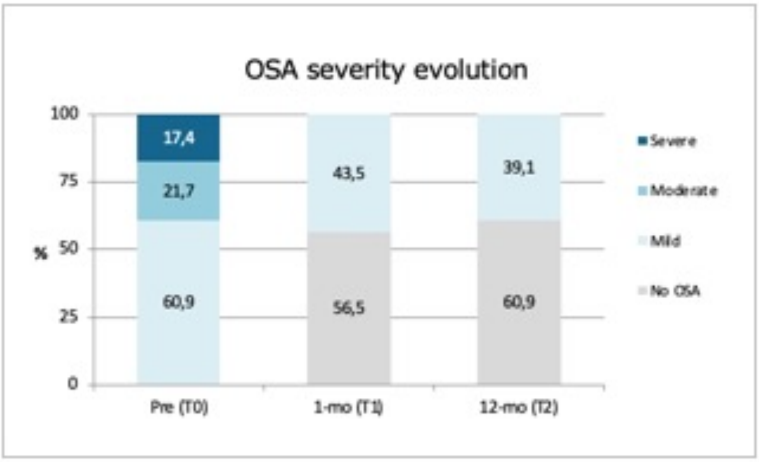

Figure 1. OSA severity evolution of the sample at 1- and 12-months follow-up.

The included patients underwent bimaxillary (82.6%) or monomandibular (17.4%) surgery, with a mean surgical advancement of 6.8 ± 6.7 mm, 14.1 ± 9.2 mm and 16.8 ± 7.8 mm for maxilla, mandible and chin, respectively ($p < 0.001$). CCW rotation of the maxillomandibular complex was performed in 82.6% of the sample (all bimaxillary procedures), whereas no CW rotational movements were performed in any patient of the sample (Table 1). Globally, a 10.4% of skeletal relapse at 12 months follow-up was reported, regardless of the surgical approach.

Table 1. Descriptive characteristics of the studied sample.

	Pre (T0) n = 23	(%)
Age (mean ± SD)	42.1 ± 11.8 years	
Gender		
Male	17	(73.9)
Female	6	(26.1)
Type of dentofacial deformity		
Class I	2	(8.7)
Class II	15	(65.2)
Class III	6	(26.1)

Type of interventions		
Bimaxillary surgery	19	82.6
Monomaxillary surgery	4	17.4
sagittal movements (mean ± SD)		
Maxillary adv	6.8 ± 6.7 mm	
Mandibular adv	14.1 ± 9.2 mm	
chin adv	16.8 ± 7.8 mm	
Rotational movements		
CW	0	0
CCW	19	82.6
No rotation	4	17.4

After OS, a mean increase of 61% of the PAV (p <0.001) and 37% of the mCSA (p <0.001) was obtained, with a mean relapse of 9.4% and 15% at 12 months follow-up, respectively. In this order, oro-, hypo- and nasopharynx significantly increased after OS by 74%, 49%, and 43%, respectively (p <0.05) (Fig. 2). No significant changes were observed for both anthropometric parameters: nor BMI neither neck perimeter (Table 2).

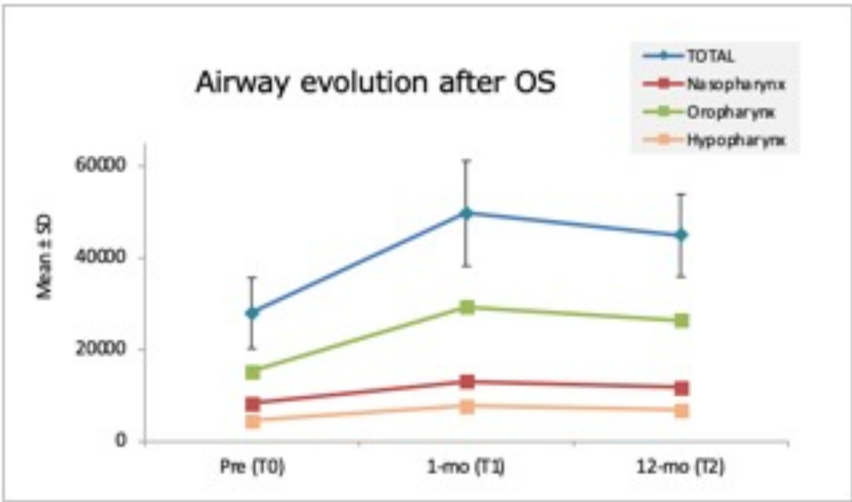

Figure 2. Upper airway evolution after OS over follow-up: at 1 and 12-months follow-up.

A significant total AHI reduction of 14.3 ± 2.1 e/h (71.7%, $p < 0.001$) was observed after OS (T1), followed by a mean relapse of 0.4 ± 1.6 e/h (7.4%, $p = 1.000$) at T2. Mean percentual differences between OSA severity subgroups (mild, moderate and severe) presented mean AHI reductions of 19.9%, 69.7%, and 93.3%, respectively. Therefore, 74% of the patients ($p < 0.001$) decreased their OSA severity level, and remained stable at long-term after OS ($p < 0.001$)) with a success rate of 100% (<20 e/h and an AHI reduction of 50%) and no longer in need of CPAP. A cure rate of 61% (AHI < 5 e/h) was obtained, so not all of them completely cured the OSA. Nocturnal oxymetry parameters (ODI, CT90%, LSpO2) and ESS score improved after OS at 12-months follow-up, although only significant for ODI ($p<0.001$) and ESS score ($p<0.001$) (Table 2).

Table 2. Type of surgery, volume and OSA-related parameters changes of the sample at 1 and 12-months follow-up.

	Pre (T0)	Post 1-month (T1) n = 23 (IQR)	Post 12-months (T2)	p value
Total PAV (mm3)	27992.6 ± 7726.2	49868.8 ± 11468.4	44992.6 ± 8956.1	p<0.001***
nasopharynx	8247.5 ± 2389.5	13,007.4 ± 3681.1	11790.2 ± 2889.4	
oropharynx	15226.8 ± 5694.9	29268.9 ± 8391.5	26483.4 ± 7155.7	
Hypopharynx	4518.2 ± 1354.6	7592.5 ± 1788.1	6718.9 ± 1106.4	
mCSA (mm2)	121.1 ± 38.9	332.1 ± 113.1	282.1 ± 102.1	
Final AHI (e/h)	20.05 ± 9.9	4.5 ± 3.7	4.8 ± 3.7	p=0.001**
OSA severity				p<0.001***
< 5 e/h No OSA	0 (0%)	13 (56.5%)	14 (60.9%)	
≥ 5 e/h	14 (60.9%)	10 (43.5%)	9 (39.1%)	
≥ 15 e/h	5 (21.7%)	0 (0%)	0 (0%)	
≥ 30e/h	4 (17.4%)	0 (0%)	0 (0%)	
ODI	10.5 (7.0-27.8)	4.3 (2.5-5.9)	4.1 (3.4-8.6)	p<0.001***
ESS score	12 (10-18)	9 (6-10)	7 (5-10)	p<0.001***
CT90%	0.4 (0.0-2.2)	0.0 (0.0-0.6)	0.0 (0.0-0.9)	p=0.768
LSpO2	88 (83-92)	90 (87-93)	90 (86-93)	p=1.000

*p<0.05; **p<0.01; ***p<0.001: median (IQR interquartile range) and Wilcoxon test with Bonferroni correction.

Abbreviations: IQR: interquartile range (1st and 3rd quartiles); PAV: pharyngeal airway volume; mCSA: minimum cross-sectional area; AHI: apnea-hypopnea index; OSA: obstructive sleep apnea; ODI: oxygen desaturation index; ESS: Epworth Sleepiness Scale; CT90%: percentage of time spent at arterial oxygen saturation below 90%; LSpO2: lower minimum oxygen saturation.

Despite the positive immediate effect of OS in PAV, mCSA and sleep-parameters, no significant correlations could be detected between the surgical parameters, and the changes in AHI and ESS score. However, notable descriptive trends (r = 0.43) were observed regarding the correlations between the clinical signs of OSA (AHI), PAV and type of surgery, as follows: a) patients who remained with a stable AHI at 12 months follow-up compared to those who did not remained stable at long-term, were those increasing their PAV mainly at the oropharynx level (p<0.15)) (Fig. 3); b) patients who underwent CCW rotation of the maxillo-mandibular complex were correlated with a greater AHI reduction (median -21.7 e/h, p<0.036), which represents an 8% more compared to those not receiving rotational movements at 12 months follow-up; and c) similarly, patients receiving LF1 segmented osteotomies compared to non-segmented LF1, were the ones who benefitted most from AHI reduction (median -26.8 e/h, p < 0.03) at 12-months follow-up, irrespective of their initial OSA diagnoses.

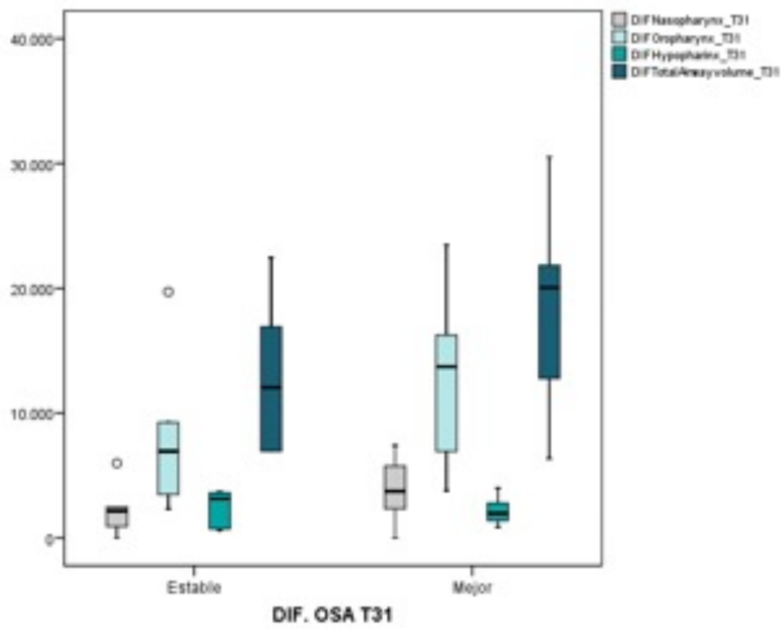

Figure 3. OSA evolution and volumetric changes distribution of the sample after OS at short and long-term.

DISCUSSION

The assessment of the long-term success predictors is essential to cure OSA after OS. This pilot study showed that there is a significant immediate positive effect of OS in the OSA-related parameters (AHI reduction), which remains stable at 12-months follow-up. Our results are consistent with those reported in previous studies (8,18,19).

The majority of the sample included in this study consisted in young patients (< 50 years) suffering from mild OSA (60.9 %) (Fig.1). This is explained because the most common reason for consultation at our Department was an underlying DFD, not a sleep disorder. In this same context, only 10 patients (43.5%) knew their OSA diagnosis in advance, the rest of the patients run undiagnosed until the enrollment stage after the sleep-screening visit with the neurophysiologist. These findings are in line with those found in the literature, where statistics show that over 50% of OSA cases go undiagnosed (2). Therefore, this young undiagnosed population would probably have developed a severe OSA over years, since with ageing PAV decreases even more (20) and OSA involving comorbidities increase (6).

OSA usually arises in patients presenting a hypoplasia of the mandible (class II patients (in our sample, 65.2%)), but also of the maxillary bone (class III patients (in our sample, 26.1%)), or both of them (class I patients (in our sample, 8.7%)). Therefore, when evaluating the relationship between OSA and a DFD, we should be aware of the skeletal facial pattern (retrusive versus protrusive) instead of the dental class (3), as Castro-Silva et al (3) who described class I and III as having statistically bigger volumetric areas than class II patients ($p<0.05$ and $p<0.001$, respectively), and finally concluding that retrognathic patients are more prone to suffer from OSA (3).

On the other hand, while all included patients denied tobacco or alcohol consumption and other OSA causing comorbidities were ruled out, all of them presented an initial hypoplastic maxilla-mandibular pattern, so we can conclude that their sleep disorder was mainly related to their underlying DFD, and thus all of them were eligible for OSA management with OS.

The positive effect of either mono- or bimaxillary OS was proven in all aspects: an immediate improvement of the sleep parameters ($p <0.001$) alongside a significant increase of the volumetric parameters ($p<0.001$) at both one- and twelve-months after surgery were observed. No significant anthropometric parameters changes were reported (neither BMI nor NP), so it is plausible to state that AHI improvement was totally induced by surgery and PAV gain (Fig. 3).

CCW rotation was the sole skeletal movement that induced a significant decrease of the AHI ($p<0.036$). Specifically, a greater amount (8%) of AHI reduction (median -21.7 e/h, $p<0.036$) was observed after 12 months when CCW rotation of the maxillomandibular complex was performed, regardless their initial OSA diagnosis. Therefore, although the literature has traditionally focused on the maxillomandibular advancement (2,8) in the context of OSA treatment, it is in fact the CCW rotation the most effective movement for this purpose (10).

Globally, a 10.4% of skeletal relapse at 12-months follow-up was reported, regardless of the surgical approach (Fig.4). However, it was insufficient to offset the final OSA-related, volumetric and cross-sectional area parameters improvement. Specifically, although an evident volumetric increase was observed at the three levels of the upper airway ($p<0.001$), a mean 9.4% of volumetric relapse at 12 months follow-up was observed. This occurs because of skeletal relapse, but also due to pharyngeal wall accommodation after maxillomandibular forward-pulling (21).

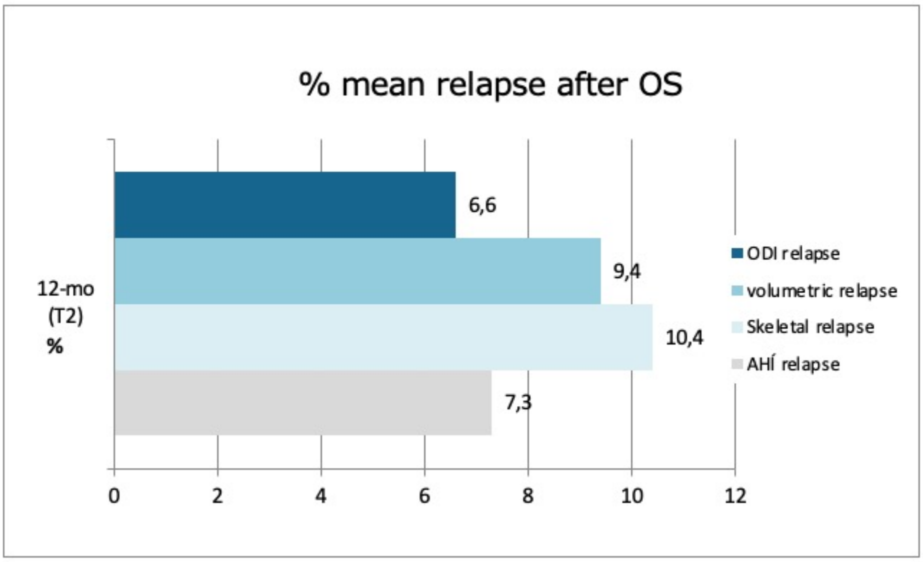

Figure 4. Mean volumetric, skeletal and OSA related parameters relapses after OS at long-term to cure OSA.

Our results showed that preoperative OSA severity is a noteworthy factor to success in the management of sleep disorders: patients with severe and moderate OSA present higher AHI reductions (93.3% and 69.7%, respectively) than the mild ones (19.9%) (Fig.5). Our results showed a mean final AHI of 4.8 ± 3.7 e/h (p=0.001) at one-year follow-up for the overall sample, and a mean final AHI of 4.1 ± 2.4 and 2.9 ± 0.2 e/h when focusing on moderate and severe cases, respectively. It is consistent with those values lately reported by the Stanford group (18) who reported a mean final AHI of 3.61±2.79 and 7.43±6.70 e/h (p=0.007) for the 1st and 2nd years of follow-up respectively, demonstrating the long-term clinical treatment effect of OS upon moderate-to-severe OSA patients (18).

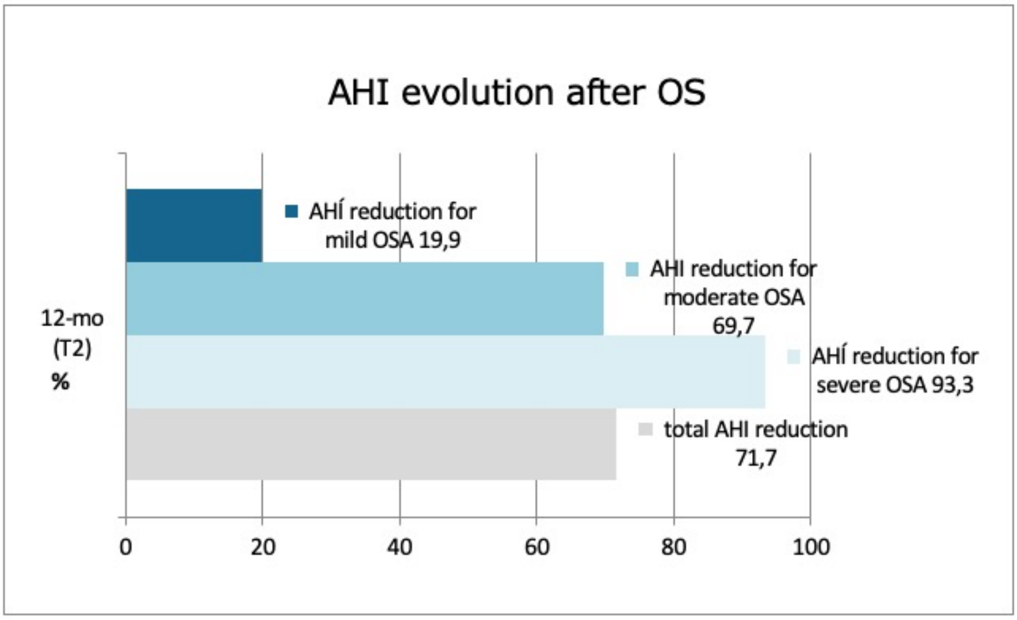

Figure 5. Long-term AHI reduction percentage regarding OSA severity

Specifically, 74% of our patients decreased their preoperative OSA severity level while the rest 26% remained stable at 12 months follow-up, and 100% no longer in need of CPAP. After OS, 60.9% of the sample cured their OSA (final mean AHI = 4.8 (2.4-8.0 e/h, p=0.001) and improved subjective OSA parameters (final mean ESS = 7 (5-10), p<0.001). Although all patients finally improved both objective and subjectively, a residual mild OSA was observed in 39.1% of the sample (Fig.1). Most of the patients (70%) with residual mild OSA after surgery, already presented an initial mild OSA. Therefore, OS shouldn't be recommended to merely treat a mild OSA, but the underlying DFD.

Last but not least, an ongoing clinical trial with a further enlargement of the sample (n=100) (ID NCT03796078 registration) will seek to be able to state firm conclusions regarding non-significant but promising results obtained in the present preliminary report.

CONCLUSIONS

In conclusion, the results of this pilot study demonstrate the positive effect of OS in the PAV, mCSA and AHI parameters at the short and long-term. However, preoperative OSA severity is a noteworthy factor in determining the long-term clinical success to cure OSA after OS. Therefore, OS should be used as the first line treatment armamentarium when planning to cure moderate-to-severe OSA in selected patients with a facial retrusive pattern.

REFERENCES

1. Haas Junior OL, Guijarro-Martínez R, de Sousa Gil AP, da Silva Meirelles L, Scolari N, Muñoz-Pereira ME, et al. Hierarchy of surgical stability in orthognathic surgery: overview of systematic reviews. Int J Oral Maxillofac Surg. 2019;
2. Giralt-Hernando M, Valls-Ontañón A, Guijarro-Martínez R, Masià-Gridilla J, Hernández-Alfaro F. Impact of surgical maxillomandibular advancement upon pharyngeal airway volume and the apnoea-hypopnoea index in the treatment of obstructive sleep apnoea: Systematic review and meta-analysis. BMJ Open Respir Res. 2019;6(1):1–13.
3. Castro-Silva L, Monnazzi MS, Spin-Neto R, Moraes M, Miranda S, Gabrielli MFR, et al. Cone-beam evaluation of pharyngeal airway space in class I, II, and III patients. Oral Surg Oral Med Oral Pathol Oral Radiol [Internet]. 2015;120(6):679–83. Available from: http://dx.doi.org/10.1016/j.oooo.2015.07.006
4. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: The challenge to effective treatment. Proc Am Thorac Soc. 2008;5(2):173–8.
5. Camacho M, Certal V, Capasso R. Comprehensive review of surgeries for obstructive sleep apnea syndrome. Braz J Otorhinolaryngol. 2013;79(6):780–8.
6. Dicus Brookes CC, Boyd SB. Controversies in Obstructive Sleep Apnea Surgery. Oral Maxillofac Surg Clin North Am [Internet]. 2017;29(4):503–13. Available from: https://doi.org/10.1016/j.coms.2017.07.005
7. Guilleminault C, Tilkian A, Dement WC. The Sleep Apnea Syndromes. Annu Rev Med [Internet]. 1976;27(1):465–84. Available from: http://www.annualreviews.org/doi/10.1146/annurev.me.27.020176.002341
8. Camacho M, Noller MW, Del Do M, Wei JM, Gouveia CJ, Zaghi S, et al. Long-term Results for Maxillomandibular Advancement to Treat Obstructive Sleep Apnea: A Meta-analysis. Otolaryngol Neck Surg [Internet]. 2019;019459981881515. Available from: http://www.ncbi.nlm.nih.gov/pubmed/30598047%0Ahttp://journals.sagepub.com/doi/10.1177/0194599818815158
9. Hernandez-Alfaro F, Guijarro-Martinez R, Mareque-Bueno J. Effect of mono- and bimaxillary advancement on pharyngeal airway volume: cone-beam computed tomography evaluation. J Oral Maxillofac Surg. 2011 Nov;69(11):e395-400.

10. Giralt-Hernando M, Valls-Ontañón A, Haas Junior OL, Masià-Gridilla J, Hernández-Alfaro F. What are the Surgical Movements in Orthognathic Surgery That Most Affect the Upper Airways? A Three-Dimensional Analysis. J Oral Maxillofac Surg. 2021;79(2):450–62.

11. Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, et al. Clinical Practice Guideline for the Treatment of Obstructive Sleep Apnea and Snoring with Oral Appliance Therapy: An Update for 2015. J Clin sleep Med JCSM Off Publ Am Acad Sleep Med. 2015 Jul;11(7):773–827.

12. Hernández-Alfaro F. Upper incisor to Soft Tissue Plane (UI-STP): A new reference for diagnosis and planning in dentofacial deformities. Med Oral Patol Oral Cir Bucal. 2010;15(5):8–10.

13. Hernandez-Alfaro F, Guijarro-Martinez R. “Twist technique” for pterygomaxillary dysjunction in minimally invasive Le Fort I osteotomy. J Oral Maxillofac Surg. 2013 Feb;71(2):389–92.

14. Hernández-Alfaro F, Giralt-Hernando M, Brabyn PJ, Haas OL, Valls-Ontañón A. Variation between natural head orientation and Frankfort horizontal plane in orthognathic surgery patients: 187 consecutive cases. Int J Oral Maxillofac Surg. 2021;(February):1–7.

15. American Academy of Sleep Medicine. Evaluation, Management and Long-Term Care of OSA in Adults Clinical Algorithm. Am Acad Sleep Med. 2015;(August):1–6.

16. Johns MW. A New Method for Measuring Daytime Sleepiness: The Epworth Sleepiness Scale. Sleep [Internet]. 1991;14(6):540–5. Available from: https://academic.oup.com/sleep/article-lookup/doi/10.1093/sleep/14.6.540

17. Wolford LM, Chemello PD, Hilliard F. Occlusal plane alteration in orthognathic surgery-part I: Effects on function and esthetics. Am J Orthod Dentofac Orthop. 1994;106(3):304–16.

18. Lin C, Chin W, Huang Y, Wang P, Li KK, Chen Y, et al. Objective and Subjective Long Term Outcome of Maxillomandibular Advancement in Obstructive Sleep Apnea. Sleep Med [Internet]. 2020; Available from: https://doi.org/10.1016/j.sleep.2020.05.024

19. Rubio-Bueno P, Landete P, Ardanza B, Vázquez L, Soriano JB, Wix R, et al. Maxillomandibular advancement as the initial treatment of obstructive sleep apnoea: Is the mandibular occlusal plane the key? Int J Oral Maxillofac Surg. 2017;46(11):1363–71.

20. Posnick JC, Adachie A, Singh N, Choi E. “Silent” Sleep Apnea in Dentofacial Deformities and Prevalence of Daytime Sleepiness After Orthognathic and Intranasal Surgery. J Oral Maxillofac Surg [Internet]. 2018;76(4):833–43. Available from: https://doi.org/10.1016/j.joms.2017.09.003

21. Araújo PM, Osterne RLV, de Souza Carvalho ACG, Azevedo NO, Gondim RF, Gonçalves Filho RT, et al. Pharyngeal airway space changes after maxillomandibular advancement: a five-year retrospective study. Int J Oral Maxillofac Surg. 2019;48(6):732–8.

04

GENERAL DISCUSSION

4.1 Rationale of the workflow of this PhD thesis

At the time this PhD thesis was set up, many authors had evaluated and assessed the UA on a 3D basis. However, to date no previous studies have examined the relationship and correlations between the impact of 3D skeletal movements of OS (mono-maxillary, mono-mandibular and bimaxillary surgeries) and the PAV- and PSG-related parameters (in terms of AHI), of patients suffering from mild, moderate and/or severe OSA at long term.

Globally, the aim of this whole investigation through a PhD project was to assess the 3D-clinical impact of OS, with regard to direction, magnitude and type of surgical movement, on the upper airway and the clinical improvement and/or cure of the OSA syndrome at long term. Thus, to verify the stability of OS surgical movements when maximizing the PAV and the minimum cross-sectional areas (mCSA), results were evaluated at three time points: pre-, immediate (1-month) and late postoperative (12-months follow-up) throughout the whole investigation. These three time points allowed the authors to be able to state firm conclusions on identifying both the surgical and volumetric gains and possible relapses (short-term) and the stability of OS (long-term).

Hence, to address the global and specific research purposes, the authors designed and implemented 5 different studies as follows though this rationale:

- A systematic review (SR) to study the current the state-of-the art regarding the impact of MMA on the PAV and the AHI in the surgical treatment and definitive cure of OSA. Our justification for this study was our perception that prior to perform the clinical work, a comprehensive review on the topic was essential to be able to design proper and adequate studies according to the missing gaps in the current literature. With this SR, the authors realized that there is a lack of homogenous and rigorous data regarding the assessment of the clinical and surgical data and methodological validation process (3D measurement assessment) though the current literature **(Paper I)**.

Assuming the scarce and lack of homogenic data on this topic:

- A retrospective cohort study was performed to demonstrate the relevance of the relationship between the head positioning through the natural head position (NHP) and the Frankfort Horizontal (FH) planes patients with different dentofacial deformities (DFD) (i.e. maxilla/mandibular retrognathia and/or prognathism) and malocclusions (i.e. class I,II or III), thus demonstrating which horizontal plane should be properly executed when planning for OS **(Paper II)**.

- As there is no rigorous data regarding the AHI reduction and volumetric, linear and cross-sectional parameters gain after OS, a retrospective longitudinal study of consecutive patients was designed and performed to study the effect of maxillary and mandibular movements (isolated or jointly) on the PAV (nasopharynx, oropharynx, and hypopharynx) and the mCSA on a 3D basis using cone-beam computed tomography (CBCT). In turn, a proposed surgical planning protocol to maximize the UA was designed and validated through this investigation **(Paper III)**.

- On the need of further studies to individualize a required magnitude and direction of surgery-induced movements to patients with DFD, a three case-series study was implemented to validate a protocol and algorithm for the surgical management of DFD in Down syndrome (DS) patients with OSA, when the main concerns are the narrowing of the UA, malocclusion, feeding and speech problems aside from aesthetics **(Paper IV)**.

- Finally, the results of a pilot study of an ongoing three arm prospective controlled clinical trial (CCT) (ClinicalTrials.gov ID NCT03796078 registration) are depicted in this PhD project to correlate the magnitude, type, and direction of these skeletal movements with the airway dimension gain or impairment at 12 months follow-up, to propose OS as the definitive and first line treatment armamentarium in selected patients to cure OSA (in terms of AHI and sleep patient-centered parameters) **(Paper V)**.

All this PhD project, coordinated by prof. Dr.Federico Hernández-Alfaro and Dr. Adaia Valls-Ontañón at the Universitat Internacional de Catalunya, started in January 2018 as a three-year program, and was granted by the competitive predoctoral fellowship ID: FI_B200134 by the AGAUR and the social European Fund.

4.2 Methodological remarks of the studies

The methodology followed by all the studies was in line and in agreement with those international guidelines to design and perform any type of clinical trials (i.e observational, cohort, case-series or CCT/RCT among others) and requires no further discussion. Then, methodology guidelines executed by our studies were as follows:

- SR: PRISMA (The Preferred Reported Items for Systematic Reviews and Meta-Analyses) guidelines [15]

- Retrospective cohort study: STROBE (Strengthening the Reporting of Observational studies in Epidemiology) guidelines [16].

- CCT: CONSORT (Consolidated Standards of Reporting Trials) guidelines[17].

Each type of methodology and data assessment is discussed in-depth in each paper **(Results section and/or Appendix I)**. However, in the following sections we would like to discuss on the linear, volumetric and cross-sectional 3D measurements assessment and superimposition protocols that followed our clinical investigations, in each **papers II,III,IV and V**.

4.3 Superimposition protocol validation and upper airway measurements

Regardless of the surgical procedures protocols for OS, either mono- or bimaxillary followed in our day-to-day basis and previously described elsewhere 18–21 , we felt the perception to further discuss the two methodological protocols executed and validated throughout this PhD investigation:

Superimposition protocol

Each patient received three CBCTs datasets (preoperative (T0), post-operative at 1 months (T1) and postoperatively at 12 months follow up (T2). These three time-point enabled us to be able to assess both the skeletal and volumetric relapses (T1) and the stability of OS at long-term (T2). The three datasets were superimposed in accordance to the voxel-based superimposition protocol 12. Data are primarily saved in DICOM (Digital Imaging and Communications in Medicine) format using a 3D software (Dolphin Imaging, version 11.0, Chatsworth, CA, USA). The software orientation calibration tool is then used along pitch (x), yaw (y) and roll (z). Orientation of both the ‘Base volume’ (original DICOM) and ‘2nd volume’ (duplicate DICOM) is undertaken to achieve the same original positions of the CBCTs (Fig.1).

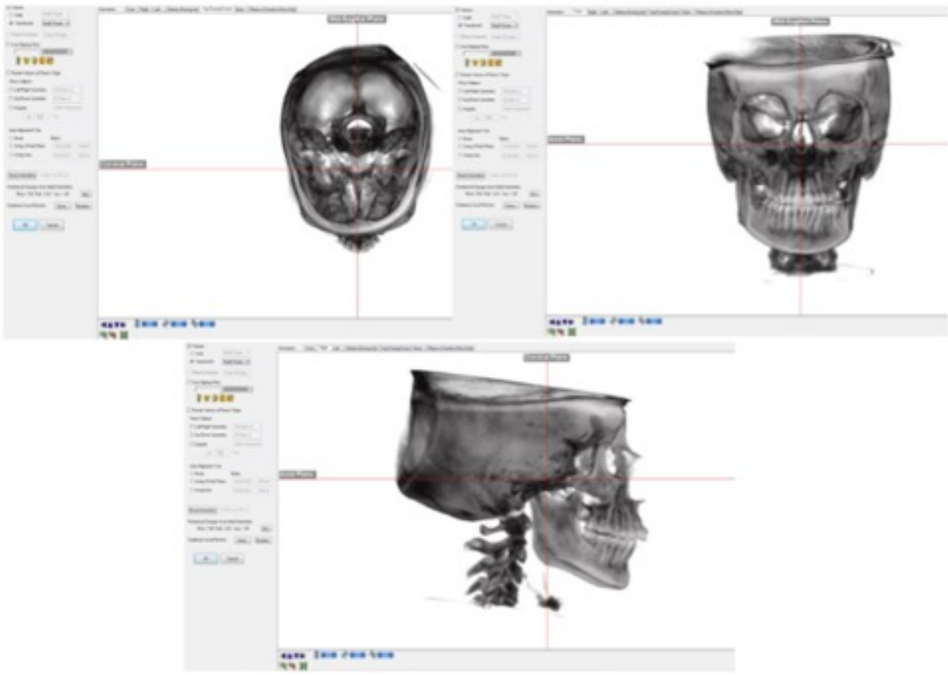

Figure 1. CBCT Head Orientation. All of the datasets are oriented according to the frontal plane (axial plane, mid-sagittal plane), right sagittal plane (coronal plane, axial plane) and coronal plane (coronal plane, mid-sagittal plane).

Then, superimposition of the preoperative CBCTs at T1 and T2 is executed using the cranial base. This reference (Cranial base) is chosen as an absolute reference as it remains stable after surgery [11,12]. Afterwards, the Dolphin software allows a proper manual adjustment following the superimposition three-step protocol (Fig.2):

1. Landmark based superimposition ('side-by-side superimposition)
2. Voxel-based superimposition ('overlay superimposition by volume sub-regions') and
3. Head orientation export ('Export to 2nd volume') 12. In other words, this means that all the three images (T0, T1, and T2) are in the same coordinate position after the voxel-based superimposition.

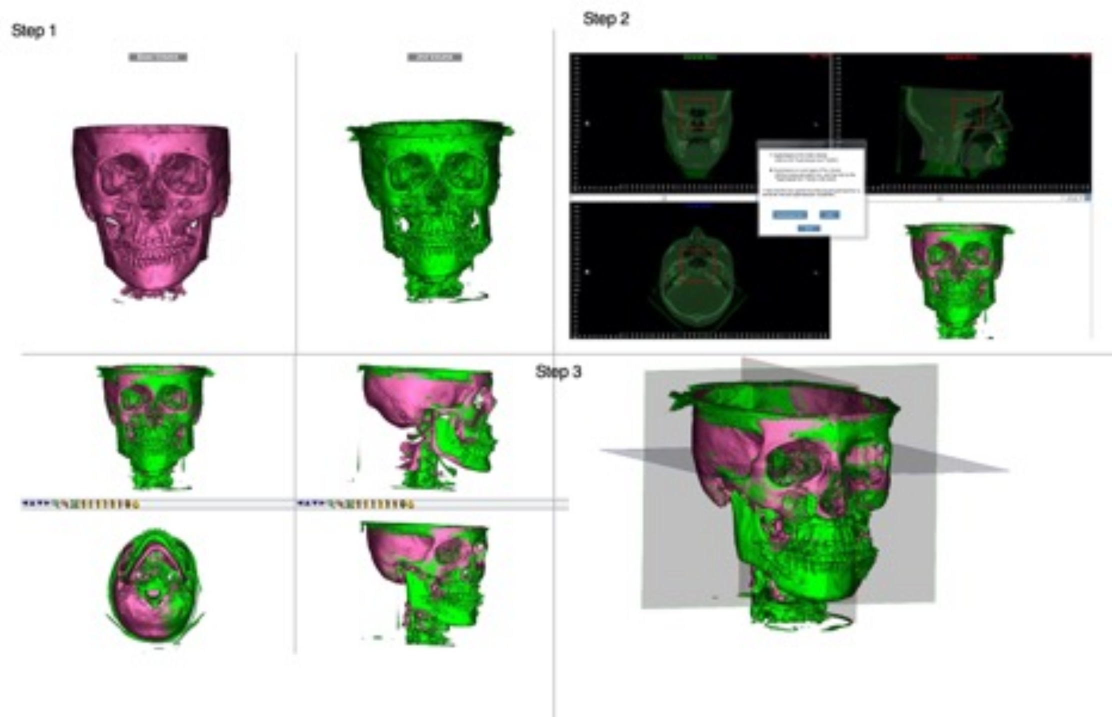

Figure 2. Voxel-based superimposition flowchart protocol (courtesy of Haas et al. 2019) 12. Step 1: Landmark superimposition ('side-by-side' superimposition of the software); step 2: Voxel superimposition ('overlay superimposition', 'volume subregion' of the software) and step 3: Head orientation ('Verify results' + 'Export orientation to 2nd volume').

This position is recommended for the baseline assessment of upper airway dimensions [22–24].

Three-dimensional linear measurements' assessment with Dolphin software

Skeletal surgical movements were evaluated in angular (º) and linear '3D line' measurements and landmarks (mm). Generally, the following measurements were assessed in each patient which enable us to depict any changes caused by OS:

- Linear and 3D landmarks: posterior nasal spine (PNS), Point A, Point B, Pogonion (Pg), most anterior point of the hyoid body (H), superior incisor (Sup I), inferior incisor (Inf I) and transversal maxilla in frontal view (Fig.3).

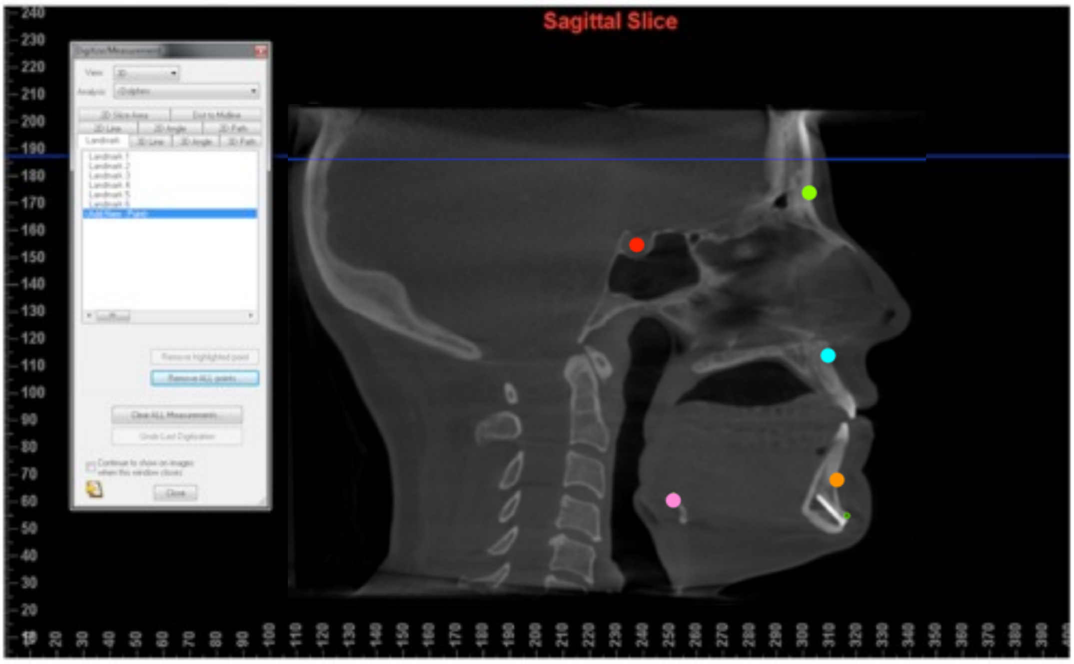

Figure 3. 3D landmarks used in Dolphin software. Color map as follows: Sella (red), Nasion (green), Point A (blue), Punto B (orange), Pogonion (dark green) and Hyoid (pink)

- The root mean square displacement of all the parameters in the reference space or system was calculated according to the following formulas:

$$\Delta\,(T1 - T0) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

$$\Delta\,(T1 - T2) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

$$\Delta\,(T2 - T0) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

- Angular: SNA, SNB, SNPg and mandibular occlusal plane (MOP) (Fig.4)

· SNA angle (Sella (S) – Nasion (Na) – Point A).
· SNB angle (S – Na – Point B).
· SNPg angle (S – Na – Pg).
· MOP angle (Lowe first molar – Inf I – Na)

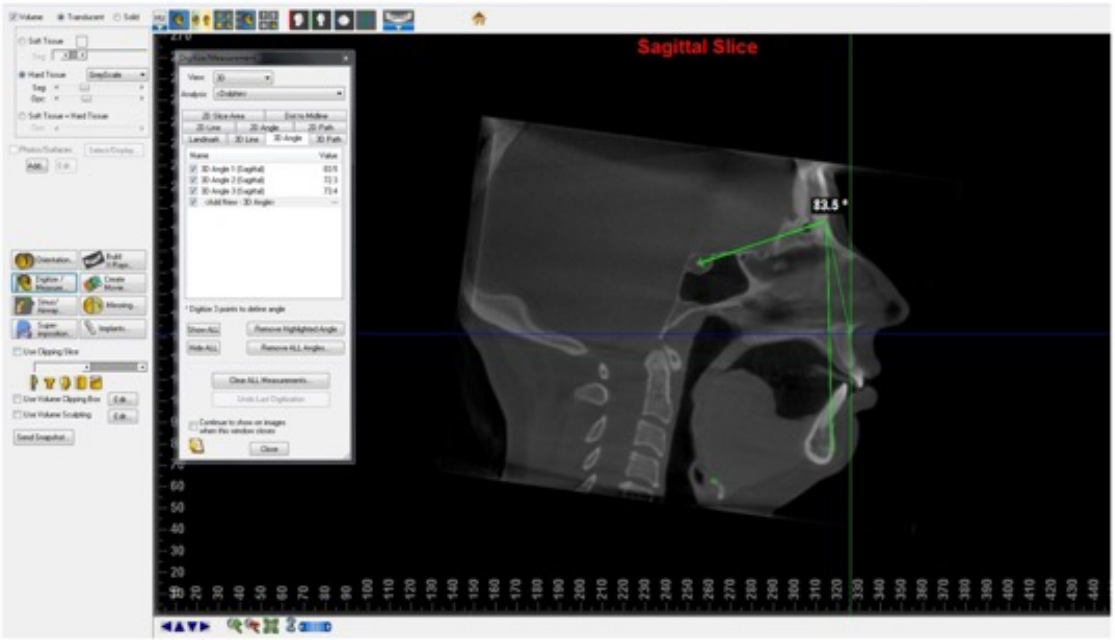

Figure 4. Angular measurement assessment in Dolphin software.

Upper airway analysis and boundaries

Manual segmentations of the pharyngeal airway anatomical limits and technical boundaries was performed as previously described by Swennen and Guijarro-Martínez [25]. For this purpose, three regions of interest are defined: naso -, oro - and hypopharynx. The nasopharynx was delimited by the Frankfort horizontal (FH) - posterior nasal spine (PNS) - sphenoid bone, extended to the soft tissue pharyngeal wall contour. The oropharynx was defined beyond the FH/PNS extended to FH – most anterior point of the body of C3 – soft tissue pharyngeal wall contour. Finally, the hypopharynx was assessed at FH/PNS parallel – most anterior point of the body of C3 – soft tissue pharyngeal wall contour to FH/PNS parallel – most anterior pole of the body of C4. An automatic threshold value of 60 was set manually to obtain the pharyngeal airway dimension (mm3) and the mCSA (mm2) (Fig.5).

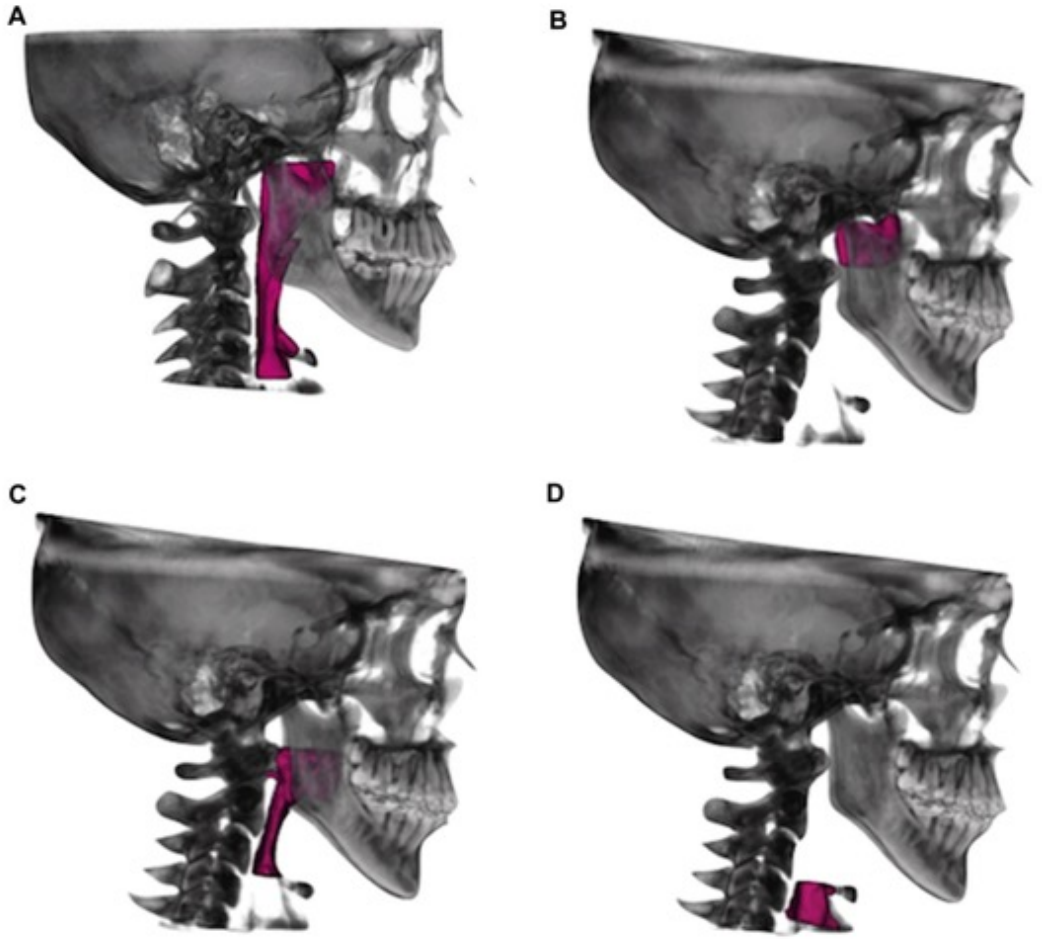

FIGURE 2. *A*, 3-dimensional total PAV assessment according to *Guijarro and Swenen, 2013* (16) PAV boundaries. *B*, 3-dimensional PAV boundaries—Delimitation of the nasopharynx PAV boundary (16). *C*, 3-dimensional PAV boundaries—Delimitation of the oropharynx PAV boundary (16). *D*, 3-dimensional PAV boundaries—Delimitation of the hypopharynx PAV boundary (16). Abbreviation: PAV, pharyngeal airway volume

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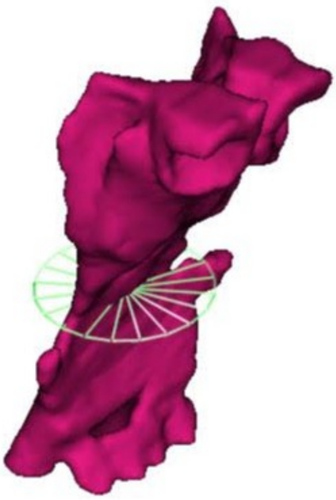

Figure 5. Three-dimensional graphical illustration of the minimal cross-sectional area (mCSA) of the pharyngeal airway (PA) (threshold value 60).

Emphasis was placed in following this UA boundaries, proposed by Swennen and Guijarro-Martínez [25] in order to avoid publication bias. However, these anatomical limits are not the only ones currently used by different authors at PAV assessment.

4.4 Key results of the investigation

Impact of OS on the PAV

In agreement with previous studies 26–33, the results of our SR led us to conclude that there is a lack of homogenous data with regard to AHI reduction and PAS/PAV gain after MMA in retrognathic patients (Paper I) 10. Nevertheless, some problems were detected in terms of AHI and UA assessment:

- Problems related to data acquisition:

  · Few articles included the methodological validation and assessment in their studies. Therefore, it is difficult for further clinicians to be able to reproduce these investigations.

  · There was a lack of homogeneity among the studies regarding the UA measurements (2D or 3D).

  · Due to the lack of homogeneity between outcome measurements assessment between studies, a subgroup analysis was made irrespective of the global sample (MMA + genioplasty (Gp) vs isolated MMA). Indeed, quantitative analysis (meta-regression analysis) was estimated at the time of assessment to avoid publication bias.

  · Some of the studies did not directly provide mean /median values, standard deviations (SD) nor interquartile ranges (IQR) – such data being calculated directly from the tables reporting individual patient values.

  · Regarding the PSG parameters, most of the studies used the AHI index as recommended 34. However, irrespective of AHI, some studies used the Respiratory Disturbance Index (RDI).

  · No firm conclusions on the impact of MMA on surgical cure rate (CR) can be stated since only two studies reported them 26,32.

- Problems related to publication bias:

  · There was a major limitation to thus study that none of the included studies were RCT. Only two were prospective 32,35 and the remainders 26–31 were of retrospective nature and, therefore, subjected to the usual biases and limitations of retrospective and observational studies.

  · However, with respect to depict publication bias and to address this aforementioned problems, funnel plots and Eager tests were used (Egger test p = 0.547 for isolated MMA and p = 0.297 for MMA + Gp). Nevertheless, homogeneity between studies was found when assessing PAV (I2 = 0%, Q = 0.64, p = 0.422).

However, this SR led us to confirm that MMA increases the UA and decreases AHI in the context of OSA, but additional multidisciplinary studies assessing aspects other than UA and AHI were needed to determine which types of maxillary, mandibular and chin movements (e.g., advancement, rotation, impaction, descent) are best for enlarging the UA in its specific compromised levels, and for finally reducing AHI, as well as patient characterization in terms of OSA severity, comorbidities and facial profile, among other factors **(Paper I)** [10].

Three-dimensional surgical planning and orientation protocol

On the purpose to depict which 'real' Horizontal plane is to be used when 3D planning for orthognathic surgery, this retrospective cohort study on consecutive patients led us to suggest that NHP-Horizontal plane should be used as an absolute reference when planning for OS (Paper II) 13. Indeed, presurgical 3D planning protocol was performed according to the in-house protocol of Hernandez-Alfaro 2010 36 – within the upper incisor soft-tissue nasion plane (UI-STP) was used an absolute reference to guide the anteroposterior positioning of the maxillomandibular complex (Fig.6) 36.

Hence, these two absolute references are recommended when planning for orthognathic surgery:

- UI-STP-Vertical plane

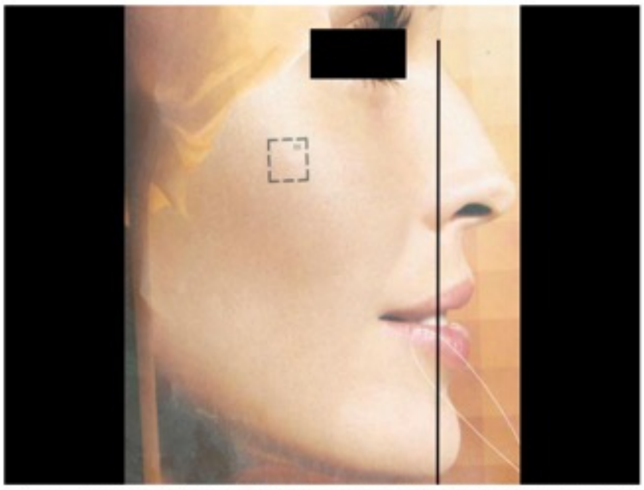

Fig. 1. A vertical line or Soft Tissue Plane (STP) is drawn passing through the soft tissue nasion (N'), and descending perpendicular to the base of the photograph. The sagital (Antero-posterior) relation with the anterior limit of the upper incisor is evaluated.

Figure 6. Courtesy of Dr.Hernández-Alfaro F, et al. 2010 [36]

- NHP-Horizontal plane

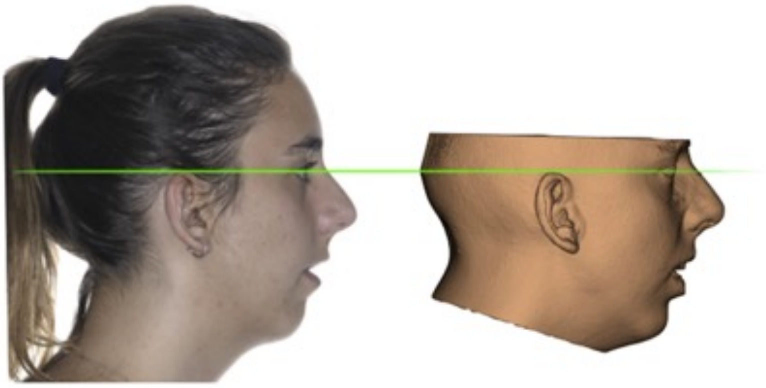

Fig. 1. Extracranial true horizontal line used by the clinicians to orient the cone-beam computed tomography. A true horizontal line was traced on the photograph (lateral view), passing through two points: the lateral canthus of the eye and at a determined point of the helix (auricular point, which varied depending on each patient).

Hernández-Alfaro F, et al. Variation between natural head orientation and Frankfort horizontal planes in orthognathic surgery patients: 187 consecutive cases, Int J Oral Maxillofac Surg (2021)[13]

The methodology followed in his study was validated by two authors (MGH and AVO):

- Examiner calibration: To ensure truly accurate and reproducible measurements, the examiners tagged all virtual models independently on two separate occasions (two weeks apart), thus avoiding inter and intra-observer differences, respectively.

  · Inter and Intra-class correlation analyses (ICC) were used to calculate examiner differences and reliability [37,38].

  · ICC between angles < 0.11º [13].

- FH-NHOº angle was measured before the intervention (T0), at 1-month (T1) and 12-months follow-up (T2). Its relationship was considered positive if the FH was located superior to the NHO plane and negative if FH was inferior to it, as follows [13]:

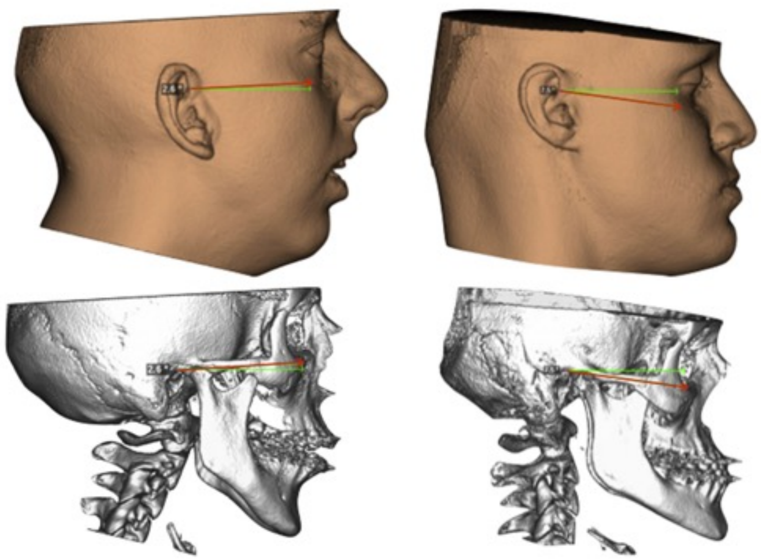

Fig. 2. Assessment of natural head orientation (NHO) and Frankfort horizontal (FH) in class II and class III patients. In these cases, NHO with respect to FH (highlighted in red) were set at 2.6° (negative) and 7.5° (positive) in class II and class III patients, respectively.

Hernández-Alfaro F, et al. Variation between natural head orientation and Frankfort horizontal planes in orthognathic surgery patients: 187 consecutive cases, Int J Oral Maxillofac Surg (2021)[13]

In this study, the majority of the selected patients underwent bimaxillary (80%) or monomaxillary (20%) surgery, of whom 55.9% and 43% received a CCW and clockwise rotation of the maxillomandibular complex, respectively.

Prior to surgery:

- FH-NHO° was significantly positive for the population eligible for orthognathic surgery ($p < 0.001$, t-test) showing significant differences between class II and class III patients ($p < 0.001$, test F) [13].

Post-operatively:

- A greater impact of surgery was evidenced in class II compared to class III patients, reporting FH-NHO° changes between T0 and T2 as follows: 2.04° ± 4.79 ($p < 0.001$) and -1.20° ± 3.03 ($p < 0.001$), respectively. Indeed, the variation between this angle significantly increases ($p = 0.006$) in patients receiving a CCW rotation of the mandible [13].

To our knowledge, this was the first study to evaluate the impact of CCW rotation in FH-NHO° after orthognathic surgery, which led us to conclude that occlusal plane changes have an impact on the cranio-cervical posture, and these differences increased after surgery [39]. Thus, extracranial references such as NHO allow the use of the true vertical and horizontal lines as optimal reference planes for surgical planning **(Paper II)** [40,41].

Validation of the surgical protocol to optimize the upper airway

Despite the obstacles that our SR detected on data acquisition at the time of PAV and mCSA assessment between studies, we were obligated to justify and to correlate the airway dimension changes depending on the type, direction and magnitude of each skeletal movement – isolated or jointly (i.e. advancement (adv), setback, CCW or CW rotation, maxillary segmentation, etc among others) on a 3D basis **(Paper III)** [14].

The evaluation of patients who underwent monomaxillary (MaxS n=25, monomandibular (MandS n=25) or bimaxillary surgery (BimaxS n=53) showed an <u>immediate positive effect of OS on the upper airway followed by a slight downward trend (stabilization of soft tissues) at 12-months follow-up, regardless of the surgical approach</u> [14].

On average, a linear mean maxillary advancement of 6.41 ± 7.72 mm, mandibular advancement of 9.92 ± 8.05 mm and a global chin advancement of 10.22 ± 10.27 mm (isolated chin 3.85 ± 2.06) were performed, with a subsequent total PAV and mCSA gains were 41.9%, (95% CI: 33.6 – 50.2%; $p < .001$) and 104% (95% CI: 87.1-122.1%; $p<.001$), respectively at 12 months follow-up. In other words - both maxillary and mandibular movements impact on the three levels of the PAV, although maxillary forward movements further widen the oro- > naso- > hypopharynx, while mandibular forward movements further widen the hypo- > oro- > nasopharynx, in these orders. However, skeletal and volumetric relapses at short term (10%) were insufficient to offset the total PAV gain and stability at long term [14]. Our results are in line with those previously reported by other studies, were OS induces positive changes in both the PAV and the mCSA [42].

Correlations between some skeletal movements which favored volume gain (either total or subregional) were significant for the three groups:

- BimaxS: CCW rotation, downward displacement of the PNS, mandibular adv, maxillary adv.

- MaxS: maxillary adv, max segmentation, centering of the maxilla and downward displacement of the PNS.

- MandS: mandibular adv, CCW of the mandible, chin adv.

Proposed surgical protocol for maximizing the upper airway

Once these correlations were found in the study, we felt the obligation to propose a surgical protocol when the main concern of the patient is the obstruction of the upper airway. Then, a proposed surgical planning protocol to maximize the UA was designed and validated through this investigation **(graphically depicted in Figure 4 Paper III)** [14]. Hence, in this hierarchical order:

- Favorable surgical movements for UA increase: CCW of the mandible, mandibular adv, maxillary adv.

- Further increase of the UA (bonus): downward maxillary displacement of the PNS, advancement genioplasty.

· This means that the descent of the posterior part of the maxilla (PNS) together with a CCW rotation enlarges the pharynx, because the muscles of the soft palate are pulled to an anterior and downward position, which favors the upper airway space [14]. At the same time, centering of the maxilla favored naso- and oropharynx PAV gain. This is explained because maxillary asymmetry may trigger some muscular constriction on one side of the upper airway. Then, to our knowledge, this study is the first to describe a potential relationship between maxillary asymmetries and constriction of the UA [14].

- Non-favorable surgical movements for UA increase: total maxillary downward movement and setback procedures.

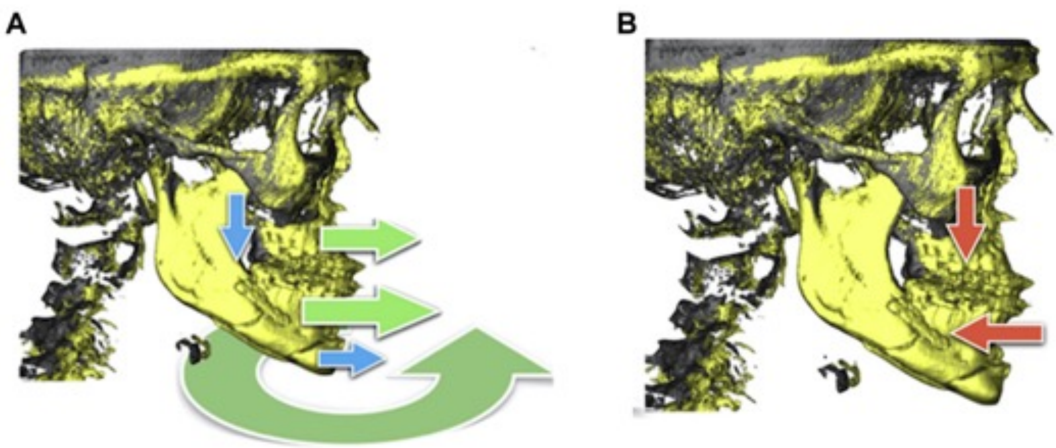

FIGURE 4. *A*, Surgical planning protocol for maximizing the upper airway. Hierarchical graphic representation of the increase/decrease in upper airway as per surgical movements in orthognathic surgery. Illustration of the favoring surgical movements to increase upper airway (CCW rotation, mandibular and maxillary advancements [*green arrows*]); movements to further increase PAV for chin advancements and posterior maxillary displacement of the PNS (*blue arrows*). *B*, Nonfavorable surgical movements (total maxillary downward and setback mandibular movements) which jeopardize the upper airway (*red arrows*). Abbreviations: CCW, counterclockwise; PAV, pharyngeal airway volume.

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OS as the first line treatment to cure OSA in selected patients

Once we know which were the skeletal movements that most increased both the airway volume and the cross-sectional areas of the UA, a prospective three-arm CTT was designed and implemented with the aim to correlate the abovementioned parameters with the improvement of OSA in patients with DFD. This study was registered at clinicalTrials.gov ID NCT03796078 **(Paper V)**.

The fundamental results of **paper V** were that all of our patients (n=25) with DFD reported both subjective and objective improvements of OSA after OS which remained stable at 12-months follow up, with a cure and success rates oof **61%** and **100%**, respectively.

Preoperatively:

- 60.9% of the patients were diagnosed with mild and 39.1% with moderate-to-severe OSA (21.7% and 17.4%, respectively).

Postoperatively:

- After OS, a total AHI reduction of 14.3 ± 2.1 e/h (71.7%, $p < 0.001$) was observed after orthognathic surgery, followed by a mean relapse of 0.4 ± 1.6 e/h (7.4%, $p = 1.000$) at 12 months follow-up **(Figure 1 paper V)**.

  · Then, most of the patients (74%, $p < 0.001$) improved their severity level and remained stable after one year (61%, $p < 0.001$) **(Figure 1 paper V)**.

  · However, a residual mild OSA was observed in 39.1% of the sample **(Figure 1 paper V)**. This is due to the preoperative OSA severity of the sample of this study (majorly mild), where OS did not induce major changes in mild OSA patients.

  · Severe and moderate OSA patients showed higher AHI reductions (93.3% and 69.7%, respectively) than the mild ones (19.9%).

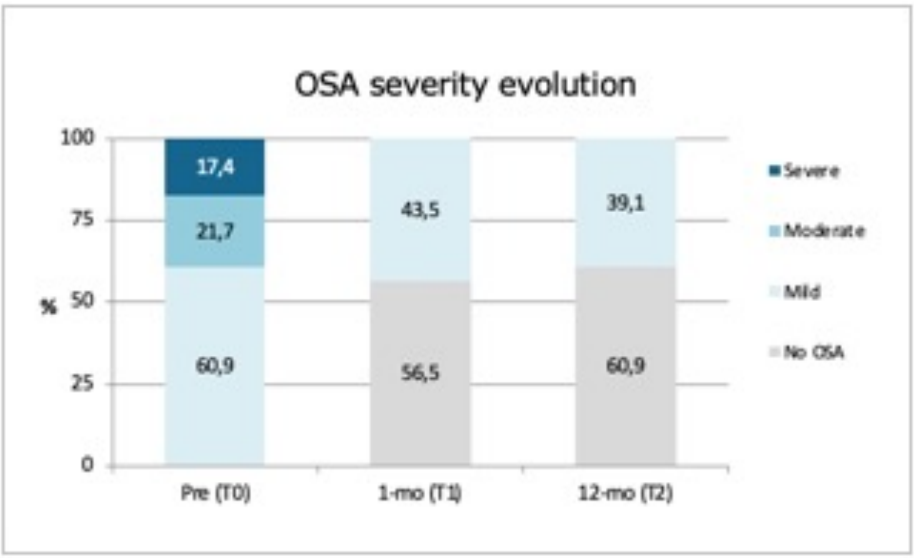

Figure 2 (paper V). Upper airway evolution after OS over follow-up: at 1 and 12-months follow-up.

- A mean volumetric relapse of 9.4% at 12 months follow-up, were as expected and in agreement with those reported in other trials [14]. This mainly occurs for the pharyngeal wall accommodation and soft tissue stability after MMA at long term [43]. However, further follow-up and increasing if the sample is needed to clarify the related risk factor that contribute to these relapses after OS.

Despite the positive immediate effect of OS in PAV, mCSA and sleep-parameters, no significant correlations could be detected between the type of surgery, and the changes in AHI and ESS score. However, it is essential to highlight that this sis a pilot study, and therefore, subjected to its natural limitations that are to be addressed on the ongoing CCT. However, all of these preliminary findings are in line with those in the latest investigations of the Stanford group [44] which demonstrates the long-term stability of OS to improve OSA [44].

Taking all these parameters into account, this pilot study led us to conclude that AHI reduction, preoperative OSA severity and underlying DFD play a major role to cure OSA. Then, the results of this study demonstrates that OS is a safe, predictable and definitive tool when planning to cure moderate-to-severe OSA. However, a further enlargement of the sample (n=100) will seek to be able to state firm conclusions in this point.

Dentofacial deformities and OSA

OSA usually arises in patients presenting hypoplasia of the mandible (class II patients (in our sample, 65.2%)), but also of the maxillary bone (class III patients (in our sample, 26.1%)), or both of them (class I patients (in our sample, 8.7%)) **(Paper V)**. <u>Therefore, when evaluating the relationship between OSA and DFDs, we should be aware of the skeletal facial pattern (retrusive vs protrusive) besides the dental class.</u> As Castro-Silva et al. [45], who described class I and III as having statistically bigger volumetric areas than class II patients ($p<0.05$ and $p<0.001$, respectively) state that retrognathic patients are more prone to suffer from OSA [45]. In this line, other authors have also speculated that patients with DFD are at a higher risk to develop OSA and, specifically, patients with a greater mandibular jaw deficiency and short face would be the most vulnerable ($p<0.001$)[46].

A diagnostic-therapeutic algorithm to treat patients with severe DFD (Down Syndrome patients) suffering from OSA

In addition to the previous ongoing CCT (total sample n= 100), the authors described a protocol for the surgical management of DFD in Down syndrome (DS) patients **(Paper IV)** [47].

The fundamental findings of this study were as follows:

- An average PAV gain of 10,954.33 mm3 (50%) was recorded immediately after surgery.

- Non-relevant skeletal and airway relapses were noted.

- Stable occlusion was achieved in all cases after postoperative orthodontic treatment. This means that all patients had a proper chewing function, and their parents referred decreased snoring levels.

- Orthodontics and OS constitute the management of choice for the occlusion disorders and associated feeding, respiratory and related problems of DS patients.

However, there are some key elements to take into account for the clinicians while treating with DS patients with specific dysmorphic orofacial features:

1. Anesthesia procedure - Difficult airway in intubation. This is explained because of a small airway due to maxillary hypoplasia, tonsillar hypertrophy, short neck and macroglossia, among others…

2. Behavioral and communicating problems - This means to establish a good and trusting professional-patient relationship. In this regard it is useful to explain the planned procedures in-depth and to indicate the expected results and eventual complications to the patient and his/her relatives. Keeping close contact through telephone support and more frequent follow-up visits may also be useful.

In agreement with the previous studies [10,13,14,47], all these outcomes point to OS as the first line treatment option, considering the characteristic orofacial dysmorphic features of individuals with DS which contribute to airway narrowing, such as retrusion or shortening of the mandible and maxillary hypoplasia [47].

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CONCLUSIONS

The conclusion of this PhD investigation are the following:

1. According to the current literature, there is a lack of homogenous data with regard to AHI reduction and PAS/PAV gain after MMA in retrognathic patients - However, MMA increases the upper airway volume and decreases AHI in the context of OSA, but additional multidisciplinary studies assessing aspects other than UA and AHI are needed to determine which types of maxillary, mandibular and chin movements (i.e. advancement, rotation, impaction, descent) are best for enlarging the UA **(Paper I)**.

2. With regard to the horizontal planes that should be used at the time of virtual surgical planning in orthognathic patients, NHO should be used as the real horizontal plane when planning for OS, given that pre- and postoperative NHO differs from FH in orthognathic patients **(Paper II)**.

3. There is a favorable effect of OS on the upper airway regardless of the surgical approach, being bimaxillary advancement and MOP changes by CCW rotation the most significant contributors **(Paper III)**.

4. Conversely, total maxillary downward displacement without rotation and mandibular setback movements penalized PAV gain at long term. However, a 10% skeletal and volumetric relapse should be expected at 12 months-follow-up **(Paper III)**.

5. In selected patients with DS presenting specific orofacial dysmorphic features, orthodontics and OS are the first management options of choice to address both occlusion and OSA. Then, the implementation of the proposed protocol together with improved medical measures, minimally invasive surgery and cutting-edge technologies allows OS to be safely performed in patients with DS **(Paper IV)**.

6. Both the underlying type of DFD and the preoperative OSA severity are noteworthy factors in determining the long-term clinical success to cure OSA after OS, irrespective of the positive effect of OS in the PAV, mCSA and AHI parameters. Therefore, OS should be used safely as the first line treatment armamentarium when planning to cure moderate-to-severe OSA in selected patients with a facial retrusive profile **(Paper V)**.

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REFERENCES

REFERENCES

1. Guilleminault C, Tilkian A, Dement WC: The Sleep Apnea Syndromes. Annu Rev Med 27: 465, 1976.
2. American Academy of Sleep Medicine: Evaluation, Management and Long-Term Care of OSA in Adults Clinical Algorithm. Am Acad Sleep Med: 1, 2015.
3. Johns MW: A new perspective on sleepiness : The Epworth Sleepiness Scale. Japanese Soc Sleep Res 8: 170, 2010.
4. Lloberes P, Durán-Cantolla J, Martínez-García MÁ, Marín JM, Ferrer A, Corral J, Masa JF, Parra O, Alonso-Álvarez ML, Terán-Santos J: Diagnosis and treatment of sleep apnea-hypopnea syndrome. Spanish Society of Pulmonology and Thoracic Surgery. Arch Bronconeumol 47: 143, 2011.
5. Durán J, Esnaola S, Rubio R, Iztueta A: Obstructive sleep apnoea-hypopnoea and related clinical features in a population-based sample of subjects aged 30 to 70 years. Am J Respir Crit Care Med 163: 685, 2001.
6. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S: The occurrence of sleep disorder breathing among middle aged adults. N Engl J Med 328: 1230, 1993.
7. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R: Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea : An American Academy of Sleep Medicine Clinical Practice Guideline. 13: 479, 2017.
8. Camacho M, Certal V, Capasso R: Comprehensive review of surgeries for obstructive sleep apnea syndrome. Braz J Otorhinolaryngol 79: 780, 2013.
9. Wolford LM, Chemello PD, Hilliard F: Occlusal plane alteration in orthognathic surgery-part I: Effects on function and esthetics. Am J Orthod Dentofac Orthop 106: 304, 1994.
10. Giralt-Hernando M, Valls-Ontañón A, Guijarro-Martínez R, Masià-Gridilla J, Hernández-Alfaro F: Impact of surgical maxillomandibular advancement upon pharyngeal airway volume and the apnoea-hypopnoea index in the treatment of obstructive sleep apnoea: Systematic review and meta-analysis. BMJ Open Respir Res 6: 1, 2019.
11. Haas Junior OL, Guijarro-Martínez R, Sousa Gil AP de, Silva Meirelles L da, Scolari N, Muñoz-Pereira ME, Hernández-Alfaro F, Oliveira RB de: Hierarchy of surgical stability in orthognathic surgery: overview of systematic reviews. Int J Oral Maxillofac Surg, 2019.
12. Haas Junior OL, Guijarro-Martínez R, Sousa Gil AP de, Méndez-Manjón I, Valls-Otañón A, Oliveira RB de, Hernández-Alfaro F: Cranial Base Superimposition of Cone-Beam Computed Tomography Images. J Craniofac Surg 00: 1, 2019.
13. Hernández-Alfaro F, Giralt-Hernando M, Brabyn PJ, Haas OL, Valls-Ontañón A: Variation between natural head orientation and Frankfort horizontal plane in orthognathic surgery patients: 187 consecutive cases. Int J Oral Maxillofac Surg: 1, 2021.
14. Giralt-Hernando M, Valls-Ontañón A, Haas Junior OL, Masià-Gridilla J, Hernández-Alfaro F: What are the Surgical Movements in Orthognathic Surgery That Most Affect the Upper Airways? A Three-Dimensional Analysis. J Oral Maxillofac Surg 79: 450, 2021.

15. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, Clarke M, Devereaux PJ, Kleijnen J, Moher D: The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 339, 2009.

16. Elm E von, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP: The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg 12: 1495, 2014.

17. Schulz KF, Altman DG, Moher D: CONSORT 2010 statement: Updated guidelines for reporting parallel group randomised trials. PLoS Med 7: 1, 2010.

18. Hernandez-Alfaro F, Guijarro-Martinez R, Mareque-Bueno J: Effect of mono- and bimaxillary advancement on pharyngeal airway volume: cone-beam computed tomography evaluation. J Oral Maxillofac Surg 69: e395, 2011.

19. Hernandez-Alfaro F, Guijarro-Martinez R, Peiro-Guijarro MA: Surgery first in orthognathic surgery: what have we learned? A comprehensive workflow based on 45 consecutive cases. J Oral Maxillofac Surg 72: 376, 2014.

20. Hernández-alfaro F, Guijarro-martínez R: " Twist Technique " for Pterygomaxillary Dysjunction in Minimally Invasive. YJOMS 71: 389, 2013.

21. Peiro-Guijarro MA, Guijarro-Martinez R, Hernandez-Alfaro F: Surgery first in orthognathic surgery: A systematic review of the literature. Am J Orthod Dentofacial Orthop 149: 448, 2016.

22. Solow B, Sandham A: Cranio-cervical posture: A factor in the development and function of the dentofacial structures. Eur J Orthod 24: 447, 2002.

23. Lin X, Edwards SP: Changes in natural head position in response to mandibular advancement. Br J Oral Maxillofac Surg 55: 471, 2017.

24. Santos RMG dos, Martino JM De, Haiter Neto F, Passeri LA: Influence of different setups of the Frankfort horizontal plane on 3-dimensional cephalometric measurements. Am J Orthod Dentofac Orthop 152: 242, 2017.

25. Guijarro-Martínez R, Swennen GRJ: Three-dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: A validation study. Int J Oral Maxillofac Surg 42: 1140, 2013.

26. Fairburn SC, Waite PD, Vilos G, Harding SM, Bernreuter W, Cure J, Cherala S: Three-Dimensional Changes in Upper Airways of Patients With Obstructive Sleep Apnea Following Maxillomandibular Advancement. J Oral Maxillofac Surg 65: 6, 2007.

27. Jones R, Badlani J, Jones C: Maxillary , mandibular and chin advancement surgery for the treatment of obstructive sleep apnoea. 55: 314, 2010.

28. Ronchi P, Cinquini V, Ambrosoli A, Caprioglio A: Maxillomandibular advancement in obstructive sleep apnea syndrome patients: a restrospective study on the sagittal cephalometric variables. J oral Maxillofac Res 4: e5, 2013.

29. Bianchi A, Betti E, Tarsitano A, Morselli-Labate AM, Lancellotti L, Marchetti C: Volumetric three-dimensional computed tomographic evaluation of the upper airway in patients with obstructive sleep apnoea syndrome treated by maxillomandibular advancement. Br J Oral Maxillofac Surg 52: 831, 2014.

30. Schendel SA, Broujerdi JA, Jacobson RL: Three-dimensional upper-airway changes with maxillomandibular advancement for obstructive sleep apnea treatment. Am J Orthod Dentofacial Orthop 146: 385, 2014.

31. Hsieh YJ, Liao YF: Effects of maxillomandibular advancement on the upper airway and surrounding structures in patients with obstructive sleep apnoea: A systematic review. Br J Oral Maxillofac Surg, 2013.

32. Veys B, Pottel L, Mollemans W, Abeloos J, Swennen G, Neyt N: Three-dimensional volumetric changes in the upper airway after maxillomandibular advancement in obstructive sleep apnoea patients and the impact on quality of life. Int J Oral Maxillofac Surg 46: 1525, 2017.

33. Ruiter MHT de, Apperloo RC, Milstein DMJ, Lange J de: Assessment of obstructive sleep apnoea treatment success or failure after maxillomandibular advancement. Int J Oral Maxillofac Surg 46: 1357, 2017.

34. Epstein LJ, Kristo D, Strollo PJ, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD, Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine: Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 5: 263, 2009.

35. Heidsieck DSP, Ruiter MHT de, Lange J de: Management of obstructive sleep apnea in edentulous patients: an overview of the literature. Sleep Breath 20: 395, 2016.

36. Hernández-Alfaro F: Upper incisor to Soft Tissue Plane (UI-STP): A new reference for diagnosis and planning in dentofacial deformities. Med Oral Patol Oral Cir Bucal 15: 8, 2010.

37. Lagravère MO, Low C, Flores-Mir C, Chung R, Carey JP, Heo G, Major PW: Intraexaminer and interexaminer reliabilities of landmark identification on digitized lateral cephalograms and formatted 3-dimensional cone-beam computerized tomography images. Am J Orthod Dentofac Orthop 137: 598, 2010.

38. Zhu S, Keeling A, Hsung TC, Yang Y, Khambay B: The difference between registered natural head position and estimated natural head position in three dimensions. Int J Oral Maxillofac Surg 47: 276, 2018.

39. Savjani D, Wertheim D, Edler R: Change in cranio-cervical angulation following orthognathic surgery. Eur J Orthod 27: 268, 2005.

40. Zebeib AM, Naini FB: Variability of the inclination of anatomic horizontal reference planes of the craniofacial complex in relation to the true horizontal line in orthognathic patients. Am J Orthod Dentofac Orthop 146: 740, 2014.

41. Meiyappan N, Tamizharasi S, Senthilkumar KP, Janardhanan K: Natural head position: An overview. J Pharm Bioallied Sci 2: 424, 2016.

42. Christovam IO, Lisboa CO, Ferreira DMTP, Cury-Saramago AA, Mattos CT: Upper airway dimensions in patients undergoing orthognathic surgery: a systematic review and meta-analysis. Int J Oral Maxillofac Surg 45: 460, 2016.

43. Araújo PM, Osterne RLV, Souza Carvalho ACG de, Azevedo NO, Gondim RF, Gonçalves Filho RT, Sant'Ana E, Nogueira RLM: Pharyngeal airway space changes after maxillomandibular advancement: a five-year retrospective study. Int J Oral Maxillofac Surg 48: 732, 2019.

44. Lin C, Chin W, Huang Y, Wang P, Li KK, Chen Y, Guilleminault C: Objective and Subjective Long Term Outcome of Maxillomandibular Advancement in Obstructive Sleep Apnea. Sleep Med, 2020.

45. Castro-Silva L, Monnazzi MS, Spin-Neto R, Moraes M, Miranda S, Gabrielli MFR, Pereira-Filho VA: Cone-beam evaluation of pharyngeal airway space in class I, II, and III patients. Oral Surg Oral Med Oral Pathol Oral Radiol 120: 679, 2015.

46. Posnick JC, Adachie A, Singh N, Choi E: "Silent" Sleep Apnea in Dentofacial Deformities and Prevalence of Daytime Sleepiness After Orthognathic and Intranasal Surgery. J Oral Maxillofac Surg 76: 833, 2018.

47. Hernandez-Alfaro F, Montes-Fernandez-Micheltorena P, Molins-Ballabriga G, Giralt-Hernando M, Mayoral-Tias A, Valls-Ontañón A: Airway Volume Changes after Orthognathic Surgery in Patients with Down Syndrome : A Diagnostic-Therapeutic Algorithm. J Otolaryng Head Neck Surg 7, 2021.

07

APPENDIX I

BMJ Open Respiratory Research

Impact of surgical maxillomandibular advancement upon pharyngeal airway volume and the apnoea–hypopnoea index in the treatment of obstructive sleep apnoea: systematic review and meta-analysis

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ABSTRACT

Background A systematic review was carried out on the effect of surgical maxillomandibular advancement (MMA) on pharyngeal airway (PA) dimensions and the apnoea–hypopnoea index (AHI) in the treatment of obstructive sleep apnoea (OSA), with the aim of determining whether increased PA in the context of MMA is the main factor conditioning the subsequent decrease in AHI.

Methods A search was made of the PubMed, Embase, Google Scholar and Cochrane databases. A total of 496 studies were identified. The inclusion criteria were a diagnosis of moderate to severe OSA, MMA success evaluated by polysomnography, reporting of the magnitude of MMA achieved, PA increase and a minimum follow-up of 6 months.

Results Following application of the eligibility criteria, eight articles were included. Metaregression analysis showed MMA to significantly increase both pharyngeal airway volume (PAV) (mean 7.35 cm^3 (range 5.35–9.34)) and pharyngeal airway space (mean 4.75 mm (range 3.15–6.35)) and ensure a final AHI score below the threshold of 20 (mean 12.9 events/hour).

Conclusions Although subgroup analysis showed MMA to be effective in treating OSA, more randomised trials are needed to individualise the required magnitude and direction of surgical movements in each patient, and to standardise the measurements of linear and nonlinear PAV parameters.

STUDY IMPACT

Continuous positive airway pressure (CPAP) is acknowledged to be the gold standard treatment for obstructive sleep apnoea (OSA), though the adherence (defined as >4 hours of night use of CPAP for 70% of nights) failure rate reportedly reaches 46%–83% over the long term. Different surgical procedures have therefore been proposed, of which maxillomandibular advancement (MMA) has been shown to be the most effective option for treating OSA in selected patients, with an 86% success rate (defined as a final apnoea–hypopnoea index value of <20 events/hour and a reduction of 50% postoperatively). However, to our knowledge, no studies have examined the relationship between the impact of MMA surgery and the pharyngeal airway volume-related and polysomnography-related parameters of patients with moderate to severe OSA.

INTRODUCTION

Obstructive sleep apnea (OSA) is defined as a sleep-related breathing disorder characterised by respiratory pauses secondary to partial (hypopnoeic) or complete (apnoeic) obstruction of the pharyngeal airway (PA), with a duration of at least 10 s.[1] The PA is occluded due to a loss of muscle tone of the dilator muscles during sleep, which leads to its narrowing or total obstruction.[1 2] As a result, there are repetitive oxygen desaturations ($SatO_2$) with snoring, unrefreshing sleep, fatigue and excessive daytime sleepiness (EDS).[1 2] Systemic arterial hypertension and heart failure may subsequently develop, with a significant increased in mortality risk.[1 2] Overall, OSA may also have a social impact in terms of poor quality of life, days of work lost and traffic accidents.[2]

It is estimated that OSA affects 5%–20%[3] of the general adult population, though some authors report figures of up to 26%.[3 4] Nevertheless, the statistics show that over 50% of all cases go undiagnosed.[3] The disorder is three times more common in men than in women.[3 4]

The diagnosis of OSA requires the recording of multiple physiological signals during sleep.[4] In this regard, polysomnography (PSG) is considered the gold standard for diagnosing the disease.[4] PSG records brain activity, breathing, heart rate, muscle activity, snoring, blood oxygen levels while resting/sleeping and repeated episodes of PA obstruction, which are measured by the apnoea–hypopnoea index (AHI).[4] In addition, the guidelines of the American Academy of Sleep Medicine[4] indicate that either PSG or home sleep apnoea testing can be used for the diagnosis of uncomplicated OSA in adults, although standard sleep channels are not monitored in the latest devices (eg, electroencephalogram).[4]

Different methods are currently used for treating patients with OSA.[5] Continuous positive airway pressure (CPAP) is considered the gold standard in this regard. However, CPAP non-adherence rates of 46%–86% have been reported[5] (adherence being defined as >4 hours of night use of CPAP during 70% of nights).[6] Different alternative treatments are available to expand the PA, such as uvulopalatopharyngoplasty (UPPP), tonsillectomy, adenoidectomy, hyoid suspension (Hs) or hyothyroidopexy,[5] though the cure rate (CR) (defined as a final AHI of <5 events/hour) does not exceed 40%, and the results do not hold up over time.[7 8]

Since Guilleminault *et al*[7] first described maxillomandibular advancement (MMA) as an effective treatment for patients with OSA with a retrusive facial profile in 1976, several studies have confirmed its benefits.[7 8] Many publications have demonstrated that MMA moves the anterior pharyngeal wall forwards, resulting in enlargement of the PA and, consequently, a decrease in AHI.[1 3 8–11] Some authors have concluded that the efficacy of MMA is equivalent to that of CPAP use over the long term.[5 7 10] Accordingly, MMA with or without adjunctive surgical procedures is the most effective and predictable surgical treatment option for patients diagnosed with moderate to severe OSA, with a 50% and 86% CR and surgical success rate (SR), respectively (SR, defined as final AHI of <20 events/hour, and its reduction by 50%).[8] Thus far, a mean MMA of 10–12 mm has been described as the standard advancement required to treat adult patients with moderate to severe OSA.[7 11–13] Mean linear maxillary and mandibular advancements of 8.07±2.60 mm and 10.8±2.34 mm, respectively, have been reported in the literature.[13] However, the magnitude of MMA required at the time of surgery in order to cure OSA depends on the patient's dentofacial characteristics (eg, retrognathia, maxillary hypoplasia and micrognathia), among other factors.[5 8 11 12]

Recent studies have evaluated PA enlargement after MMA, reporting significant changes in pharyngeal airway volume (PAV) (a mean 80.43% vol gain), related to a mean decrease in AHI of 83.01% (p<0.001).[13] These volumetric parameters are usually quantified using cone beam CT (CBCT),[2 5 8–10 14 15] since the use of three-dimensional (3D) computer-aided planning technology with CBCT, compared with conventional planning with two-dimensional (2D) cephalometry, has been proven to be more accurate at treatment planning and follow-up and thus more beneficial for the patient.[16] Nowadays, there is an emerging interest in the 3D study of the impact of orthognathic surgery on PAV, evaluating the impact of each single maxillomandibular movement on the three dimensions and at each level of the PA in the context of OSA approach.[16]

The aim of the present systematic review and meta-analysis was to assess the impact of MMA on PAV and AHI in the treatment of OSA.

MATERIALS AND METHODS

Search strategy

A systematic search was conducted of the PubMed, Embase, Cochrane Library and Google Scholar Beta databases on the upper airway and polysomnographic changes following MMA for OSA treatment. The study was based on the following PICO question (population: patients with OSA, intervention: MMA, comparison: magnitude of MMA, outcome: final PA dimensions and final AHI): how does MMA surgery affect PAV and, consequently, AHI in patients with OSA?

The PubMed search was conducted with the following Medical Subject Headings (MeSH) entry terms and thesaurus vocabulary for indexing articles: ((“Orthognathic surgery” OR “Orthognathic Surgeries” OR “Surgeries, Orthognathic” OR ”Surgery, Orthognathic” OR “Maxillofacial Orthognathic Surgery” OR “Maxillofacial Orthognathic Surgeries” OR “Orthognathic Surgeries, Maxillofacial” OR “Orthognathic Surgery, Maxillofacial” OR “Surgeries, Maxillofacial Orthognathic” OR “Surgery, Maxillofacial Orthognathic” OR “Jaw Surgery” OR “Jaw Surgeries” OR “Surgeries, Jaw” OR “Surgery, Jaw” OR “Orthognathic Surgical Procedures“ OR “mandibular setback” OR “ mandibular advancement” OR “maxillary setback” OR “maxillary advancement” OR “bimaxillary surgery” OR” maxillomandibular advancement”) AND (“Polysomnographies” OR “Monitoring, Sleep” OR “Sleep Monitoring” OR “Somnography” OR “Somnographies” OR “oximetry” OR “Oximetry” OR “Oximetries” OR “Oximetry, Pulse” OR “Oximetries, Pulse” OR “Pulse Oximetries” OR “Pulse Oximetry”) AND (“Sleep Disordered Breathing” OR “Apneas, Obstructive Sleep” OR “Obstructive Sleep Apneas” OR “Sleep Apneas, Obstructive” OR “Obstructive Sleep Apnea Syndrome” OR “Obstructive Sleep Apnea” OR “OSAHS” OR “Syndrome, Sleep Apnea, Obstructive” OR “Apnea, Obstructive Sleep” OR “Sleep Apnea Hypopnea Syndrome” OR “Syndrome, Obstructive Sleep Apnea” OR “Upper Airway Resistance Sleep Apnea Syndrome” OR “Syndrome, Upper Airway Resistance, Sleep Apnea” or “Apnea Syndrome, Sleep” OR “Apnea Syndromes, Sleep” OR “Sleep Apnea Syndrome” OR “Apnea, Sleep” OR “Apneas, Sleep” OR “Sleep Apnea” OR “Sleep Apneas” OR “Sleep Hypopnea” OR “Hypopnea, Sleep” OR “Hypopneas, Sleep” OR “Sleep Hypopneas” OR “Sleep-Disordered Breathing”

OR "Breathing, Sleep-Disordered" OR "Sleep Disordered Breathing" OR "Sleep Apnea, Mixed Central and Obstructive" OR "Mixed Central and Obstructive Sleep Apnea" OR "Sleep Apnea, Mixed" OR "Mixed Sleep Apnea" OR "Mixed Sleep Apneas" OR "Sleep Apneas, Mixed" OR "Hypersomnia with Periodic Respiration")).

The same strategy was used in the case of the Cochrane Library, since it also employs MeSH terms.

The Embase database was searched using the Emtree preferred terms and supplementary data: "Orthognathic surgery"/exp AND "Obstructive Sleep Apnea"/syn.

Grey literature from the Google Scholar Beta database was also searched in order to retrieve studies published in journals not indexed in the major databases. All duplicates from the four systematic searches were subsequently removed.

Study selection

The electronic search was conducted by two authors (MG-H and AV-O) to avoid subjectivity. Those studies that fulfilled the inclusion criteria were retrieved for full-text reading.

The inclusion criteria were intervention studies; patients >18 years of age with moderate to severe OSA (AHI ≥15 events/hour) eligible for MMA; studies assessing the effect of orthognathic surgery on PA dimensions; studies assessing the impact of orthognathic surgery on PSG-related parameters; a minimum follow-up period of 6 months; and reporting of the magnitude of advancement of the maxilla, mandible and chin. Studies in which patients underwent turbinectomy and/or septoplasty as adjunctive procedures were also included, since these procedures do not modify PA dimensions. The exclusion criteria were case reports; literature reviews; and studies reporting patients undergoing setback orthognathic surgery or Hs, tonsillectomy, adenoidectomy or UPPP as adjunctive procedures, since these procedures may modify PA dimensions.

In the event of disagreement between the authors, the identified papers were subjected to full-text reading, and eligibility under discussion was then assessed. If any doubts arose, a third reviewer (FH-A) screened and read in full the included articles, and it was then discussed whether one of the authors had rejected it.

The level of inter-rater agreement between authors was assessed by Cohen's kappa coefficient (κ).

Data extraction

Demographic, surgical and methodological data were compiled from the included studies. Any discrepancies were resolved by consensus between the authors (MG-H and AV-O).

Outcome measures

The following outcome measures were evaluated: AHI, PA dimensions, and SRs and CRs, respectively.

Regarding the AHI assessment, it was established as the final postoperative score (final AHI) and the presurgery versus postsurgery difference (AHI reduction). Moreover, final AHI was assessed to establish the 'SRs' and 'CRs' of surgical treatment of OSA after MMA, as described elsewhere.[1 4–6 17–25] A final AHI of <20 events/hour, with a reduction of 50% postoperatively, defines surgical success.[1 5 7] A final AHI of <5 events/hour is regarded as a surgical cure criterion.[1 4–6 17–25]

As to PA enlargement evaluation, both 3D and 2D measures assessed by CBCT and cephalometric analysis, respectively, were included as primary indicators of the anatomical changes as follows: PAV and pharyngeal airway space (PAS) gain (in cm^3 and mm, respectively).

Finally, as key independent variables, the magnitudes of maxillary and mandibular (in mm) advancement, as well as the ratio between maxillary and mandibular advancement, were extracted from the included studies.

Statistical analysis

The statistical analysis included a demographic study (mean, SD, range and median for continuous variables, and absolute and relative frequencies for categorical variables). Paired t-tests were used to compare preoperative and postoperative mean values. Statistically significant differences were considered for $p<0.05$. The R V.3.0.2 statistical package was used throughout.

Study of heterogeneity and risk of bias

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses[26] statements were used as a basis to ensure transparency of the systematic review, comprising 27 checklist items (referred to title, abstract, introduction, methods, results, discussion and funding) and a four-phase flowchart (identification, screening, eligibility and inclusion).[26 27] Heterogeneity among the included items was assessed using the I^2 statistics and a corresponding statistical null test. Galbraith plots were used to visualise the degree of heterogeneity. In situations of significant heterogeneity, the source was explored through sensitivity analysis.

Subgroup analyses were made to examine the different surgical techniques of the studies since genioplasty (Gp), the surgical correction of the projection of the chin, can add an increase in the PA. Thus, two surgical factors were considered for the two group analyses: (1) 'MMA group' (n=108), which excluded studies with Gp,[17 20 22 24] and (2) 'MMA±Gp' group (n=159), including all articles regardless of Gp.[17–24] Forests plots were used to show the effects. A metaregression model was developed to assess the association between the largest number of studies regarding maxillary and/or mandibular advancement. These random effects were supported by the inverse variance method of DerSimonian and Laird.[28] A 95% CI was pooled.

The quality of the papers was assessed using the adaptation of the bias analysis used by Haas *et al*.[16 29] The criteria

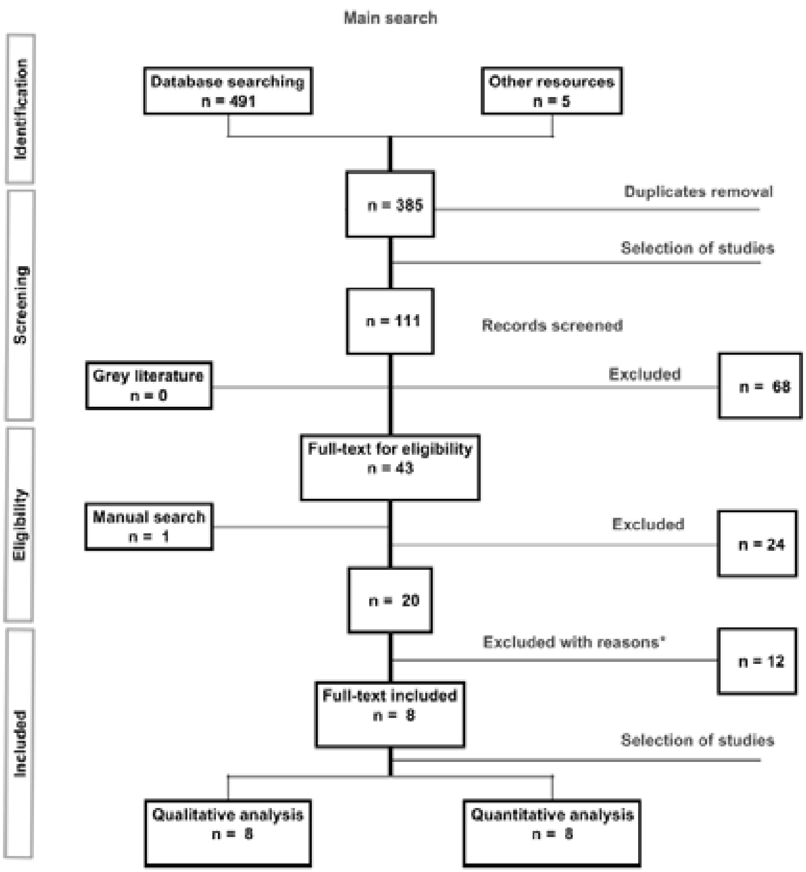

Figure 1 Systematic Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart. *No response or inappropriate data were received from the authors of the excluded studies.

based on sample selection, blinding of the authors, comparison between treatments, statistical analysis and outcome validation measured the degree of bias, definition of inclusion and exclusion criteria, and postoperative follow-up. They were categorised as low risk if all the criteria were met, uncertain risk when only one criterion was missing, and high risk if two or more criteria were missing according to the analysis of Haas *et al*.[16] With respect to publication bias, funnel plots and the Egger test were used.

RESULTS

Search strategy and study selection

The strategies of the main search and grey literature search were applied up to December 2017. A four-phase flowchart (identification, screening, eligibility and inclusion) is provided of each step of the systematic search, confirming the thoroughness of the screening process. The aim of this diagram was to help the authors improve the reporting of systematic reviews (figure 1).[26 27]

The main electronic search yielded a total of 496 articles. Of these, 491 were found in PubMed and 5 were found in the Cochrane Library and Embase databases. The titles and abstracts of 111 articles were scrutinised independently by the two investigators (MGH and AVO) after the removal of duplicates. Of these studies, 43 were subjected to full-text reading. The inter-rater agreement coefficient was κ=0.856 (95% CI 0.773 to 1) for study selection.

Study eligibility

The same two authors independently evaluated the 43 articles subjected to full-text reading. Of these, 20 met the criteria for inclusion. The authors of four studies[13 30–32] were contacted by email for further information, since some doubts arose during the selection process. A period of 4 weeks was allowed for their reply in providing the missing data, but no reply for further information was obtained from any of the authors.[13 30–32]

Twelve articles[11 13 30–39] were excluded from the systematic review. Of the excluded studies, one[35] failed to report the magnitude of movement during orthognathic surgery; eight studies[11 30 31 33–37] did not report PA measurements; and three studies[36 38 39] reported setback procedures.

Eight studies[17–24] were therefore included in the quantitative analysis. The inter-rater agreement regarding study eligibility was considered excellent, with κ=0.813 (95% CI 0.663 to 1.0).

Data extraction

Data from the included studies are shown in table 1.

The included studies were mainly retrospective,[17–21 24] and only two involved a prospective design.[22 23] The meta-analysis sample consisted of a total of 159 patients from the eight included studies. Of these, four articles assessed the efficacy of MMA alone (n=108),[17 20 22 24] while four trials[18 19 21 23] evaluated the effectiveness of MMA+Gp as an adjunctive procedure, though not necessarily in all the patients (n=51).[18 19 21 23] Since Gp may add an increase in PA, subgroup analyses were made to examine the different surgical techniques used in the studies: (1) MMA group (n=108), which excludes studies with Gp,[17 20 22 24] and (2) MMA±Gp group (n=159), which includes all articles regardless of Gp[17–24] (tables 1 and 2).

No gender differences were identified in any study, though the male sample was larger in all the included studies (total of 116 men and 28 women).[17–24] The mean age was 39 years (range 33–61).[17–24]

All of the studies[17–24] included patients with moderate to severe OSA assessed by PSG. In relation to the PSG parameters, most of the studies used the AHI.[17 19 24] However, one publication[18] used the respiratory disturbance index (consisting of the apnoeas+hypopnoeas and arousals). Both metrics were considered equivalent when assessing OSA severity.[5] In particular, the patients eligible for MMA included in this systematic review were not able to adhere to CPAP therapy (defined as >4 hours of night use of CPAP during 70% of nights)[6] or failed previous adjunctive surgery, such as UPPP, Hs or adenoidectomy, among others.[17–24]

Regarding the imaging techniques used, the majority of the studies[17 20–23] assessed the PA measurements with 3D methods (CBCT). In all studies, patients were scanned sitting in an upright position in the Frankfort horizontal plane. This position is closer to the natural head position and is recommended for the baseline assessment of upper airway dimensions.[8–14] Of these publications, five reported 3D PA measurements (PAV),[17 20–23] and three reported 2D PA measurements[18 19 24] in the sagittal plane (PAS), consisting of the minimum distance between the base of the tongue and the posterior pharyngeal wall[18 19 24] (table 3).

Quantitative analysis

The meta-analysis estimated the effects of the PSG parameters (final AHI, AHI reduction, SR and CR) and PA measurements (3D PAV gain or 2D PAS gain) in relation to the maxillary and mandibular advancement achieved in the eight studies regardless of Gp (MMA±Gp group).[17–24] In a second stage, the analyses were replicated for the studies reporting only MMA (MMA group)[17 20 22 24] in order to evaluate the sole effect of the MMA, without Gp. Metaregression was estimated at the time of assessment of the effects in terms of the magnitude of maxillary and mandibular advancement and the maxillary:mandibular ratio related to AHI as independent variables.[40]

Effect of MMA on AHI

Data on the outcomes assessed in this meta-analysis can be extracted from tables 2 and 3.

Regarding the *final AHI* in both groups: (1) MMA±Gp group[17–24]: the mean postoperative AHI scores for the global sample of 159 patients ranged from 4.8[22] to 29.4 events/hour,[18] with a mean final AHI of 12.4 events/hour (95% CI 7.18 to 17.6, p<0.001) (figure 2A). The results suggest that the treatment ensures a final AHI value below the threshold of 20 on average. Specifically, the p values for metaregression of the maxillary, mandibular and maxillary:mandibular ratio were 0.073, 0.747 and 0.316, respectively. A strong tendency was seen, though no significant effects were detected for any of them separately. (2) MMA group[17 20 22 24]: a global sample of 108 patients who did not undergo Gp yielded a mean postoperative AHI score of 4.8[22] to 18.6[17] events/hour. The mean final AHI score was 12.9 events/hour (95% CI 6.94 to 18.85, p<0.001), which suggests that the treatment ensures a final AHI value below the threshold of 20.[17 20 22 24] Individually, no significant effect was shown for maxillary advancement (p=0.200), though a statistically significant effect was detected for both mandibular advancement and the maxillary:mandibular ratio (p=0.025 and 0.002, respectively). For every additional 1 mm of mandibular advancement, the final AHI score was reduced by an average of 1.45 events/hour,[17 20 22 24] and for every additional unit of maxillary:mandibular ratio, the final AHI score was reduced by an average of 0.81 events/hour,[17 20 22 24] respectively.

On the other hand, results regarding AHI reduction were as follows: (1) MMA±Gp group[17–24]: the average reduction values ranged between 30.9[17] and 50.6 events/hour.[19] The mean estimated overall effect for AHI reduction was 38.0 events/hour (95% CI 31.7 to 44.3) (p<0.001) (figure 2B). Metaregression analysis referred to the magnitude of maxillary and mandibular advancement, and the maxillary:mandibular ratio yielded no statistically significant results for any of the groups (p=0.977, 0.263 and 0.520, respectively). (2) MMA group[17 20 22 24]: the average reduction values ranged between 30.9[22] and 50.6 events/hour[17] for the sample of 108 patients. A statistically significant mean decrease in AHI of 39.0 events/hour (95% CI 31.5 to 46.6, p<0.001) was obtained. In particular, the maxillary advancement had a significant effect on the reduction of AHI (p=0.044). Hence, for each additional 1 mm of maxillary advancement, the AHI further decreased by 1.34 events/hour. However, no

Table 1 Demographic data of the included studies

Author, year	Country, place of study+years of intervention	Study design	Sample*	Gender	Age (years), mean±SD	Dental classes I, II and III	Type of OSA: moderate or severe	Evaluation: 3D or 2D	Type of surgery: MMA or MMA+Gp
Fairburn *et al*,[17] 2007	University of Alabama at Birmingham, Birmingham, AL, USA, 2000–2003	R	n=20	M: 13 F: 7	47.6±10.0	NA	Severe	3D	MMA
Jones *et al*,[18] 2010	University of Adelaide, Australia, 2002–2004	R	n=20	NA	NA	NA	Severe	2D	MMA±Gp
Ronchi *et al*,[19] 2013	Sant'Anna Hospital Como, Italy, San Raffaele Hospital, Milan	R	n=15	M: 11 F: 4	42.3±9.5	I: 5 II: 9 III: 1	Severe	2D	MMA±Gp
Bianchi *et al*,[20] 2014	Sant'Orsola Malpighi University Hospital, Bologna, Italy, 2008–2011	R	n=10	M: 10 F: 0	45±14	NA	Severe	3D	MMA
Schendel *et al*,[21] 2014	Stanford University, Stanford, California, USA	R	n=10	M: 8 F: 2	46.4±9.7	I: 2 II: 8	Severe	3D	MMA±Gp
Hsieh *et al*,[22] 2014	Chang Gung Memorial Hospital, Taoyuan, Taiwan	P	n=16	M: 12 F: 4	33±7.9	I: 1 II: 15	Severe	3D	MMA
Veys *et al*,[23] 2017	Bruges, Belgium, January–December 2015	P	n=11 (only six assessed: pts 1, 2, 3, 5, 7 and 11	M: 8 F: 3	44.7±9.5	NA	Moderate to severe	3D	MMA±Gp
de Ruiter *et al*,[24] 2017	Academic Medical Centre of the University of Amsterdam, 2011–2015	R	n=62	M: 54 F: 8	54 (47–61)	NA	Severe	2D	MMA

*In the sample of Veys *et al*,[23] only six pts were assessed out of 11.

F, female; Gp, genioplasty; M, male; MMA, maxillomandibular advancement; NA, not assessed by the authors; P, prospective; pt, patient; R, retrospective.

Table 2 Data referred to outcome measures of the included studies

Author, year	Sample*	Pre-BMI (kg/m^2)	Post-BMI (kg/m^2)	Type of surgery: MMA or MMA±Gp	Pre-AHI mean±SD (events/hour)	Post-AHI mean±SD (events/hour)	Success rate	Cure rate
Fairburn *et al*,[17] 2007	n=20	32.24±4.7	31.74±5.0 (p=0.61)	MMA	69.2±35.8	18.6±6.3	90%	50%
Jones *et al*,[18] 2010	n=20	33.9±8.5 (p=0.61)	34.7±9.2 (p=0.61)	MMA±Gp	61.41±19.6 (p>0.01)	29.4±19.4 (p>0.01)	65%	NA
Ronchi *et al*,[19] 2013	n=15	NA	NA	MMA±Gp	58.7±16 (p<0.001)	8.1±7.8 (p<0.001)	100%	NA
Bianchi *et al*,[20] 2014	n=10	NA	NA	MMA	56.8±16.6 (p<0.005)	12.3±5.5 (p<0.005)	100%	NA
Schendel *et al*,[21] 2014	n=10	28.6	NA	MMA±Gp	42.9±21.2	5.2±8.3	100%	NA
Hsieh *et al*,[22] 2014	n=16	22±3.3	NA	MMA	35.7±18.0 (p<0.001)	4.8±4.4 (p<0.001)	100%	NA
Veys *et al*,[23] 2017 *	n=11	NA	NA	MMA±Gp	27.7±14.7 (p=0.005)	8.5±10 (p=0.005)	70%	40%
de Ruiter *et al*,[24] 2017	n=62	29 (27–33) (p=0.609)	NA	MMA	52±10 (p=0.515)	16±10 (p=0.515)	71%	NA

*In the sample of Veys *et al*,[23] only six pts were assessed out of 11 (pts 1, 2, 3, 5, 7 and 11).
†P values <0.05 were considered as significant (95% CI).
AHI, apnoea–hypopnoea index; BMI, body mass index; Gp, genioplasty; MMA, maxillomandibular advancement;NA, not assessed by the authors; pt, patient.

significant effect was shown for mandibular advancement (p=0.544) or maxillary:mandibular ratio (p=0.258).

Finally, in relation to SR, both groups achieved high surgical SRs. An overall SR of 87.5% (95% CI 76.8% to 98.2%) and 90.3% (95% CI >76.8%) was obtained for the MMA±Gp and MMA groups, respectively (figure 3). However, no statistically significant associations were found between maxillary, mandibular advancement and maxillary:mandibular ratio (p=0.289, p=0.901 and p=0.394, respectively) in any group.

Effect of MMA on PAS and PAV

With regard to the *2D PAS* increase, the following results were found in each group: (1) MMA±Gp group[17–19 21 24]: five studies comprising a sample of 127 patients reported 2D PA measurements. The overall mean PAS gain was 4.75 mm (95% CI 3.15 to 6.35) and proved to be statistically significant (p<0.001) (figure 4). Metaregression analysis yielded no statistically significant results for maxillary advancement or the maxillary:mandibular ratio (p=0.211 and 0.560, respectively). However, mandibular advancement was found to be statistically significant in terms of PAS gain (p<0.001). Our results suggest that the greater the mandibular advancement, the greater the PAS gain: each additional 1 mm of mandibular advancement implied a 0.5 mm gain in PAS.

(2) MMA group: only two studies[17 24] comprising a total of 82 patients reported 2D PA measurements with a mean PAS gain of 6.48 mm (95% CI 5.31 to 7.64, p<0.001). Since only two papers are included in this group, a reliable metaregression analysis was not possible.

On the other hand, only two studies,[20 22] included within both groups (MMA±Gp and MMA), reported data on absolute *3D PAV gain*. The mean PAV gain was 7.35 cm^3 (95% CI 5.35 to 9.34) and proved to be statistically significant (p<0.001). Since only two papers are included in this group, a reliable metaregression analysis was not possible.

Correlation between PAS/PAV gain and AHI

Regarding *2D PA* measurements, only four studies corresponding to the MMA±Gp group (comprising a sample of 107 patients) reported information on PAS gain and final AHI/AHI reduction.[17 19 21 24] A statistically significant association was found between PAS gain and final AHI (r=0.41, p=0.023), meaning that for each 1 mm of PAS gain, AHI was reduced in 3.58 events/hour (95% CI 0.49 to 6.68). Therefore, a greater change in PAS would result in a lower final AHI[17 19 21 24] (online supplementary figure S1).

With regard to the *3D PA* measurements, two papers,[20 22] included within both groups (MMA±Gp and MMA), provided correlations between PAV and AHI reduction in a sample of 72 patients. Both studies obtained positive correlations (Pearson correlation coefficient (r) 0.576 according to Bianchi[20] and 0.76 according to de Ruiter *et al*.[24] The global effect estimated for the correlation was 0.75 (95% CI 0.65 to 0.85), reflecting a

Table 3 Analyses of the included studies regarding PA, MMA and PAS

Author, year	Point PA	Pre-PA mean±SD (cm³)	Post-PA mean±SD (cm³)	Max ADV (mm)	Mand ADV (mm)	Max:mand ADV ratio	Pre-PAS mean±SD (mm)	Post-PAS mean±SD (mm)	Change in PAS mean±SD
Fairburn *et al*[17] 2007	PAS	NA	NA	NA	10	NA	11.125	16.96	5.8±3
Jones *et al*[18] 2010	PAS	NA	NA	12.05±2.7	16.23±5.72	NA	9.5±3.66	13.28±5.72	2.55±3.18 (p>0.01)
Ronchi *et al*[19] 2013	PAS	NA	NA	5.2±4.5	9.5±8.7	1.83	5±2.2	9.5±3.3	4.5±2.75 (p=0.74)
Bianchi *et al*[20] 2014	PAS	12.9±4.0 (p<0.005)	20.7±3.5 (p<0.005)	10	10	1.00	NA	NA	NA
Schendel *et al*[21] 2014	PAS	74.1	176.9	9.4	9.5	1.01	6.07±2.3	9.60±4.1	3.53±3.2
Hsieh *et al*[22] 2014	PAS	17.1±7.0 (p<0.001)	23.2±8.6 (p<0.001)	NA	NA	NA	NA	NA	NA
Veys *et al*[23] 2017	PAS	28.78±8.4 (p=0.002)	38.97±15.07 (p=0.002)	8.0±2.1	9.8±1.8	1.23	NA	NA	NA
de Ruiter *et al*[24] 2017	PAS	NA	NA	7±2.2 (p=0.164)	7±3.7 (p=0.248)	1.00	7±3.7	14±4.4	7±4.05

*In the sample of Veys *et al*,[23] only six patients were assessed out of 11 (pts 1, 2, 3, 5, 7 and 11).
†P values <0.005 were considered significant (95% CI).
ADV, advancement; mand, mandibular; max, maxillary; MMA, maxillomandibular advancement;NA, not assessed by the authors; PA, pharyngeal airway; PAS, pharyngeal airway space; pt, patient.

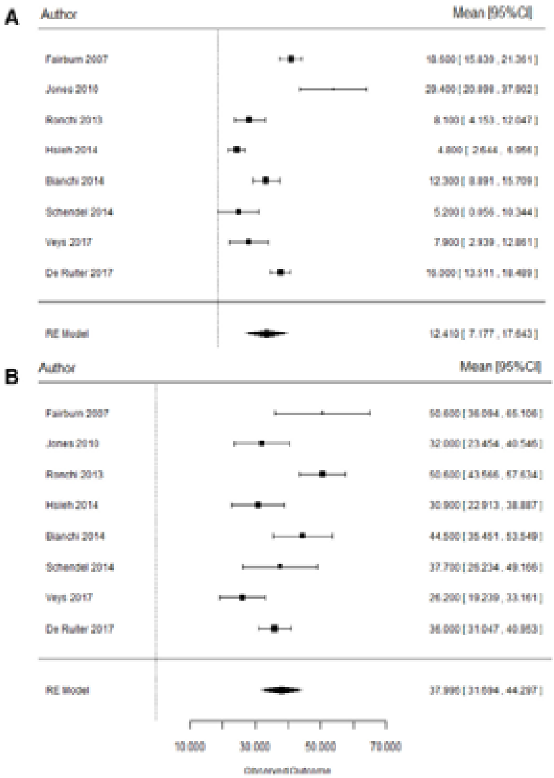

Figure 2 Forest plots representing the final mean AHI (A) and AHI reduction (B) for both groups. AHI, apnoea–hypopnoea index.

strong relationship between changes in both variables. Therefore, the greater the volume gain, the greater the corresponding AHI reduction.

Analysis of publication bias

Data reporting the risk of bias are shown in table 4. The risk of bias of the papers included in this systematic review was classified as high for five studies[17–19 21 24] and as medium/unclear for three studies.[20 22 23] None of the studies reported blind assessment.

Funnel plots were used to depict the risk of publication bias. No publication bias was detected for final AHI (Egger test p=0.547 for MMA and p=0.297 for MMA±Gp) or PAS gain (Egger test p=0.156 for MMA and p=0.109 for MMA±Gp). Sensitivity analysis of the estimates identified two publications[17 18] as potentially being responsible for most of the heterogeneity between studies. Disparity between data was due to the patient sample regarding OSA severity. In terms of final AHI, heterogeneity accounted for 94.6% of the total variability, with Q=102.9 (p<0.001). The problem seemed to point primarily to one study,[18] with a fairly high value in comparison with the other studies. No publication bias was likewise suggested with respect to PAS gain.

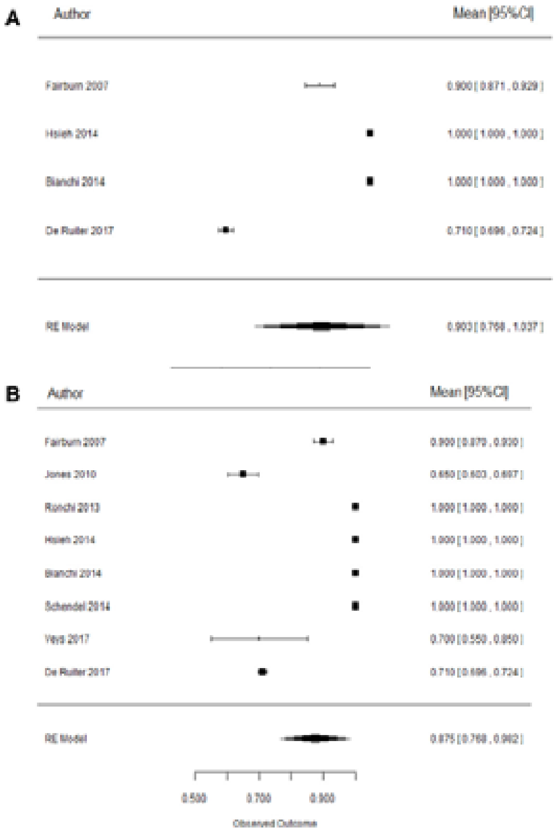

Figure 3 Forest plots corresponding to the success rate for both groups, (A) 'MMA' and (B) MMA±genioplasty'. MMA, maxillomandibular advancement.

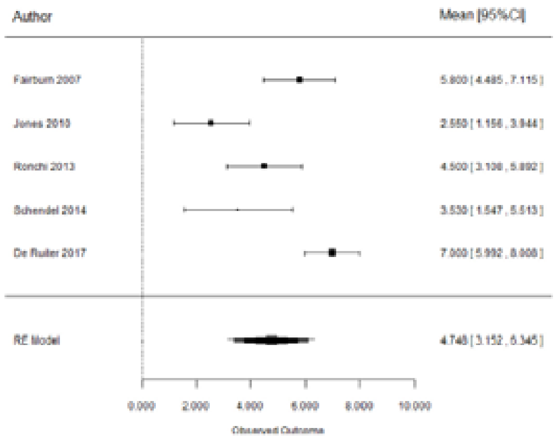

Figure 4 Forest plots representing pharyngeal airway space gain for both the 'MMA' and 'MMA±genioplasty' groups. MMA, maxillomandibular advancement.

Table 4 Results of the quality analysis of the included studies

Quality criteria	Fairburn *et al*[17]	Jones *et al*[18]	Ronchi *et al*[19]	Bianchi *et al*[20]	Schendel *et al*[21]	Hsieh *et al*[22]	Veys *et al*[23]	de Ruiter *et al*[24]
Sample randomisation	No	No	No	No	No	No	No	No
Comparison between treatments	No	No	No	No	Yes	No	No	No
Blind assessment	No	No	No	No	No	Yes	Yes	No
Description of measurements	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Statistical analysis	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Defined inclusion/exclusion criteria	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Report of follow-up	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Risk of bias	High	High	High	High	Unclear	Unclear	Unclear	High

*Risk of bias assessment: high=0–4, 'yes'; unclear=5–6, 'yes'; low=7, 'yes'.

However, regarding AHI reduction, sensitivity analysis suggested that all the aforementioned heterogeneity could be due to maxillary advancement in the MMA group, given the adjustment found (I^2=0.0%, Q=0.85, p=0.357). This could be due to studies[17] that reported large reductions in AHI. The Egger test yielded a low p value (p=0.144), taking into account its limited power in application to these sample sizes. In contrast, homogeneity between studies was found on assessing PA (I^2=0%, Q=0.64, p=0.422).

DISCUSSION

The aim of the present systematic review with metaregression analysis was to assess the impact of MMA on PA dimensions and AHI in the treatment of OSA, as there is limited evidence regarding their exact correlations.[17–24] Indeed, it has been widely reported that MMA increases PA and decreases AHI in the context of OSA, but additional multidisciplinary studies assessing aspects other than PA and AHI are needed to determine which types of maxillary, mandibular and chin movements (eg, advancement, rotation, impaction and descent) are best for enlarging the PA in its specific compromised levels and for finally reducing AHI, as well as patient characterisation in terms of OSA severity, comorbidities and facial profile, among other factors.[5 41–43]

With regard to MMA surgery according to the analysed articles,[17–24] the positive effect of the intervention was clearly evidenced by the surgical SR obtained (87.5%). However, while most of the included studies[19 20 22] obtained SR values of 100%, Jones *et al*[18] recorded the lowest rate (65%). Specifically, a mean final AHI of 12.4 events/hour (95% CI 7.18 to 17.6, p<0.01)[17–24] was achieved in all of the literature reviewed. Hence, orthognathic surgery in application to OSA ensures surgical success with a final AHI of <20 events/hour and an AHI reduction of at least 50% according to the criteria defined by Riley *et al*.[34] However, some patients would still require ongoing CPAP treatment after MMA, since OSA may not be cured (AHI <5 events/hour),[5 34] and would eventually have more difficulty in adhering to CPAP after surgery.[44] None of the included studies reported the number of patients requiring ongoing CPAP after MMA.[17–24] However, the surgical success criterion remains subject to controversy.[5 44] In this regard, some authors suggest that surgical success in OSA should be assessed on the basis of improvement or resolution of the clinical signs and symptoms of OSA, the normalisation of sleep, AHI reduction (AHI <20) and quality of life.[44] On the other hand, surgical CRs (AHI <5 events/hour) were assessed by only two studies (Fairburn *et al*[17] and Veys *et al*,[23] with CRs of 50% and 40%, respectively (table 2).[17 23] Thus, we were not able to draw definitive conclusions on the impact of MMA on CRs.[17 23]

Scarce data are available on the required MMA advancement to benefit patients with OSA.[5 42] In terms of the amount of surgical movement achieved, to date, an MMA of 10 mm has been considered the gold standard orthognathic surgery treatment in patients with OSA.[34] Nevertheless, the combination of MMA with counterclockwise rotation has proven to be the movement with the strongest impact on PA.[1 7 8 13 17–24 34 41–43] However, there is not enough evidence to establish the magnitude and direction of maxillary or mandibular movement required in order to cure OSA.[5] Our results in this meta-analysis showed that for each additional 1 mm of mandibular advance, the final AHI is reduced by 1.45 events/hour on average,[17 22] but further in-depth investigations would be helpful to carry out patient-tailored surgeries, depending on their skeletal facial profile, PA shape, OSA characteristics and patients' comorbidities.[45 46]

The surgical treatment of OSA through MMA is occasionally performed in combination with additional procedures such as septoplasty, turbinectomy, tonsillectomy, adenoidectomy, UPPP or genial tubercle advancement (GTA).[5 35 41 42] As specified by the inclusion criteria, studies where patients underwent turbinectomy and/or septoplasty as adjunctive procedures were included since it is considered that these procedures do not modify PA dimensions.[18 19 21 23] Hs, tonsillectomy, adenoidectomy or UPPP as adjunctive procedures were excluded since they may alter PA dimensions.[18 19 21 23] Regarding GTA and Gp, these procedures were included, provided that the magnitude of advancement was reported.[18 19 21 23] However, in order to discard any independent effect or impact of Gp in MMA in terms of AHI reduction, variation in PAS and PAV gains of the two group analyses assessing MMA alone and MMA with Gp were carried out.[17–24]

In the past decades, the effectiveness of MMA in modifying PAS and PA has been evaluated using 2D or 3D methods, respectively.[14] All of the studies[17–24] assessed PAV by means of CBCT or cephalometry, both techniques (2D and 3D) being considered a safe and predictable way to measure PA, though the former lacks the option of evaluating the transverse dimension.[17–24] The PA was assessed two dimensionally in three of the included studies,[18 19 24] taking the minimum distance between the base of the tongue and the posterior pharyngeal wall, though not all of them indicated the exact landmarks/reference points used.[18 19 24] A significant difference of 4.75 mm (95% CI 3.15 to 6.35) between preoperative PAS and postoperative PAS was found. Particularly, mandibular advancement was seen to be statistically significant when considering PAS gain (p<0.001): 1 mm of mandibular advancement implied 0.5 mm gain in PAS.[17–19 21 24] However, only Hsieh *et al*[22] and Veys *et al*[23] reported 3D airway measurements, and these were evaluated at three different levels with respect to the limits of the PA subregions: nasopharynx, oropharynx and hypopharynx.[14] Taking into account that orthognathic surgery impacts three dimensionally and in different subregions of the PA,[14] further studies reporting volumetric data with different PA levels of measurement are needed, in addition to those included in our review[17 22 23 41 43] Thus, it is important to standardise the PA measurements for homogeneity purposes and thus be able to draw relevant conclusions.[14 45]

Regarding the correlations between changes in PAS/PAV and AHI reduction in terms of MMA, a statistically significant association between PAS gain and final AHI was found in four of the studies included in the meta-analysis (p=0.023).[17 19 21 24] For each 1 mm PAS gain, AHI was reduced by 3.58 events/hour.[17 19 21 24] With regard to the 3D studies, PAV gain and AHI reduction were positively correlated (r=0.75, 95% CI 0.65 to 0.85),[20 24] reflecting a strong relationship between changes in both dimensions. Thus, the greater the volume gain, the greater the AHI reduction.

OSA severity and its clinical signs and symptoms, as well as special patient features such as comorbidities and facial profile, among others, should be considered when dealing with patients with OSA.[5] Regarding OSA severity, to date, MMA is indicated only in moderate to severe cases and not in mild OSA cases (AHI of <5).[5] All of the included articles established the type of OSA as moderate to severe in their inclusion criteria[17–24] (table 1). However, it should be noted that two studies[17 22] reported AHI values at baseline that moved further away from the average (mean 57.9 events/hour, range 35.7±18.0[17] to 69.2±35.8).[22] Thus, further studies are needed in order to evaluate the impact of MMA in patients with mild OSA. Another relevant issue is the importance of a comprehensive assessment of the global OSA symptoms of the patient for diagnostic and disease monitoring purposes.[4] EDS and quality of life can be subjectively evaluated through the use of multiple clinical tools and questionnaires, such as the Epworth Sleepiness Scale (ESS) and the OSA Functional Outcomes of Sleep Questionnaire, respectively.[3 5 23] Improvement of daytime sleepiness assessed by ESS was reported by one of the included studies.[23] A significant decrease in EES from 14 (10–18) to 6 (4–7), preoperatively and postoperatively, was observed (p=0.0014).[23]

Moreover, anatomical factors such as body mass index (BMI) are relevant factors that compromise OSA.[5 47] In our review, only two studies[17 18] addressed preoperative and postoperative BMIs. In this context, a 10% of weight loss has been associated with a 26% decrease in final AHI.[47] Nonetheless, untreated obesity is also considered a major risk factor for the progression of OSA.[5 47] Another crucial factor is the patient's facial profile, since the maxillomandibular complex sustains the PA soft tissues. Facial analysis of many patients with OSA evidences maxillary or mandibular hypoplasia, which generally can be corrected by orthognathic surgery.[48] Accordingly, mandibular advancement devices—apart from being an option for treating mild to moderate OSA—are also useful in deciding which patients may benefit from surgical mandibular advancement in the context of OSA. Unfortunately, no similar maxillary devices for predicting the impact of maxillary advancement on OSA are available.[5]

The importance of non-anatomical factors in relation to sleep disturbance surgery outcomes has been underscored, including neuromuscular tone, rostral fluid shift, airway collapsibility and loop gain.[46 49] Li *et al*[49] attributed an average of 61% of the recorded variation in postoperative AHI to these parameters (r=0.47, p<0.01).[49] Therefore, anatomical and non-anatomical factors are of great value in the diagnosis and treatment of patients with OSA.[45–47] Hence, the current literature suggests that a multidisciplinary strategy is strongly advisable, taking into account all the related factors in order to ensure the long-lasting success of surgical treatment.[5 45 49]

Finally, our study has a number of significant limitations: (1) the main limitation is the fact that none of the included studies were randomised controlled clinical trials[25]; (2) few articles were included in the meta-analysis; (3) definitive generalisations cannot be made, given that of the eight studies included,[17–24] only two were prospective; the remainder were retrospective and therefore subjected to the usual biases and limitations of retrospective studies[40]; (4) there was a lack of homogeneity among the studies regarding the PA measurements (2D or 3D); (5) some of the studies did not directly provide mean values or SD, such data being calculated directly from the tables reporting individual patient values; (6) regarding the PSG parameters, most of the studies used the AHI[17 19 24]; however, one publication[18] used the respiratory disturbance index; and (7) no firm conclusions on the impact of MMA on surgical CR can be stated since only two studies reported CRs.

CONCLUSIONS

There is a lack of homogeneous and detailed data in the current literature regarding AHI reduction and PAS/PAV gain after MMA in patients with a retrusive facial profile. However, within the limitations of this systematic review, there is sufficient evidence to conclude that MMA significantly increases PA dimensions and ensures a final AHI score below the threshold of 20 events/hour, obtaining a mean SR of 87.5%. However, further studies are needed to individualise the required magnitude and direction of surgery-induced movements for each patient.

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REFERENCES

1 Knudsen TB, Laulund AS, Ingerslev J, *et al*. Improved apnea-hypopnea index and lowest oxygen saturation after maxillomandibular advancement with or without counterclockwise rotation in patients with obstructive sleep apnea: a meta-analysis. *J Oral Maxillofac Surg* 2015;73:719–26.
2 Lloberes P, Durán-Cantolla J, Martínez-García Miguel Ángel, *et al*. Diagnosis and treatment of sleep apnea-hypopnea syndrome. Spanish Society of pulmonology and thoracic surgery. *Arch Bronconeumol* 2011;47:143–56.
3 Durán J, Esnaola S, Rubio R, *et al*. Obstructive sleep Apnea–Hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 Yr. *Am J Respir Crit Care Med* 2001;163:685–9.
4 Kapur VK, Auckley DH, Chowdhuri S, *et al*. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea : An American Academy of Sleep Medicine Clinical Practice Guideline 2017;13:479–504.
5 Dicus Brookes CC, Boyd SB. Controversies in obstructive sleep apnea surgery. *Oral Maxillofac Surg Clin North Am* 2017;29:503–13.
6 Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. *Proc Am Thorac Soc* 2008;5:173–8.
7 Guilleminault C, Tilkian A, Dement WC. The sleep apnea syndromes. *Annu Rev Med* 1976;27:465–84.
8 Holty J-EC, Guilleminault C. Maxillomandibular advancement for the treatment of obstructive sleep apnea: a systematic review and meta-analysis. *Sleep Med Rev* 2010;14:287–97.
9 Hernández-Alfaro F, Guijarro-Martínez R, Mareque-Bueno J. Effect of mono- and bimaxillary advancement on pharyngeal airway volume: cone-beam computed tomography evaluation. *J Oral Maxillofac Surg* 2011;69:e395–400.
10 Guijarro-Martínez R, Swennen GRJ. Cone-Beam computerized tomography imaging and analysis of the upper airway: a systematic review of the literature. *Int J Oral Maxillofac Surg* 2011;40:1227–37.
11 Prinsell JR. Obstructive sleep Apnea—Surgical treatment. in: current therapy in oral and maxillofacial surgery. *Elsevier* 2012:1048–63.
12 Prinsell JR. Maxillomandibular advancement surgery in a site-specific treatment approach for obstructive sleep apnea in 50 consecutive patients. *Chest* 1999;116:1519–29.
13 Butterfield KJ, Marks PLG, McLean L, *et al*. Linear and volumetric airway changes after maxillomandibular advancement for obstructive sleep apnea. *J Oral Maxillofac Surg* 2015;73:1133–42.
14 Guijarro-Martínez R, Swennen GRJ. Three-Dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: a validation study. *Int J Oral Maxillofac Surg* 2013;42:1140–9.
15 Christovam IO, Lisboa CO, Ferreira DMTP, *et al*. Upper airway dimensions in patients undergoing orthognathic surgery: a systematic review and meta-analysis. *Int J Oral Maxillofac Surg* 2016;45:460–71.
16 Haas Jr. OL, Becker OE, de Oliveira RB. Computer-Aided planning in orthognathic surgery—systematic review. *Int J Oral Maxillofac Surg* 2015;44:329–42.
17 Fairburn SC, Waite PD, Vilos G, *et al*. Three-Dimensional changes in upper airways of patients with obstructive sleep apnea following maxillomandibular advancement. *J Oral Maxillofac Surg* 2007;65:6–12.
18 Jones R, Badlani J, Maxillary JC. Mandibular and chin advancement surgery for the treatment of obstructive sleep apnoea 2010;55:314–21.
19 Ronchi P, Cinquini V, Ambrosoli A, *et al*. Maxillomandibular advancement in obstructive sleep apnea syndrome patients: a restrospective study on the sagittal cephalometric variables. *JOMR* 2013;4:e5.
20 Bianchi A, Betti E, Tarsitano A, *et al*. Volumetric three-dimensional computed tomographic evaluation of the upper airway in patients with obstructive sleep apnoea syndrome treated by maxillomandibular advancement. *Br J Oral Maxillofac Surg* 2014;52:831–7.
21 Schendel SA, Broujerdi JA, Jacobson RL. Three-Dimensional upper-airway changes with maxillomandibular advancement for obstructive sleep apnea treatment. *Am J Orthod Dentofacial Orthop* 2014;146:385–93.
22 Hsieh Y-J, Liao Y-F, Chen N-H, *et al*. Changes in the calibre of the upper airway and the surrounding structures after maxillomandibular advancement for obstructive sleep apnoea. *Br J Oral Maxillofac Surg* 2014;52:445–51.
23 Veys B, Pottel L, Mollemans W, *et al*. Three-Dimensional volumetric changes in the upper airway after maxillomandibular advancement in obstructive sleep apnoea patients and the impact on quality of life. *Int J Oral Maxillofac Surg* 2017;46:1525–32.
24 de Ruiter MHT, Apperloo RC, Milstein DMJ, *et al*. Assessment of obstructive sleep apnoea treatment success or failure after maxillomandibular advancement. *Int J Oral Maxillofac Surg* 2017;46:1357–62.
25 Schulz KF, Altman DG, Moher D, *et al*. Consort 2010 statement: updated guidelines for reporting parallel group randomized trials. *Ann Intern Med* 2010;152:726.
26 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. preferred reporting items for systematic reviews and meta-analyses. *BMJ Br Med J* 2010;8.
27 Liberati A, Altman DG, Tetzlaff J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6:e1000100.
28 DerSimonian R, Laird N. Meta-Analysis in clinical trials. *Control Clin Trials* 1986;7:177–88.
29 Higgins JPT, Altman DG, Gøtzsche PC, *et al*. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928–9.
30 Susarla SM, Abramson ZR, Dodson TB, *et al*. Upper airway length decreases after maxillomandibular advancement in patients with obstructive sleep apnea. *J Oral Maxillofac Surg* 2011;69:2872–8.
31 Giarda M, Brucoli M, Arcuri F, *et al*. Efficacy and safety of maxillomandibular advancement in treatment of obstructive sleep apnoea syndrome. *Acta Otorhinolaryngol Ital* 2013;33:43–6.
32 Abramson Z, Susarla SM, Lawler M, *et al*. Three-Dimensional computed tomographic airway analysis of patients with obstructive sleep apnea treated by maxillomandibular advancement. *J Oral Maxillofac Surg* 2011;69:677–86.
33 Waite PD, Wooten V, Lachner J, *et al*. Maxillomandibular advancement surgery in 23 patients with obstructive sleep apnea syndrome. *Journal of Oral and Maxillofacial Surgery* 1989;47:1256–61.
34 Riley RW, Powell NB, Li KK, *et al*. Surgery and obstructive sleep apnea: long-term clinical outcomes. *Otolaryngol Head Neck Surg* 2000;122:415–20.
35 Abrahão M, Gregório LC, Gregório LC, *et al*. Genioplasty for genioglossus muscle advancement in patients with obstructive sleep apnea-hypopnea syndrome and mandibular retrognathia. *Braz J Otorhinolaryngol* 2007;73:480–6.
36 Hasebe D, Kobayashi T, Hasegawa M, *et al*. Changes in oropharyngeal airway and respiratory function during sleep after orthognathic surgery in patients with mandibular prognathism. *Int J Oral Maxillofac Surg* 2011;40:584–92.
37 Barrera JE. Virtual surgical planning improves surgical outcome measures in obstructive sleep apnea surgery. *Laryngoscope* 2014;124:1259–66.
38 Gokce SM, Gorgulu S, Gokce HS, *et al*. Evaluation of pharyngeal airway space changes after bimaxillary orthognathic surgery with a 3-dimensional simulation and modeling program. *Am J Orthod Dentofacial Orthop* 2014;146:477–92.
39 Uesugi T, Kobayashi T, Hasebe D, *et al*. Effects of orthognathic surgery on pharyngeal airway and respiratory function during sleep in patients with mandibular prognathism. *Int J Oral Maxillofac Surg* 2014;43:1082–90.
40 Thompson SG, Higgins JPT. How should meta-regression analyses be undertaken and interpreted? *Stat Med* 2002;21:1559–73.
41 Tan SK, Leung WK, Tang ATH, *et al*. How does mandibular advancement with or without maxillary procedures affect pharyngeal airways? an overview of systematic reviews. *PLoS One* 2017;12:e0181146–20.

42 Bartolucci ML, Bortolotti F, Raffaelli E, *et al*. The effectiveness of different mandibular advancement amounts in OSA patients: a systematic review and meta-regression analysis. *Sleep Breath* 2016;20:911–9.
43 Sher AE, Schechtman KB, Piccirillo JF. The efficacy of surgical modifications of the upper airway in adults. *Sleep* 1976;19:156.
44 Hobson JC, Robinson S, Antic NA, *et al*. What is "Success" following surgery for obstructive sleep apnea? The effect of different polysomnographic scoring systems. *Laryngoscope* 2012;122:1878–81.
45 American Academy of Sleep Medicine. Time for surgeons to think outside the anatomical box. *JCSM* 2017;13:1023–4.
46 Sin DOND, Fitzgerald F, Parker JD, *et al*. Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. *Am J Respir Crit Care Med* 1999;160:1101–6.
47 Romero-Corral A, Caples SM, Lopez-Jimenez F, *et al*. Interactions between obesity and obstructive sleep apnea: implications for treatment. *Chest* 2010;137:711–9.
48 Ristow O, Rückschloß T, Berger M, *et al*. Short- and long-term changes of the pharyngeal airway after surgical mandibular advancement in class II patients—a three-dimensional retrospective study. *Journal of Cranio-Maxillofacial Surgery* 2018;46:56–62.
49 Li Y, Ye J, Han D, *et al*. Physiology-Based modeling may predict surgical treatment outcome for obstructive sleep apnea. *J Clin Sleep Med* 2017;13:1029–37.

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Research Paper
Orthognathic Surgery

Variation between natural head orientation and Frankfort horizontal planes in orthognathic surgery patients: 187 consecutive cases

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Abstract. The purpose of this study was to assess the relationship between the Frankfort horizontal (FH) and natural head orientation (NHO), their correlation between patients' malocclusion, and the impact of counterclockwise rotation (CCW) on the FH-NHO angle variation after orthognathic surgery. An evaluation of 187 consecutive patients was performed at the Maxillofacial Institute (Teknon Medical Center, Barcelona). FH-NHO° was measured pre- and postoperatively at 1 and 12 months, after three-dimensional (3D) superimposition using a software (Dolphin®). Patients were classified as follows: 3.2%, 48.7% and 48.1%, class I, II and III, respectively. Baseline FH-NHO° was significantly positive for patients with dentofacial deformities (2.73° ± 4.19 (2.12–3.33°, $P < 0.001$). The impact of orthognathic surgery in FH-NHO° was greater in class II when compared with class III patients, with a variation of 2.04° ± 4.79 ($P < 0.001$) and −1.20° ± 3.03 ($P < 0.001$), respectively. FH-NHO° increased when CCW rotational movements were performed ($P = 0.006$). The results of this study suggest that pre- and postoperative NHO differs from FH in orthognathic patients. The angle between FH and NHO is significantly larger in class III than in class II patients at baseline, which converges after orthognathic surgery when CCW rotation is performed. Therefore, NHO should be used as the real horizontal plane when planning for orthognathic surgery.

Keywords: Patient positioning; Orthognathic surgery; Dentofacial deformities; Three-dimensional imaging; Cone-beam computed tomography.

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Head orientation is a key factor in cephalometric and facial analysis for orthodontic and orthognathic surgery treatment planning, because it influences the anteroposterior perception of the maxillomandibular complex and may result in an incorrect diagnosis.[1]

Various reference planes have been described for head orientation, both extracranial and intracranial.[2] One of the most commonly used is the Frankfort horizontal (FH) plane, which was first described in the Frankfort Craniometric Agreement (1882),[3] and was defined as a plane that passes through the upper rim of the external acoustic meatus (porion, Po) and the lowest point of the orbital rim (orbitale, Or).[2,3] However, a potential variability has been observed with the FH plane and similar planes that use only intracranial landmarks, because the anatomical landmarks are influenced by individual biological variability.[4] The FH plane has been found to deviate from the true horizontal plane depending on head inclination, especially in patients with dental or facial deformities.[5]

Extracranial reference planes, such as the natural head position (NHP) and natural head orientation (NHO) are alternatives to the intracranial reference planes, enabling the use of true vertical and horizontal lines for clinical facial analysis.[6] The concept of NHP was introduced in cephalometric analysis in the 1950s and is defined as the physiological position of the head that feels most natural to a living person.[6,7] Thus, NHP has been described as the ideal reference in cephalometric analysis due to its reliability and reproducibility, as it focuses on a distant point and therefore is not influenced by cranial base variability.[5,8] Although there are different methods for the patient to achieve NHO, the most common is to indicate the individual to look straight ahead at a point in front of them at eye level (e.g., looking into a mirror).[6] However, there is a slight subjectivity in head orientation as it depends on the patient who has to be told how to achieve a natural posture, and it sometimes requires certain experience of the clinician.[9]

Furthermore, NHO is influenced by other factors such as the visual and vestibular apparatus, local proprioceptors, craniocervical posture, facial and neck muscles, temporomandibular joints, maxillo-mandibular relation and dental occlusion.[10] Consequently, because the maxillomandibular relation is one of the defining factors of head positioning, NHO should theoretically change after orthognathic surgery, and even more when counterclockwise (CCW) rotational movements are performed, due to its effect on the accommodation of the head on the cervical column.[11,12]

Therefore, the main objectives of this research were to assess the relationship between FH and NHO and its correlation between patients' dental class, and the impact of CCW rotation on the FH-NHO angle variation after orthognathic surgery.

Materials and methods

To address the research purpose, the investigators designed and implemented a retrospective cohort study. The study population consisted of consecutive patients with dentofacial deformities who underwent orthognathic surgery (either mono- or bimaxilar) at the Maxillofacial Institute (Teknon Medical Centre in Barcelona, Spain) during 2019. Clinical data and three-dimensional (3D) radiological images were obtained from the Institute's database. Each patient provided written informed consent to access their cone-beam computed tomography (CBCT) data. This study was approved by the Teknon Medical Hospital Institutional review board (IRB) (Barcelona, Spain) (Ref.2019/60-CMF-TEK),and was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its subsequent amendments. All participants signed an informed consent agreement.

Patients of any gender, over the age of 18 years with completed growth of the maxillofacial complex and who underwent orthognathic surgery (mono- or bimaxillary) were included in the study. Patients with craniofacial syndromes or craniocervical posture pathology, patients with missing follow-up photographs and CBCTs or those who were not willing to sign the informed consent were excluded from the study.

Presurgical 3D planning protocol, as described elsewhere, was performed with a three-party software and the upper incisor soft-tissue nasion plane (UI-STP) was used as an absolute reference to guide the anteroposterior positioning of the maxillomandibular complex.[13] Intermediate and final surgical splints were designed and printed in house. Patients were operated on under general anaesthesia by the same surgeon (FHA) following the mandible-first proto-

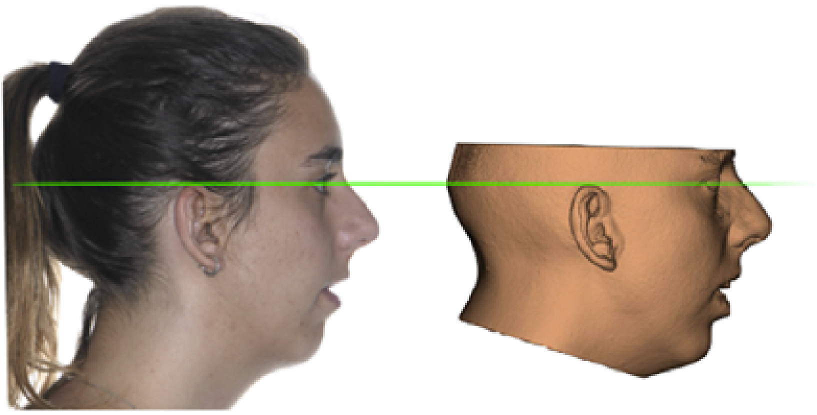

Fig. 1. Extracranial true horizontal line used by the clinicians to orient the cone-beam computed tomography. A true horizontal line was traced on the photograph (lateral view), passing through two points: the lateral canthus of the eye and at a determined point of the helix (auricular point, which varied depending on each patient).

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col. A mandibular bilateral sagittal split osteotomy (BSSO) was performed using the Dal Pont–Obwegeser method and/or a maxillary LeFort I osteotomy was carried out using the minimally invasive 'twist technique' described elsewhere.[14] Surgical data was collected regarding type of mono- or bimaxillary surgery and whether clockwise or CCW rotation movements were performed.

All included patients had followed the standard pre- and postoperative imaging workflow protocol for orthognathic surgery of the Department, which involves facial and occlusal pictures and CBCT at three time points: preoperatively (T0) and postoperatively at 1- (T1) and 12- (T2) months follow-up. These two postoperative time points were chosen in order to evaluate the short- and long-term effects of orthognathic surgery in NHO.

The CBCT scans were performed using an i-CAT Vision system (iCAT, Imaging Sciences International, Hatfield, PA, USA). For both records (CBCT and photographs), patients were previously instructed by trained clinical personnel in order to achieve a proper head orientation: they were indicated to adopt a standing position and to look straight ahead at a point at eye level located on the wall in front of them (1 m away).[6] In addition, a 2-mm centric relation wax bite was placed to avoid occlusal interferences.

Each patient had three CBCT datasets (preoperative (T0), postoperative at 1 month (T1) and postoperative at 12 months (T2)). Data were primarily saved in DICOM (Digital Imaging and Communications in Medicine) format using 3D software (Dolphin Imaging, version 11.95 premium, Chatsworth, CA, USA). Routine photographic records in NHO were used to orient and match up the CBCT 'virtual patient' ('soft tissue layer') as follows: a true horizontal line was traced on the photograph (lateral view), passing through two points: the lateral canthus of the eye and at a determined point of the helix (auricular point, which varied depending on each patient). Then, this true horizontal line from the photographs were transferred to the CBCT 'soft tissue virtual patient', resulting in a re-oriented CBCT 'virtual patient'. This true horizontal line was used to orient the CBCT 'virtual patient' in NHO (Fig. 1). The software orientation calibration tool was used along pitch (x), yaw (y) and roll (z). Orientation of both the 'Base volume' (original DICOM) and '2nd volume' (duplicate DICOM) was undertaken to achieve the same original positions of the CBCTs ('hard tissue layer').[15] Then, the FH plane was marked as a line connecting the right porion (Po, the upper rim of the external acoustic meatus) and right orbitale (Or, the lowest point of the orbital rim) ('hard tissue layer').[3]

The angle between FH and NHO (FH-NHO°) was measured by two investigators (M.G.H. and A.V.O.) before the intervention (T0), at 1 month (T1) and 12 months follow-up (T2). Its relationship was considered positive if the FH was located above the NHO plane and negative if FH was below it (Fig. 2). In order to ensure truly accurate and reproducible measurements, the examiners tagged all virtual models independently on two separate occasions (2 weeks apart), thus avoiding inter- and intra-observer differences, respectively. Inter- and intra-class correlation analyses (ICCs) were used to calculate examiner differences and reliability.[16,17]

Statistical analysis (IBM SPSS Statistics for Windows, version 25; IBM Corp., Armonk, NY, USA) was used to investigate the relationship between FH and NHO before, and 1 month and 1 year after surgery. Descriptive analysis evaluated the most relevant statistics for all analysed variables, and a Kolmogorov–Smirnov test was used to check the normal distribution of FH-NHO dimensions. In order to compare measurements at different time points and their correlation with dental class and surgical procedure, an inferential analysis was performed using the analysis of variance (ANOVA) test and the Bonferroni correction. Two-sided P-values <0.05 were considered significant for all

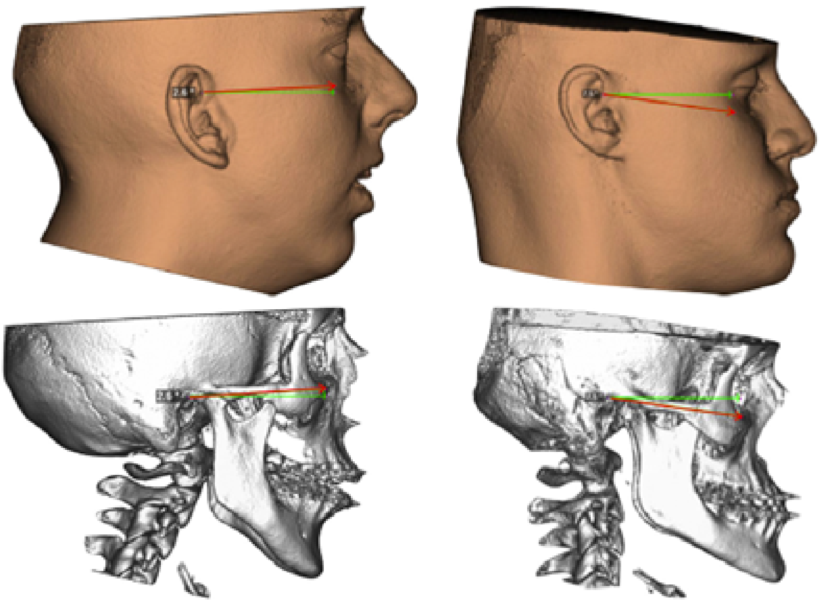

Fig. 2. Assessment of natural head orientation (NHO) and Frankfort horizontal (FH) in class II and class III patients. In these cases, NHO with respect to FH (highlighted in red) were set at 2.6° (negative) and 7.5° (positive) in class II and class III patients, respectively.

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of the statistical tests. A mixed ANOVA model reached a statistical power of 98% when detecting mean differences in NHO between groups, with a medium effect size ($f = 0.25$) and a 95% confidence interval. The statistical power was 88% with a small to medium effect size ($f = 0.15$) for intra-observer variation and differences over time (T0, T1, T2).

Results

A sample of 187 consecutive patients who underwent orthognathic surgery were included in the study. The sample comprised 124 women (66.3%) and 63 men (33.7%), with a mean age of 33.9 ± 11.2 years (range 15–67). Patients were classified as dental class I (3.2%), class II (48.7%) or class III (48.1%) according to Angle's malocclusion classification.[18] All of the selected patients underwent bimaxillary (80%) or monomaxillary (20%) surgery, of whom 55.9% and 43% received a CCW and clockwise rotation of the maxillomandibular complex, respectively. No rotational movements were performed in 1% of the sample (Table 1). The ICC obtained for angle measurements was <0.11°.

The mean baseline FH-NHO° was 2.73° ± 4.19° (2.12–3.33°, $P < 0.001$). FH-NHO° was significantly positive for the population eligible for orthognathic surgery ($P < 0.001$, *t*-test). In particular, regarding FH-NHO° related to Angle's dental class, statistically significant differences between class II and III patients in each group were observed ($P < 0.001$, test F) (Fig. 3).

Regarding FH-NHO° changes after surgery, there were no significant differences for the total sample, neither at 1-month (2.86° ± 3.12)($P = 1.000$) nor at 12-months follow-up (3.15° ± 3.19) ($P = 0.539$) (Table 2). However, a variation in FH-NHO° was observed between dental class II and III patients ($P < 0.001$) (Fig. 4). A greater impact of surgery was evidenced in class II compared with class III patients, reporting FH-NHO° changes between T0 and T2 as follows: 2.04° ± 4.79 ($P < 0.001$) and −1.20° ± 3.03 ($P < 0.001$), respectively.

No significant changes could be detected based on the type of surgery (mono- and bimaxillary surgery) ($P = 0.318$). Nevertheless, patients who received a CCW rotation in the context of a bimaxillary surgery (compared with those patients with CW or without rotational movement), FH-NHP° increased significantly ($P = 0.006$) (Fig. 5)

A multivariate model was calculated including each single independent variable in order to rule out eventual bias and confounding factors. Results showed that FH-NHO° changes significantly depend on the dental class of the patient ($P < 0.001$) and the CCW rotation performed at surgery in the bimaxillary group ($P = 0.082$) (Fig. 6).

Discussion

The head positioning of the CBCT is essential for the virtual planning of orthognathic surgery. The results of the present study show that FH is not equivalent to NHO and that a positive angle between FH-NHO exists (2.73° ± 4.19, $P < 0.001$, *t*-test). This implies that FH is located superior to the NHO plane in most cases, which is in agreement with the published literature.[5] However, when grouping patients according to dental class, class II patients showed a smaller FH-NHO angle (1.35° ± 4.29), whereas class III patients presented an increased relationship (4.15° ± 3.60) ($P < 0.001$) (Fig. 3). Emphasis should be placed when adjusting the head position of the patient during NHO registration to avoid diagnostic errors, as Class II and Class III facial types tend to compensate for their head position.[19] Class II subjects tilt their head upwards, whereas class III subjects tilt their heads downwards, thus the FH represents an upward or downward inclination in relation to the true horizontal plane, respectively.[19] Thus, it is plausible that NHO should be the 'gold standard' reference plane instead of FH, because a reliable reference plane is necessary for a correct 3D facial analysis, which becomes even more evident in patients with dentofacial deformities.[4] Needless to say, both treating orthodontists and surgeons should use the same reference plane in order to use a common terminology for treatment planning, and therefore align treatment goals, increase accuracy and improve final outcomes.

Reproducibility of NHO in the sagittal, coronal and axial planes with 3D imaging has been proven to be as reliable as with cephalometric radiographs.[17,20,21] When recording NHO three-dimensionally, a CBCT in an upright position without external immobilizers is recommended, rather than a conventional computed tomography in a supine position.[21] Although it would be desirable for patients to undergo the scan with a proper NHO, some unexpected changes in head position during the recording process are unavoidable. For this reason, new tools and softwares have been designed to record, transfer and adjust NHO properly; such as stereophotogrammetry, laser surface scanner, or digital gyroscope, among others.[17,22,23] However, the devices themselves may influence the accuracy of re-orientated head position, and in some cases may cause soft tissue distortion.[20,24,25] Therefore, surgeons usually use a simple virtual skull re-orientation method according to NHO based on frontal and lateral photographic records.[26]

As stated previously, extracranial references such as NHO allow the use of true vertical and horizontal lines as optimal reference planes for surgical planning.[27,28] In this context, the authors used a soft tissue vertical line that passes through nasion soft tissue as an absolute reference to guide the anteroposterior positioning of the maxillomandibular complex, further described elsewhere.[11]

Besides, when Class I was obtained after surgery, FH-NHO angulation in-

Table 1. Descriptive characteristics of the studied sample.

	n = 187	%
Gender		
Male	63	33.7
Female	124	66.3
Type of dentofacial deformity		
Class I	6	3.2
Class II	91	48.7
Class III	90	48.1
Type of interventions		
Bimaxillary surgery	149	79.6
Monomaxillary surgery	38	20.4
Rotational movements		
CW	80	43
CCW	104	55.9
No rotation	3	1.1
Age (mean ± SD)	33.9 ± 11.2	

CW, clockwise rotation; CCW, counterclockwise rotation; SD, standard deviation.

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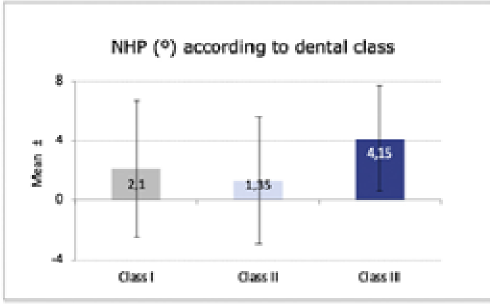

Fig. 3. Mean angle between Frankfort horizontal and natural head orientation (FH-NHO°) for class I, II and III patients. NHP, natural head position.

creased in class II patients (3.40° ± 3.41), while it reduced in class III (2.95° ± 3.04). Remarkably, final FH-NHO relationship for both groups converged after treatment yielding to a more similar value, which was close to the overall postsurgical FH-NHO value of the entire sample (3.15° ± 3.19), which can be considered a close approximation to the standard FH-NHO relationship of class I patients (Fig. 4). Therefore, this relationship was still positive, which reaffirms the earlier statement that FH is not equivalent to NHO.

The relationship between the final FH-NHO° and the patients' dentofacial deformity was greater in class II than in class III patients, which reverses the initial situation of the angle (Fig. 4). This is explained by the previous adaptation of the cranio-cervical posture, facial and neck muscles, temporomandibular joints, visual and vestibular apparatus and local proprioceptors which counteract the presurgical dental class and pattern of maxillomandibular imbalance.[12,29]

To our knowledge, this is the first study to evaluate the impact of CCW rotation on FH-NHO° after orthognathic surgery. Although head and neck posture changes after orthognathic surgery have been widely reported in the literature,[30,31] our study has demonstrated that CCW rotation of the maxillomandibular complex is significantly related to FH-NHO° changes ($P = 0.006$) (Fig. 5), which suggests that occlusal plane changes have an impact on the cranio-cervical posture.[11] This is explained by the patients' tendency to adapt their cervical spine based on their specific underlying dentofacial deformity. Then, once it is surgically corrected, there is no need for this adaptation.

The type of surgery did not induce significant changes in the NHO, but the rotational movements performed did. Therefore, when CCW rotation was performed in the context of bimaxillary surgery, FH-NHO angulation increased at 1-month follow-up (from 1.83° to 2.81°) and to a greater extent at 12-month follow-up (from 2.81° to 3.32°) (Fig. 5). Similarly, the same pattern was observed in class II patients: FH-NHO° increased immediately after surgery and even further at long-term follow-up (T0–T1–T2: 1.35°–2.84°–3.40°, respectively). However, FH-NHO° decreased significantly after surgery and remained stable over time in class III patients (T0 – T1 = T2, from 4.15° to 2.95°) (Fig. 4). This suggests that the period of adaptability of the abovementioned influencing factors in NHO is longer in class II patients when CCW rotation is performed than in class III patients.

A potential limitation to this study was the reliability analysis of NHO determination and measurement assessment. To overcome this problem, emphasis was placed on landmark identification and angle measurement. In order to ensure truly accurate and reproducible measurements, and to avoid landmark errors produced by magnification and distortion, both examiners (M.G.H. and A.V.O.) previously calibrated each virtual model by independently tagging landmarks on two separate occasions (2 weeks apart), thus avoiding inter- and intra-observer differences, respectively. ICC (inter- and intra-) analyses were performed throughout the present study.

With regard to NHO re-orientation reliability, 3D imaging techniques do not maintain the previously recorded NHO of the patient; therefore, subjective re-orientation by expert clinicians of the 3D images is needed (Fig. 1).[17] Considering this, some authors[17] have determined a moderate reliability for both intra- and inter-rater reliability in re-orientating 3D images to the estimated natural head position.[17] In their study, Zhu et al.[17] found a small median ICC difference for roll and yaw, but larger for pitch. This means that clinicians tend to position the chin posteriorly (6.3 ± 5.2 mm), reducing the perceived severity of the dentofacial deformity in the antero-posterior direction. Therefore, this data highlights the importance of orientating the 3D images prior to measuring and planning. Both calibration and ICC analyses followed those from Lagravere et al.,[16] and Zhu et al.,[17] previous studies, and measurements were taken in the three axes (x, y, z) as mentioned above. In this study, the ICC obtained by the authors for the angle variability was <0.11°. Thus, our ICC analyses for this study are in line with those previously accepted in the literature, which demonstrates the accuracy of the followed approach on NHO determination and landmark identification among different examiners.[16]

In conclusion, the results of this study suggest that pre- and postoperative NHO differs from FH in orthognathic patients. The angle between FH and NHO is significantly larger in class III patients than in class II patients at baseline, which converges after orthognathic surgery when CCW rotation is performed. Therefore, NHO should be used as the real horizontal plane when planning for orthognathic surgery.

Table 2. Mean changes in the angle between Frankfort horizontal and natural head orientation (FH-NHO°) short term (T1–T0), stability (T2–T1) and long term (T2–T0) for dental class II and III patients.

	T0	T1	T2	T1–T0	T2–T1	T2–T0
Class II	1.35 ± 4.29	2.84 ± 3.22	3.40 ± 3.41	1.48 ± 4.08 **P < 0.001*** **	0.56 ± 2.77 $P = 0.121$	2.04 ± 4.79 **P < 0.001*** **
Class III	4.15 ± 3.60	2.95 ± 3.08	2.95 ± 3.04	−1.20 ± 2.80 **P = 0.004** **	0.01 ± 2.42 $P = 1.000$	−1.20 ± 3.03 **P = 0.015***

Statistically significant results are presented in bold; $P < 0.05$. Mean ± SD and t-test from analysis of variance (ANOVA) and Bonferroni correction.

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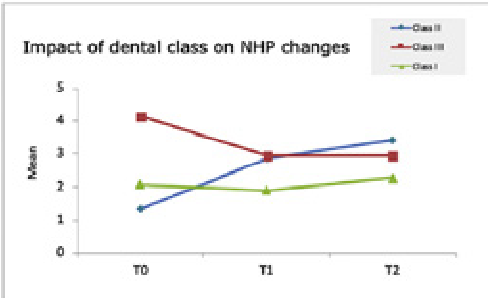

Fig. 4. Impact of dental class (I, II and III) on the angle between Frankfort horizontal and natural head orientation (FH-NHO°) over time (T0, T1 and T2). NHP, natural head position.

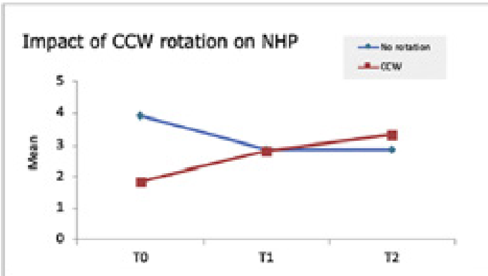

Fig. 5. Impact of counterclockwise (CCW) rotation on Frankfort horizontal and natural head position (FH-NHP°) over time (T0, T1 and T2).

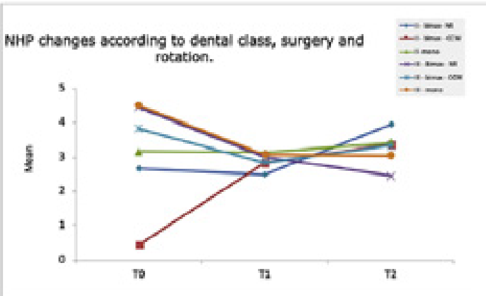

Fig. 6. Multivariate analysis of changes in the angle between Frankfort horizontal and natural head orientation (FH-NHO°) over time according to dental class (I, II or III), type of surgery (mono- or bimaxillary) and rotation [no rotation (NR) or counterclockwise (CCW)], in the short and long term.

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Competing interests

There are no competing interests.

Ethical approval

This study was approved by the Teknon Medical Hospital Institutional review board (IRB) (Barcelona, Spain) (Ref.2019/60-CMF-TEK).

Patient consent

Patient written informed consent was provided to access the CBCT database.

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References

1. Barbera AL, Sampson WJ, Townsend GC. Variation in natural head position and establishing corrected head position. *Homo* 2014;**65**(3):187–200.
2. Naini FB. The Frankfort plane and head positioning in facial aesthetic analysis – the perpetuation of a myth. *JAMA Fac Plast Surg* 2013;**15**(5):333–4.
3. Garson JG. The Frankfort Craniometric Agreement, with Critical Remarks Thereon. *Source: J Anthropol Inst Great Britain Ireland* 1885;**14**:64–83.
4. Lundström A, Lundström F. The Frankfort horizontal as a basis for cephalometric analysis. *Am J Orthod Dentofac Orthop* 1995;**107**(5):537–40.
5. Bjerin R. A comparison between the Frankfort horizontal and the sella turcica–nasion as reference planes. *Acta Odontol Scand* 1957;**15**(1):1–12.
6. Lundström A, Lundström F, Lebret. Moorrees CFA. Natural head position and natural head orientation – basic considerations in cephalometric analysis. *Eur J Orthod* 1995;**17**:111–20.
7. Moorrees CFA, Kean MR. Natural head position, a basic consideration in the interpretation of cephalometric radiographs. *Am J Phys Anthropol* 1958;**16**(2):213–34.
8. Cuccia AM, Carola C. The natural head position. Different techniques of head positioning in the study of craniocervical posture. *Minerva Stomatol* 2009;**3**(58):601–12.
9. Capon T. Standardised anatomical alignment of the head in a clinical photography studio. A comparison between the Frankfort Horizontal and the natural head position. *J Vis Commun Med* 2016;**39**(3–4):105–11.
10. Solow B, Sonnesen L. Head posture and malocclusions. *Eur J Orthod* 1998;**20**(6):685–93.
11. Savjani D, Wertheim D, Edler R. Change in cranio-cervical angulation following orthognathic surgery. *Eur J Orthod* 2005;**27**(3):268–73.
12. Paya-Argoud M, Tardieu C, Cheynet F, Raskin A, Borel L. Impact of orthognathic surgery on the body posture. *Gait Posture* 2019;**67**:25–30.
13. Hernández-Alfaro F. Upper incisor to soft tissue plane (UI-STP): A new reference for diagnosis and planning in dentofacial deformities. *Med Oral Patol Oral Cir Bucal* 2010;**15**(5):8–10.

14. Hernandez-Alfaro F, Guijarro-Martinez R. Twist technique" for pterygomaxillary dysjunction in minimally invasive Le Fort I osteotomy. *J Oral Maxillofac Surg* 2013;**71**(February (2)):389–92.
15. Haas Junior OL, Guijarro-Martínez R, Sousa Gil APde, Méndez-Manjón I, Valls-Otañón A, de Oliveira RB, et al. Cranial base superimposition of cone-beam computed tomography images. *J Craniofac Surg* 2019;**30**:1809–14.
16. Lagravère MO, Low C, Flores-Mir C, Chung R, Carey JP, Heo G, et al. Intraexaminer and interexaminer reliabilities of landmark identification on digitized lateral cephalograms and formatted 3-dimensional cone-beam computerized tomography images. *Am J Orthod Dentofac Orthop* 2010;**137**(5):598–604.
17. Zhu S, Keeling A, Hsung TC, Yang Y, Khambay B. The difference between registered natural head position and estimated natural head position in three dimensions. *Int J Oral Maxillofac Surg* 2018;**47**(2):276–82.
18. Wolford LM, Chemello PD, Hilliard F. Occlusal plane alteration in orthognathic surgery – part I: effects on function and esthetics. *Am J Orthod Dentofac Orthop* 1994;**106**(3):304–16.
19. Arnett GW, Gunson MJ. Facial planning for orthodontists and oral surgeons. *Am J Orthod Dentofac Orthop* 2004;**126**(3):290–5.
20. Weber DW, Fallis DW, Packer MD. Three-dimensional reproducibility of natural head position. *Am J Orthod Dentofac Orthop* 2013;**143**(5):738–44.
21. Cassi D, De Biase C, Tonni I, Gandolfini M, Di Blasio A, Piancino MG. Natural position of the head: review of two-dimensional and three-dimensional methods of recording. *Br J Oral Maxillofac Surg* 2016;**54**(3):233–40.
22. Hsung TC, Lo J, Li TS, Cheung LK. Recording of natural head position using stereophotogrammetry: a new technique and reliability study. *J Oral Maxillofac Surg* 2014;**72**(11):2256–61.
23. Yang HJ, Han JJ, Hwang SJ. Accuracy of 3D reproduction of natural head position using three different manual reorientation methods compared to 3D software. *J Craniomaxillofac Surg* 2018;**46**(9):1625–30.
24. Damstra J, Fourie Z, Ren Y. Simple technique to achieve a natural position of the head for cone beam computed tomography. *Br J Oral Maxillofac Surg* 2010;**48**(3):236–8.
25. Manders PJD, Wolke JGC, Jansen JA. Bone response adjacent to calcium phosphate electrostatic spray deposition coated implants: an experimental study in goats. *Clin Oral Implants Res* 2006;**17**(5):548–53.
26. Xia JJ, McGrory JK, Gateno J, Teichgraeber JF, Dawson BC, Kennedy KA, et al. A new method to orient 3-dimensional computed tomography models to the natural head position: a clinical feasibility study. *J Oral Maxillofac Surg* 2011;**69**(3):584–91.
27. Zebeib AM, Naini FB. Variability of the inclination of anatomic horizontal reference planes of the craniofacial complex in relation to the true horizontal line in orthognathic patients. *Am J Orthod Dentofac Orthop* 2014;**146**(6):740–7.
28. Meiyappan N, Tamizharasi S, Senthilkumar KP, Janardhanan K. Natural head position: an overview. *J Pharm Bioallied Sci* 2016;**2**(2):424–7.
29. Cuccia AM, Carola C. The measurement of craniocervical posture: a simple method to evaluate head position. *Int J Pediatr Otorhinolaryngol* 2009;**73**(12):1732–6.
30. Lin X, Edwards SP. Changes in natural head position in response to mandibular advancement. *Br J Oral Maxillofac Surg* 2017;**55**(5):471–5.
31. Cho D, Choi DS, Jang I, Cha BK. Changes in natural head position after orthognathic surgery in skeletal Class III patients. *Am J Orthod Dentofac Orthop* 2015;**147**(6):747–54.

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What are the Surgical Movements in Orthognathic Surgery That Most Affect the Upper Airways? A Three-Dimensional Analysis

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Purpose: Most studies have focused on airway changes after maxillomandibular advancement; however, airway size will change depending on the type, direction, and magnitude of each skeletal movement. The aim of this study was to assess the effect of the maxillary and/or mandibular movements on the pharyngeal airway volume and the minimum cross-sectional area using 3-dimensional cone-beam computed tomography voxel-based superimposition.

Patients and methods: The investigators designed and implemented a retrospective cohort study composed of patients with dentofacial deformity subjected to orthognathic surgery. The predictor variables were the surgical movements performed at surgery. The primary outcome variables were the pharyngeal airway volume and minimum cross-sectional area measured preoperatively, at 1- and 12-month follow-up. Skeletal and volumetric relapse and stability were recorded as secondary outcomes at 1 and 12 months, respectively. Descriptive, bivariate and correlation analyses were computed. Significance was set at $P < .05$.

Results: The sample was composed of 103 patients grouped as follows: bimaxillary (53), maxillary (25), or isolated mandible (25). All of the surgical treatments resulted in a significant linear pattern of initial immediate increase of 33.4% (95% confidence interval [CI]: 28.2 to 38.7%; $P < .001$) in volumetric (nasopharynx [28.7%, CI: 22.7 34.9%; $P < .001$], oropharynx [36.2%, CI: 29.0 to 43.5%; $P < .001$], and hypopharynx [31.5%, CI: 25.7 to 37.3%; $P < .001$]) and minimum cross-sectional area parameters (bimaxillary = 104%, [CI: 87.1 to 122.1%; $P < .001$], maxillary = 39.5%, [CI: 18.4 to 60.7%; $P < .05$], and mandible = 65.8%, [CI: 48.1 to 83.6%; $P < .05$]), followed by a slight downward trend (stabilization) at 12-month follow-up. Airway increase was favored by mandibular advancement ($P < .05$) and mandibular occlusal plane changes by counterclockwise rotation ($P < .05$).

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Conclusions: The results of this study suggest that there is a favorable effect of orthognathic surgery in the upper airway regardless of the surgical approach, with bimaxillary advancement and mandibular occlusal plane changes by counterclockwise rotation being the most significant contributors.

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The combination of orthognathic surgery and orthodontic treatment aims to reestablish facial esthetics and optimize dental occlusion while moving the jaws. Although orthognathic surgery corrects bone discrepancies by means of osteotomies and jaw repositioning, it also implies soft tissue changes of the facial envelope.[1] Similarly, repositioning of the muscles attached to jaws and pharyngeal walls creates significant volumetric changes in the pharyngeal airway: in general terms, the pharyngeal airway walls are expanded or diminished when the facial skeletal framework is repositioned either forward or backward, respectively.[1] Thus, pharyngeal airway dimensions will change depending on the type, direction, and magnitude of the skeletal movements.[2] As widely reported, a mean 10-mm maxillomandibular advancement (MMA) results in a mean increase in the pharyngeal airway space of 4.75 mm (range 3.15 to 6.35) and a mean pharyngeal airway volume (PAV) gain of 7.35 cm^3 (range 5.35 to 9.34) over the long-term.[3] Conversely, there is evidence to support a significant narrowing of the pharyngeal airway space after sole mandibular setback procedures (mean decrease of 4.46 mm in men and 3.20 mm in women) for treating mandibular prognathism.[4] However, no studies have evaluated the impact of the type, direction, and magnitude of the different skeletal movements on upper airway size changes in the long-term.

Therefore, we have designed the present study considering the following gaps that exist in the current literature which require more in-depth evaluation: *1)* Orthognathic surgery involves repositioning of both the maxillary and mandibular bones, and each individual repositioning is related to specific pharyngeal airway changes. Separate study is therefore required of the impact of isolated maxillary, mandibular (and chin) movements, as well as study of the maxillomandibular complex jointly; *2)* Orthognathic surgery is a procedure that implies 3-dimensional (3D) movements (counterclockwise [CCW]/clockwise rotation, advancement/setback, impaction/descent, leveling, and constriction/segmentation procedures), which behave differently at the pharyngeal level and should be evaluated separately; *3)* There are not clear guidelines or references to determine where the maxilla and mandible should be repositioned to simultaneously maximize airway volume, still not compromising facial esthetics; *4)* Orthognathic surgery impacts 3-dimensionally on PAV (sagittal, vertical, and transversal planes), so linear, volumetric, and cross-sectional measurements of the pharyngeal airway are required; *5)* Orthognathic surgery induces changes in all 3 levels of the pharyngeal airway (nasopharynx, oropharynx, and hypopharynx), so all of them need to be assessed; and finally, *6)* Pharyngeal airway changes induced by orthognathic surgery may relapse over time, so long-term trials (12 months of follow-up) are compulsory.

The purpose of this study was to assess the effect of maxillary and mandibular movements (isolated or jointly) on the pharyngeal airway (nasopharynx, oropharynx, and hypopharynx) and the minimum cross-sectional area (mCSA) on a 3D basis. The authors hypothesize that each surgical movement during orthognathic surgery impacts differently to increase the upper airway size. Thus, the specific aims of this study were to correlate the magnitude, type, and direction of these skeletal movements with the airway dimension gain or impairment and their stability or relapse at the 12-month follow-up.

Materials and Methods

STUDY DESIGN/SAMPLE

To address the research purpose, the investigators designed and implemented a retrospective cohort study. The study population was composed of consecutive patients with a dentofacial deformity who underwent orthognathic surgery between January 2018 and January 2019 at the Maxillofacial Institute (Teknon Medical Center in Barcelona, Spain). Clinical data and 3D radiological images were obtained from the institute's database.

To be included in the study sample, patients were included as study participants if they met the following criteria: *1)* age ≥ 18 years, *2)* good systemic health (American Society of Anesthesiologists score I or II), *3)* completed growth of the maxillofacial complex, *4)* patients subjected to orthognathic surgery because of occlusal, skeletal, or esthetic problems, and *5)* signed informed consent. Patients were excluded from the study if they presented *1)* any systemic/disease background capable of compromising bone healing, *2)* congenital anomalies, *3)* incomplete postoperative follow-up; and *4)* missing radiological tests.

This study followed the STROBE (Strengthening the Reporting of Observational studies in Epidemiology) statement guidelines[5] (www.strobe-statement.org), including a checklist of 22 items considered essential to report analytical observational studies, and Dodson 2015[6] updated guidelines on how to report a patient-oriented manuscript. This study was approved by the Teknon Medical Hospital Institutional Review Board (Barcelona, Spain), and all participants signed an informed consent agreement (Ref. 3D-OS-VAS). The study was carried out in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

SURGICAL PROTOCOL

All patients were operated under general anesthesia and controlled hypotension by the same surgeon (FHA). A mandible first protocol was followed in all cases. Mandibular sagittal osteotomy was performed following the Obwegeser[7] technique and settled with a hybrid technique (1 miniplate fixed with 4 monocortical screws and a retromolar bicortical screw). Maxillary procedures included Le Fort I osteotomy with or without segmental maxillary osteotomies and always through a minimally invasive approach using the twist technique described elsewhere.[8,9] All patients were extubated in the operating room, maintaining a dynamic intermaxillary fixation with guiding elastics. Antibiotics, anti-inflammatory drugs, and a closed-circuit cold mask at 17°C were prescribed during admission. Patients were discharged 24 hours after surgery. Functional training with light guiding elastics was prescribed for 1 month, with a soft diet during the same period of time.

STUDY VARIABLES

Demographic characteristics of the sample were included: age (years), gender, and type of dentofacial deformity (I, II, or III). The primary outcomes measured were PAV (mm^3) and mCSA (mm^2); the secondary outcomes measured were surgical movements (mm) and skeletal relapse (%), preoperatively and postoperatively at 1 (T1) at 12 months (T2) after surgery. Patients were divided as per the orthognathic surgery procedure involved as follows: *1)* BimaxS: combined surgery involving segmented or nonsegmented Le Fort I maxillary osteotomy and mandibular bilateral sagittal split osteotomy with or without genioplasty; *2)* MaxS: isolated segmented or nonsegmented Le Fort I maxillary osteotomy; and *3)* MandS: isolated bilateral sagittal split osteotomy with or without genioplasty. All these surgical techniques were evaluated in linear and angular measurements—advancement, setback, upward, downward, centering, noncentering, clockwise rotation, CCW rotation, and mandibular occlusal plane (MOP).

DATA COLLECTION

All patients followed the standard preoperative and postoperative imaging workflow for orthognathic surgery of the department, which involves cone-beam computed tomography (CBCT) at 3 time points: preoperatively (T0) and postoperatively at 1 (T1) and at 12 (T2) months of follow-up. The CBCT scans were performed using an i-CAT Vision system (iCAT, Imaging Sciences International, Hatfield, PA), and patients were previously instructed by trained personnel to achieve the standard key points for orthognathic surgery diagnosis and planning: the patient breathing quietly without swallowing, sitting upright in the natural head position with the Frankfort and bipupilar planes parallel to the floor; indicating the patient to look straight ahead at a point in front of them at eye level (looking into a mirror), the tongue in a relaxed position, and the mandible in centric relation with a 2-mm wax bite in place to avoid direct contact between teeth. An expert clinician paid special attention during the preoperative and postoperative CBCT to minimize posture influence in the airway evaluation.

Presurgical 3D planning was performed with Dolphin software and the soft tissue–nasion plane was used as an absolute reference to guide anteroposterior positioning of the maxillomandibular complex.[10] Intermediate and final surgical splints were printed in-house.[11]

Each patient had 3 CBCT data sets (T0, T1, and T2) that were superimposed in accordance with the voxel-based superimposition protocol described previously by the authors.[12] All CBCT scans were evaluated by the same researcher (MGH). Data were primarily saved in DICOM (Digital Imaging and Communications in Medicine) format using a 3D software (version 11.0; Dolphin Imaging, Chatsworth, CA). The software orientation calibration tool was used along pitch (x), yaw (y), and roll (z). Orientation of both the base volume (original DICOM) and second volume (duplicate DICOM) was undertaken to achieve the same original positions of the CBCTs. Then, superimposition of the preoperative CBCTS at T1 and T2 was performed using the cranial base, as it remains stable after surgery. The software allows a proper manual adjustment following the superimposition 3-step protocol: *1)* Landmark-based superimposition (side-by-side superimposition), *2)* Voxel-based superimposition (overlay superimposition by volume subregions), and *3)* Head orientation export (export to second volume).[12] This means that all the 3 images (T0, T1, and T2) were in the same coordinate position after the voxel-based superimposition (Fig 1). This position is recommended for the baseline assessment of upper airway dimensions.[13-15]

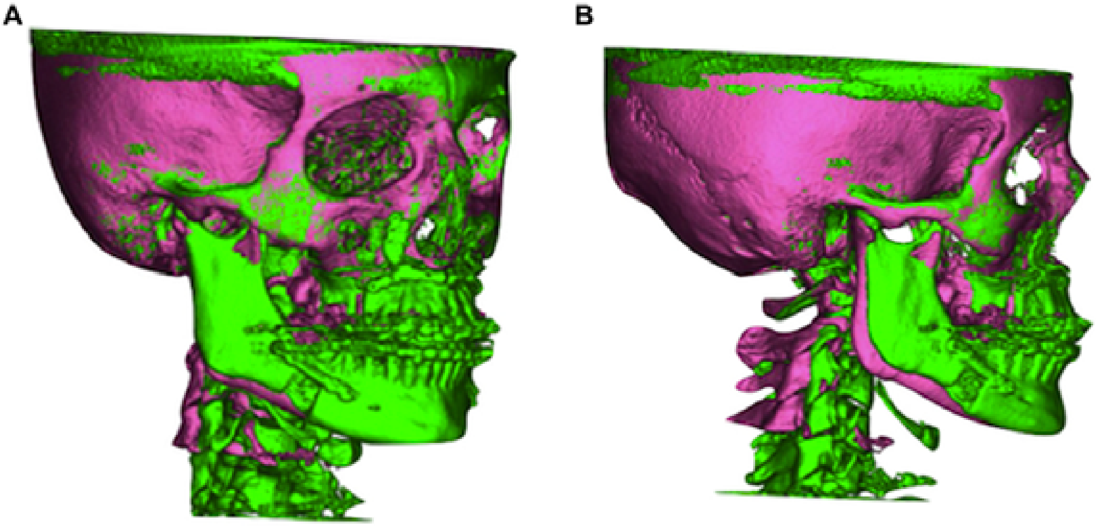

FIGURE 1. *A*, Preoperative and postoperative color map superimposition—front view. Color legend as follows: Pink, preoperative CBCT (T0); Green, postoperative CBCT (T1 or T2).*B*, Preoperative and postoperative color map superimposition—lateral view. Color legend as follows: Pink, preoperative CBCT (T0); Green, postoperative CBCT (T1 or T2).

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DATA ANALYSES

Skeletal surgical movements were assessed from angular (o) and linear measurements (mm). Upper airway data were evaluated in terms of volumetric (mm^3) and cross-sectional areas (mm^2).

Surgical Movements

The following measurements were assessed in each patient: *1)* angular: sella-nasion point A (SNA), sella-nasion point B (SNB), sella-nasion pogonion (SNPg), and MOP; and *2)* linear: posterior nasal spine (PNS), point A, point B, pogonion, most anterior point of the hyoid body, superior incisor, inferior incisor, and transversal maxilla in frontal view. The root mean square displacement of all the parameters in the reference space or system was calculated as per the following formulas:

$$\Delta\ (T1 - T0) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

$$\Delta\ (T1 - T2) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

$$\Delta\ (T2 - T0) = \sqrt{(x_2 - x_1)^2 + (y_2 - y_1)^2 + (z_2 - z_1)^2}$$

Upper Airway Analysis

Manual segmentation was performed to delimit the anatomic and technical boundaries of the upper airway at the anterior, posterior, upper, and lower limits, respectively, as reported by *Swennen and Guijarro-Martínez*.[16] In relation to the upper airway dimensions, 3 regions of interest were defined for this purpose, measuring the nasopharynx, oropharynx, and hypopharynx. The nasopharynx was delimited by the Frankfort horizontal (FH)—PNS—sphenoid bone, extended to the soft tissue pharyngeal wall contour. The oropharynx was defined beyond the FH/PNS extended to FH—most anterior point of the body of C3—soft tissue pharyngeal wall contour. Finally, the hypopharynx was assessed at FH/PNS parallel—most anterior point of the body of C3—soft tissue pharyngeal wall contour to FH/PNS parallel—most anterior pole of the body of C4. An automatic threshold value of 60 was set manually to obtain the pharyngeal airway dimension (mm^3) and mCSA (mm^2) (Fig 2).

STATISTICAL ANALYSES

The data analysis was performed using SPSS for Windows, version 25.0.0, software (SPSS Inc, Chicago, IL). Power analysis was conducted from results of a pilot study carried out on 15 patients. It was concluded that a minimum sample size of 50 patients for the global sample should be included to reach 80% power to detect volumetric changes, assuming a medium effect size (d = 0.5) and 95% of confidence. The descriptive analysis included the most relevant statistics for all analyzed variables: mean, standard deviation, minimum, maximum and median for continuous variables and absolute and relative frequencies (percentages)

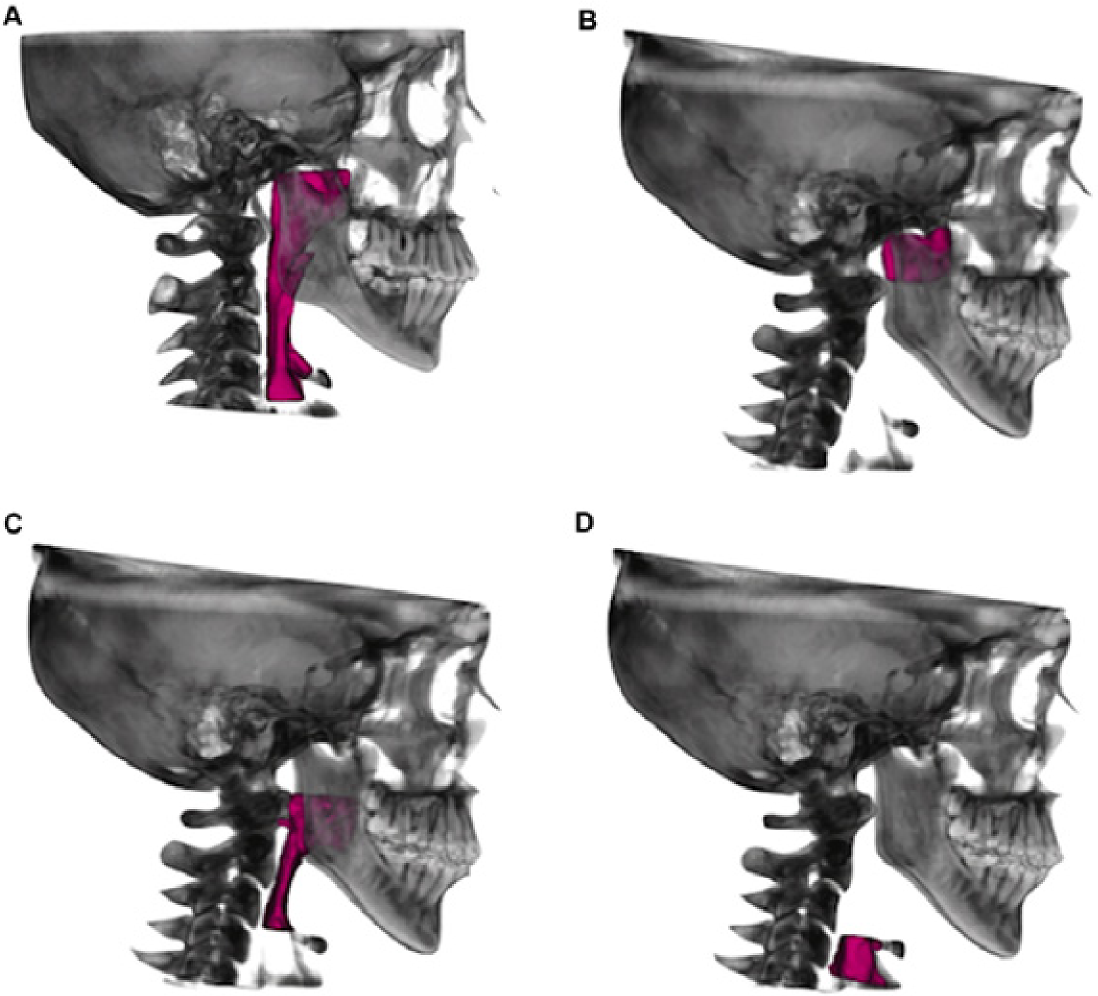

FIGURE 2. *A*, 3-dimensional total PAV assessment according to *Guijarro and Swenen, 2013* (16) PAV boundaries. *B*, 3-dimensional PAV boundaries—Delimitation of the nasopharynx PAV boundary (16).*C*, 3-dimensional PAV boundaries—Delimitation of the oropharynx PAV boundary (16). *D*, 3-dimensional PAV boundaries—Delimitation of the hypopharynx PAV boundary (16). Abbreviation: PAV, pharyngeal airway volume

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for qualitative variables. The comparative analysis included the assessment of normal distribution of the measurements using the Kolmogorov-Smirnov test. The inferential analysis included the following statistical methods: *1)* The analysis of variance general linear model for repeated measures was used to compare the evolution of the skeletal and volumetric parameters over follow-up. Multiple comparisons were made with Bonferroni correction to avoid type I error and allowed the evaluation at short-term (T1-T0), stability (T2-T1), and long-term (T2-T0) effects; *2)* Pearson's linear correlation coefficient (r) was used to estimate the degree of association between volumetric and skeletal changes, likewise in different periods; *3)* Student *t* test for independent samples (t), with use of the nonparametric Mann-Whitney U-test (MW) and Kruskal-Wallis test to assess differences in volumetric changes as per aspects of the patient profile and type of surgery; and *4)* Exploratory factor analysis of main components (principal component analysis) was performed to identify the underlying dimensions or common movement patterns of both skeletal and airway parameters between T0 and T2. For all analyses, the level of statistical significance was set at .05.

Results

The study sample comprised a total of 103 patients, 36 men (35%) and 67 women (65%), with a mean age of 31.9 ± 10.9 years (range 18 to 60). Preoperatively, 52.4% of the sample presented dentofacial deformity Class II, 45.6% Class III, and 2% Class I dentofacial deformities. Descriptive and demographic data with regard to the surgical characteristics involved in each group (Bimax, MaxS, or MandS) are presented in Table 1. The analysis regarding the linear and angular skeletal changes in the 3 groups are presented in Table 2. In turn, Table 3 displays the preoperative, postoperative (short- and long-term), and final percentages of variations (long-term gain and relapse) in the volumetric and mCSA measurements. Overall, an immediate positive effect (T1-T0) of orthognathic surgery on the skeletal, volumetric, and cross-sectional parameters was observed, followed by a slight downward trend and stabilization over time (T2) in all the 3 groups.

BIMAXILLARY ORTHOGNATHIC SURGERY

Although there was a small skeletal relapse at the long-term (T1-T2), with statistical significance being

Table 1. DESCRIPTIVE STATISTICS FOR STUDY POPULATION FOR THE 3 GROUPS (BIMAXS, MAXS, AND MANDS) (N = 103)

	BimaxS (n = 53)		MaxS (n = 25)		MandS (n = 25)	
Demographic Variables	n	%	n	%	n	%
Gender						
Male	15	28.3	12	48	16	64
Female	38	71.7	13	52	9	36
Type of dentofacial deformity						
Class I	0	0	2	8	0	0
Class II	32	60.4	0	0	22	88
Class III	21	39.6	23	92	3	12
Maxilla						
Segmented LeFort I	28	52.8	9	36	-	-
Nonsegmented LeFort I	25	47.2	16	64	-	-
Advancement	53	100	25	100	-	-
Setback	0	0	0	0	-	-
Upward (impaction)	16	30.2	4	16	-	-
Downward (descend)	11	20.8	12	48	-	-
No vertical movement	26	49.1	9	3.6	-	-
Centering	21	39.6	5	20	-	-
No centering	32	60.4	20	80	-	-
Mandible						
BSSO	43	81.1	-	-	23	92
Setback	2	3.8	-	-	2	8
Centering	27	50.9	-	-	17	68
No centering	26	49.1	-	-	8	32
Chin						
Advancement genioplasty	26	49.1	-	-	3	12
No sagittal genioplasty	27	50.9	-	-	22	88
Downwards (descend)	5	9.4	-	-	2	8
No vertical genioplasty	48	90.6	-	-	23	92
Rotational movements						
CW	4	7.5	0	0	0	0
CCW	49	92.5	25	100	3	12
No rotation	0	0	0	0	22	88
Age (mean ± SD)	29.6 ± 9.4		39.7 ± 9.2		29.1 ± 12	

Abbreviations: BimaxS, bimaxillary surgery; BSSO, bilateral sagittal split osteotomy; CW, clockwise rotation; CCW, counterclockwise rotation; MandS, mandibullary surgery; MaxS, maxillary surgery; SD, standard deviation.

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Table 2. LINEAR AND ANGULAR SKELETAL CHANGES AT 1- AND 12-MONTH FOLLOW-UP IN THE 3 GROUPS (BIMAXS, MAXS, AND MANDS)

Angles and Skeletal Movements*	BimaxS			MaxS			MandS		
	T1-T0	T1-T2	T2-T0	T1-T0	T1-T2	T2-T0	T1-T0	T1-T2	T2-T0
Max adv	**5.9 ± 4.9**	**1.2 ± 0.6**	**5.6 ± 4.8**	**14.4 ± 9.5**	**0.1 ± 0.1**	**14.4 ± 9.5**	0.03 ± 0.14	0.0 ± 0.0	0.03 ± 0.14
Mand adv	**14.2 ± 11.4**	**2.9 ± 10.8**	**12.7 ± 8.1**	**0.5 ± 1.9**	**0.01 ± 0.03**	**0.5 ± 1.9**	**5.1 ± 3.5**	**0.5 ± 0.3**	**5.2 ± 3.6**
Chin adv	**16.8 ± 10.3**	**1.4 ± 1.1**	**16.6 ± 10.2**	0.6 ± 2.3	0.00 ± 0.02	0.5 ± 2.3	**6.4 ± 4.1**	**0.4 ± 0.3**	**6.4 ± 4.2**
SNA	**4.4 ± 2.8**	**−0.7 ± 1.0**	**3.7 ± 2.9**	**4.3 ± 3.5**	−0.07 ± 0.15	**4.2 ± 3.5**	−0.01 ± 0.12	0.01 ± 0.09	0.0 ± 0.1
SNB	**6.2 ± 4.1**	−0.1 ± 0.9	**6.1 ± 4.2**	02 ± 1.6	−0.02 ± 0.08	0.1 ± 1.6	**2.9 ± 3.3**	−0.2 ± 0.7	**2.7 ± 3.0**
SNPg	**7.4 ± 5.1**	−0.2 ± 1.6	**7.2 ± 5.2**	−0.2 ± 1.5	−0.01 ± 0.04	−0.2 ± 1.2	**2.6 ± 3.1**	−0.02 ± 1.58	**2.6 ± 2.6**
PNS	**5.7 ± 3.9**	**1.2 ± 1.1**	**5.9 ± 3.7**	**12.4 ± 9.0**	**0.1 ± 0.1**	**12.4 ± 9.03**	0.06 ± 0.22	0.01 ± 0.04	0.07 ± 0.22
Hyoid	**18.0 ± 13.3**	**2.5 ± 6.8**	**17.1 ± 11.7**	1.5 ± 3.8	0.01 ± 0.03	1.5 ± 3.8	**9.9 ± 5.6**	**0.4 ± 0.4**	**9.9 ± 5.7**
Max Exp.	**4.0 ± 4.4**	−0.05 ± 0.4	**3.9 ± 4.3**	**2.2 ± 3.5**	0.0 ± 0.0	**2.2 ± 3.5**	0.07 ± 3.83	0.1 ± 0.4	0.2 ± 3.6
MOP	**5.3 ± 4.6**	0.4 ± 1.8	**5.7 ± 4.9**	−0.5 ± 6.0	0.2 ± 0.4	−0.3 ± 62	1.5 ± 5.3	−0.3 ± 1.0	1.2 ± 5.6

Note: Statistically significant parameters are presented in bold: $P < .05$. Mean ± SD and t test from analysis of variance and Bonferroni correction. Angular SNA, SNB and SNPg measurements are given in terms of rotation. Values are presented as mean ± SD.

Abbreviations: Chin adv, pogonion advancement (pogonion); Mand adv, mandibular advancement (B point); Max adv, maxillary advancement (A point); Max exp, maxillary transversal expansion; MOP, mandibular occlusal plane (MOP reduction in terms of rotation); SD, standard deviation; SNA, sella-nasion point A; SNB, sella-nasion point B; SNPg, sella-nasion pogonion.

* Max adv, Mand adv, Chin adv, Hyioid, PNS, and Max Exp. are given in mm and SNA, SNB, SNPg, and MOP are given in.

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Table 3. VOLUMETRIC CROSS-SECTIONAL MEASUREMENTS AND PERCENTAGE VARIATION IN THE 3 GROUPS PREOPERATIVELY AND POSTOPERATIVELY AT 1- (T1) AND 12-MONTH FOLLOW-UP (T2)

PAV Subregions*	T0	T1	T2	Long-Term Gain (%)	95% CI	*P*-Value
BimaxS						
Nasopharynx	7397.9 ± 1973.4	11426.3 ± 3219.9	10475.7 ± 2883.3	41.6	30.9 to 52.3	<.001§
Oropharynx	16200.6 ± 5397.6	26850.0 ± 7539.5	23199.2 ± 6510.7	43.2	32.1 to 54.3	<.001§
Hypopharynx	4111.5 ± 1274.2	6703.8 ± 1471.3	5692.0 ± 1310.7	38.4	29.7 to 47.2	<.001§
Total PAV	27720.6 ± 6534.3	44905.8 ± 9881.0	39336.8 ± 8338.1	41.9	33.6 to 50.2	<.001§
mCSA	120.9 ± 59.3	290.9 ± 96.5	247.4 ± 76.9	104	87.1 to 122.1	<.001§
MaxS						
Nasopharynx	8980.3 ± 1545.9	11745.1 ± 2637.2	11000.2 ± 1928.9	22.5	13.6 to 31.4	<.001§
Oropharynx	17649.2 ± 4662.1	23988.4 ± 6632.8	22755.3 ± 6039.0	28.9	14.8 to 43.1	<.001§
Hypopharynx	4356.6 ± 844.9	5153.7 ± 971.6	5049.5 ± 1040.3	18.3	9.1 to 27.5	.001‡
Total PAV	30986.2 ± 6010.3	41143.0 ± 8689.7	38909.3 ± 7421.9	26	15.7 to 35.5	<.001§
mCSA	168.2 ± 67.1	239.8 ± 89.2	234.7 ± 86.2	39.5	18.4 to 60.7	<.05†
MandS						
Nasopharynx	8602.6 ± 1612.1	10210.0 ± 2463.8	9635.2 ± 2048.2	12	2.2 to 21.8	<.001§
Oropharynx	16603.6 ± 4157.9	24666.7 ± 6355.1	21541.5 ± 5494.4	29.7	16.1 to 43.4	<.001§
Hypopharynx	4174.8 ± 948.7	6208.5 ± 1613.1	5,466.2 ± 1297.1	30.9	18.1 to 43.8	<.001§
Total PAV	29381.1 ± 5803.1	41085.3 ± 8689.7	36643.0 ± 6656.5	25	15.4 to 34.1	<.001§
mCSA	136.5 ± 54.4	231 ± 56.9	226.5 ± 58.9	65.8	48.1 to 83.6	<.05†

Note: Values are presented as mean ± standard deviation unless indicated.

Abbreviations: BimaxS, bimaxillary group; CI, confidence interval; MandS, isolated mandibular group; mCSA, minimum cross-sectional area; MaxS, monomaxillary group; PAV, pharyngeal airway volume.

* Nasopharynx, oropharynx, hypopharynx, and total PAV are given in mm^3 and mCSA are given in mm^2.

† $P < .05$.

‡ $P < .01$.

§ $P < .001$.

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reached only for SNAo (-0.6 ± 1.0°; $P < .001$; Table 2), no significant changes were observed for PAV and for mCSA. On average, the final PAV and mCSA gains were 41.9%, (95% CI: 33.6 to 50.2%; $P < .001$) and 104% (95% CI: 87.1 to 122.1%; $P < .001$), respectively (Table 3).

Correlation analysis showed volume gain (total or subregional) at T2 to be favored by certain surgical movements (vs the absence of them): maxillary CCW rotation—downward displacement of PNS at nasopharynx (7,456.5 vs 4,121.5 mm^3, r = 0.045, $P < .05$); mandibular CCW rotation at oropharynx (9,837.7 vs 5,845.6 mm^3, t = 0.013, $P < .05$); centering of the maxilla at oropharynx (8,922.2 vs 5,736.3 mm^3, t = 0.041, $P < .05$); and sagittal mandibular advancement at hypopharynx (2,500 vs 523 mm^3, MW = 0.012, $P < .05$). The total PAV was mainly influenced by maxillary CCW rotation (18,652.5 vs 9,757 mm^3, Kruskal-Wallis test = 0.032, $P < .05$), centering of the mandible (13,313.3 vs 9,853.6 mm^3, t = 0.049, $P < .05$), and MOP increase (r = 0.272, $P = .049$). Therefore, when quantifying major volumetric variations based on skeletal changes, hypopharynx volume gain was increased by 61.4 mm^3 for every 1 mm of mandibular advancement ($P < .001$) and by 102.4 mm^3 for every 1 mm of downward movement of the posterior maxilla in terms of PNS displacement (r = 0.304, $P < .05$). In relation to cross-sectional parameters, changes in mCSA were directly correlated with a further increment in size of the upper airway ($r^2 = 0.421$, $P < .001$). In particular, for every 1 mm^2 of mCSA increase, a mean gain of 31.88 mm^3 in total PAV was observed ($r^2 = 0.177$, $P < .001$).

SINGLE-JAW ORTHOGNATHIC SURGERY (MaxS OR MandS)

Regarding skeletal relapse rates, the MaxS group presented significant relapse of final PAV when vertical movement of the maxilla without rotation was performed (23%, mean relapse of 6,850.5 mm^3 Kruskal-Wallis test = 0.020, $P < .05$), but this proved irrelevant compared with the total volume gain at T2 (mean 38,909.3 ± 7,421.9 mm^3). In the case of the MandS group, the greater the setback movement (pogonion reduction), the greater the observed PAV relapse at hypopharynx level (mean reduction of 1,789 mm^3, $r^2 = 0.367$, $P < .001$; Table 2).

Total PAV gain for single-jaw surgeries was smaller when compared with the BimaxS group, with a 26%

increase for MaxS (95% CI: 15.7-5.5; $P < .001$) and 25% for MandS (95% CI: 15.4-34.1; $P < .001$). In the same line as for PAV, the cross-sectional parameters increased significantly by 39.5% (95% CI: 18.4 to 60.7%; $P < .05$) and 65.8% (95% CI: 48.1 to 83.6%; $P < .05$) in the MaxS and MandS groups, respectively. As per Angle's classification, the total volume gain was greater in Class II than in Class III malocclusion (12,958 vs 3,054 mm^3; $P < .05$; Table 3).

Correlations between beneficial surgical movements (vs the absence of them) in terms of PAV and mCSA gains were identified for both groups: *1)* MaxS: segmentation at nasopharynx level (2,370 vs 1,594 mm^3, MW = 0.032, $P < .05$) and displacement of the PNS at oropharynx level—maxilla CCW rotation with posterior downward displacement (6,324 vs 3,712 mm^3, r = 0.571, $P = .003$). The total PAV gain was positively influenced by maxillary advancement (9,107 vs 6,724.5 mm^3, r = 0.605, $P = .001$) and by centering of the maxilla (8,156.2 vs 6,990.8 mm^3, MW = 0.075, $P < .05$) and *2)* MandS: mandibular advancement at hypopharynx level (1,457.1 vs -613.5 mm^3, MW = 0.013, $P < .05$), CCW rotation (5,139.77 vs 3,457.33 mm^3, MW 0.027, $P < .05$), and sagittal chin advancement (with genioplasty) (6,791.3 vs 4,585.1 mm^3, MW = 0.046, $P < .05$) at oropharynx level. The total PAV was enlarged by mandibular advancement (7,981.1 vs 1,009 mm^3, r = 0.494, $P = .012$). Finally, vertical upward (2.27 ± 5.99 mm) and sagittal forward displacements (2.58 ± 5.44 mm) of the hyoid bone were correlated to mandibular advancement and greater PAV gain at the long-term (r = 0.435, $P = .030$). Then, quantification analyses of relevant PAV and cross-sectional changes were as follows: *1)* MaxS: 1 mm of maxillary advancement implied 373.3 mm^3 total volume gain ($P = .020$); 1 mm of PNS displacement implied an average total PAV gain of 556.9 mm^3 ($P = .002$); 1° of SNA increase by CCW rotation of the maxilla implied a mean nasopharynx gain of 151.6 mm^3 ($P = .011$) and *2)* MandS: 1° of MOP CCW resulted in 605.4 mm^3 total PAV gain ($r^2 = 0.628$, $P = .003$). No correlations between mCSA and 1-jaw surgeries were found in our study.

Discussion

The purpose of this study was to assess the effect of maxillary and mandibular movements on the pharyngeal airway on a 3D basis in patients subjected to orthognathic surgery, either bimaxillary or monomandibular. The authors hypothesized that each surgical movement during orthognathic surgery impacted differently to increase or decrease the upper airway dimension. Thus, to address this hypothesis, the authors identified 3 groups of patients who underwent bimaxillary or monomandibular surgery (Bimax, MaxS, and MandS) to evaluated the PAV and mCSA changes at 1- and 12-month follow-up.

Overall, the positive effect of either monomandibular or bimaxillary surgery was proven in all aspects (linear, cross-sectional, and volumetric analysis): an immediate increase in PAV and mCSA, with bimaxillary advancement and MOP changes by CCW rotation, was the most significant contributor. Our results show that forward surgical procedures in both the maxilla and the mandible were carried out in almost the entire sample, regardless of the initial dentofacial deformity involved (Class I, II or III). In fact, only 4 patients (2 BimaxS and 2 isolated MandS cases) received mandibular setback surgery. This is consistent with the upper incisor-to-soft tissue plane surgical 3D planning protocol used by the authors and previously described elsewhere[10] and which is used as an absolute reference to guide the anteroposterior positioning of the maxillomandibular complex, irrespective of the previous occlusal problems (Class II or III). Once in Class I, the complex is displaced and rotated so both the upper incisor and soft tissue pogonion lie (1 to 5 mm) in front of this plane.[10] However, the PAV gain was greater in patients with Class II occlusion than in patients with Class III occlusion (patients with Class II occlusion presenting 12% [95% CI: 10.1 to 22.1] more PAV gain than patients with Class III occlusion, [MW: 0.020, $P < .05$]). This is explained because this population in general requires greater mandibular advancement, which is considered to be the main factor for increasing PAV.

Our results are in line with those of many authors who have found that MMA increases PAV and that the effect remains stable at 1 year of follow-up.[17-19] A linear mean maxillary advancement of 6.41 ± 7.72 mm, mandibular advancement of 9.92 ± 8.05 mm, and a global chin advancement of 10.22 ± 10.27 mm (isolated chin 3.85 ± 2.06) were achieved, with a subsequent mean total PAV increase of 33.4% (95% CI: 28.2 to 38.7%; $P < .001$) for the global sample—the results being more significant in the BimaxS group 42% (95% CI: 33.6 to 50.2%; $P < .001$) (nasopharynx, oropharynx, and hypopharynx increments of 41.6, 43.2, and 38.4%, respectively). When isolated maxillary or mandibular surgeries were performed, volume gain was obtained but to a lesser extent compared with the BimaxS group, with an average PAV increase of 26% (95% CI: 15.7 to 35.5; $P < .001$) in the MaxS group (nasopharynx, oropharynx, and hypopharynx: 22.5, 28.9, and 18.3%, respectively) and 25% (95% CI: 15.4 to 34.1; $P < .001$) in the MandS group (nasopharynx, oropharynx, and hypopharynx: 12, 29.7, and 30%, respectively; Table 3). It thus can be affirmed that both maxillary and mandibular movements impact on the 3 levels of the PAV, although

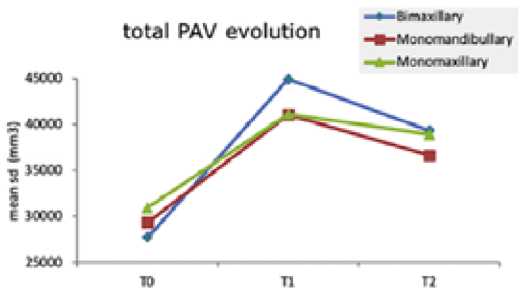

FIGURE 3. Total upper airway evolution as per type of surgery at long-term (T2-T0) in the 3 groups. Abbreviation: PAV, pharyngeal airway volume

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maxillary forward movements further widen the oropharynx > nasopharynx > hypopharynx, whereas mandibular forward movements further widen the hypopharynx > oropharynx > nasopharynx, in these orders. Obviously, bimaxillary surgeries that move the entire maxillomandibular complex increase total PAV and cross-sectional parameters even further (Fig 3). In this regard, it is important to underscore that 1-jaw surgeries (MaxS and MandS) yielded similar volumetric gains in our study—only the MandS group achieving less volume compared with the MaxS group, which is explained because most isolated mandibular surgeries involved only mandibular centering without any advancement or CCW rotation.

As previously stated, some movements significantly favored PAV gain, whereas some jeopardized it. With regard to 2-jaw surgeries, mandibular advancement ($P < .05$) and CCW rotation of the mandible ($P < .05$) favored PAV gain at oropharynx and hypopharynx level. Hypopharynx airway volume was increased by 61.4 mm^3 for every 1 mm of mandibular advancement. Our results suggest that 55% of the PAV changes after orthognathic surgery are explained by mandibular surgical movements ($r^2 = 0.547$, $P < .001$). This is in line with the literature,[2,3] which suggests that the influence of the mandible plays a major role in widening both mCSA and PAV in the long-term. In the same way as for mandibular advancement, a mean 5.74 ± 4.90° reduction of the MOP ($r^2 = 0.272$, $P = .049$) in terms of CCW rotation significantly incremented both total PAV ($P < .05$) and nasopharynx volume ($P < .05$), with a 68.2% (95% CI: 42.8 to 88.3%, $P < .05$) more of total PAV gain when compared with the absence of rotation. Thus, our results support that MOP stabilization ($P < .05$) by CCW rotation determines the final volume gain. This is owing to the advancement of the suprahyoid muscles by both the mandibular advancement and the correction of the MOP at the time of surgery, allowing further expansion of airway size, with a subsequent volume gain.[17] Previous studies focused on the normalization of the MOP to achieve an increment in the upper airway. Our findings are in agreement with those published by Rubio et al.,[17] who associated a 6- to 10-mm mandibular advancement with concomitant correction of MOP by CCW rotation to be essential for incrementing mCSA and PAV.

A positive effect of the downward movement of the posterior maxilla in terms of PNS displacement was observed in relation to total PAV and hypopharynx for BimaxS and MaxS ($P < .05$ and $P < .001$), respectively. One millimeter of downward movement of the posterior maxilla (PNS) resulted in 102.4 mm^3 of hypopharynx gain. The descent of the posterior part of the maxilla (PNS) together with a CCW rotation enlarges the pharynx because the muscles of the soft palate are pulled to an anterior and downward position, which favors the upper airway space. In addition, segmentation/expansion and sagittal advancement of the maxilla incremented nasopharynx and total PAV gain ($P < .05$). Greater oropharyngeal and total volume were achieved when centering of the maxilla was performed compared with noncentering (8,922.2 mm^3 vs 5,736.3 mm^3; $P < .05$). This occurs because maxillary asymmetry may trigger muscular constriction on 1 side of the upper airway. To our knowledge, the present study is the first to describe a potential relationship between maxillary asymmetries and constriction of the upper airway.

On the other hand, concomitant chin advancement during mandibular advancement significantly improved the airway at oropharynx level ($P < .05$). Chin advancement involves forward movement of the genial tubercles, which together with the hyoid movements, potentially leads to more airway flow.[20] In addition, a recent meta-analysis has evidenced that MMA together with genioplasty significantly increase PAV ($P < .001$).[3] In this same line, there was a clear relationship between mandibular advancement and hyoid advancement and ascent, with a subsequent PAV increase ($P < .05$). The hyoid bone is a mobile structure anchored to both the pharyngeal wall and to mandibular anatomical structures, exerting a pulley function between them. Thus, this structure assumes a major role in widening the upper airway when hyoid-mandibular muscles are straightened or tensed.[21]

Finally, mention must be made of the relationship between mCSA increase and final PAV gain. Our results showed that for each square millimeter of mCSA increase, there was a 32 mm^3 of total PAV gain after bimaxillary surgery ($P < .001$). Thus, minimal CSA increase is extremely important in terms of maximizing airflow through the oropharynx and minimizing friction and resistance of air penetration to the respiratory region. It should be noted that the mCSA increase doubled in size (104%, [95% CI: 87.1 to 122.1%; $P < .001$]) in the BimaxS group compared with the effect of isolated maxillary procedures (39.5% [95% CI: 18.4 to 60.7%; $P < .05$]) or sole mandibular surgery (65.8%, [95% CI: 48.1 to 83.6%; $P < .05$]). An explanation for this is that the pharyngeal walls are complex structures mainly composed of muscles (superior, middle, and inferior constrictors muscles among others) that delimit upper airway flow. However, although monomaxillary procedures increased mCSA and increased the pharyngeal volume, bimaxillary procedures, by moving the whole maxillomandibular complex together, allow further widening of the airway and constriction areas. Therefore, bimaxillary surgery should be contemplated to secure further increase in terms of mCSA and PAV. In addition, other studies associated the differences in constriction areas between patients with Class II and Class III occlusion with tongue position as well as adenoid and tonsillar hypertrophy[22]—though constriction areas are mainly found in the oropharynx and hypopharynx regions, owing to severe systemic consequences such as obstructive sleep apnea (OSA).[23] In this same line, Schendel et al.[24] observed a relationship between OSA and constriction areas, reporting a high probability of developing OSA when mCSA was < 52 mm^2; an intermediate probability when 52 to 110 mm^2; and a low probability when > 110 mm^2. Hence, 3D surgical planning in individuals potentially at risk of suffering from or developing OSA should be patient-tailored and considered in all future primary studies.[3]

In contrast, other surgical movements penalized volume gain: total vertical downward movement of the maxilla without rotation reduced nasopharynx volume (MaxS; $P < .05$), and isolated setback procedures in the mandible reduced hypopharynx volume gain (BimaxS and MandS; $P < .05$ and $P < .01$, respectively). Our results are also consistent with the data found in the literature,[25,26] where mandibular setback procedures were found to result in higher upper airway constriction ($P < .05$) and became a risk factor for developing OSA when exceeding 4-8 mm of setback movement of the mandible.[26] Likewise, as reported by Lee et al.[27], isolated either maxillary (maxillary setback Le Fort I osteotomy) or mandibular setback surgery decreased both oropharynx and hypopharynx volumes and significantly reduced mCSA ($P < .05$). However, no cases of isolated maxillary setback were reported in our study.

Overall, a linear pattern of initial immediate increase in pharyngeal airway volumetric parameters followed by a slight downward trend related to skeletal relapse was observed during the study in all 3 groups (Fig 3). Global relapse was 10%, which was insufficient to offset the total PAV and mCSA gains, regardless of the surgical approach involved. Greater PAV relapse occurred mainly at oropharynx level ($-2,936.41$ mm^3), compared with > nasopharynx (-809.45 mm^3) and > hypopharynx (-762.85 mm^3), though statistical significance was not reached. The oropharynx was probably the most relapse-prone area, owing to the impact of both maxillary and mandibular bones relapses, apart from being the most enlarged area after surgery. In our study, skeletal relapses referred to the different groups only proved significant for maxillary procedures: SNA in terms of rotation ($P < .001$) and downward vertical movement of the maxilla without rotation ($P < .05$). This is consistent with the observations of Haas Junior et al.,[28] who together with our team proposed a hierarchical pyramid to assess the stability of orthognathic surgery as per surgical movements. The authors found surgical movements in the maxilla to be more relapse-prone (unstable) than mandibular procedures (highly stable).[28,29] Hence, we highlight this pyramid as an additional tool for helping surgeons to choose the technique with the best surgical outcomes and for reducing (but not avoiding) skeletal and volumetric relapse to a certain degree.

To avoid measurement error, emphasis was placed on the 3D voxel-based superimposition protocol in measurement assessment throughout the study. This protocol was chosen because it enables unbiased analysis of surgical outcomes based on a software application that affords accuracy and precision and avoids complex, technically demanding, and time-consuming measurements.[12] This study exemplifies the recommended method. The results of this study, however, should be interpreted with caution. Although many authors fail to give information on the protocol used for 3D skeletal and volumetric measurements in their primary studies, it is important to standardize these factors for homogeneity purposes and thus to be able to draw relevant conclusions from our studies.

A limitation to this study is that it was a retrospective study and therefore subjected to the usual biases of its nature. Then, the improvement of the clinical symptoms of OSA was not assessed. In particular, although our results confirm the use of MMA as a stable procedure to enlarge the upper airway dimensions, the relationship between our results and patient sleep parameters could not be evaluated by polysomnography preoperatively and postoperatively (at T1 and T2). As a result, we were unable to establish which surgical movement is more effective in terms of treating OSA, as well as to equate skeletal and volumetric changes with the changes in clinical symptoms of OSA. An ongoing prospective study (ClinicalTrials.gov ID NCT03796078 registration) regarding sleep and patient-centered parameters will determine whether there are any correlations between the direction, magnitude, and type of surgical movement and the increase in PAV and cross-sectional areas with definitive curing of OSA, and whether orthognathic surgery

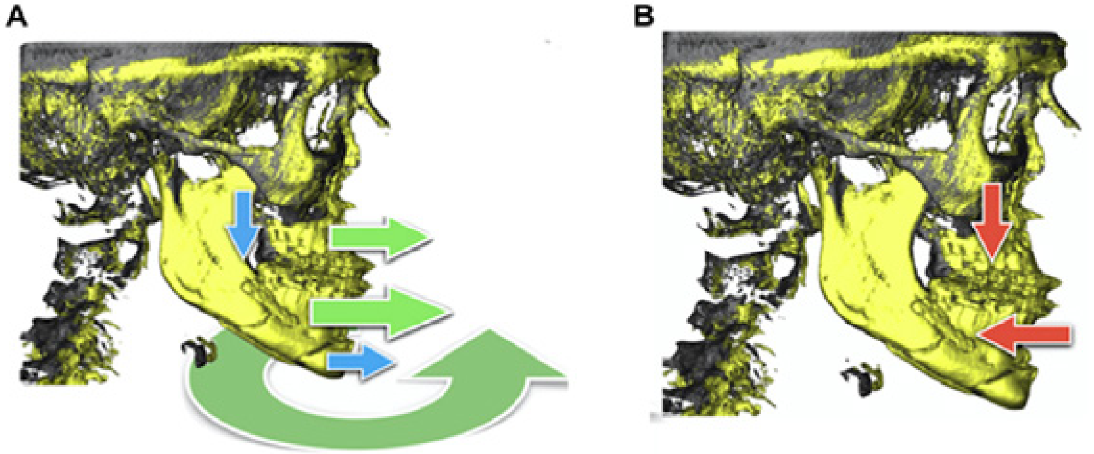

FIGURE 4. *A*, Surgical planning protocol for maximizing the upper airway. Hierarchical graphic representation of the increase/decrease in upper airway as per surgical movements in orthognathic surgery. Illustration of the favoring surgical movements to increase upper airway (CCW rotation, mandibular and maxillary advancements [*green arrows*]); movements to further increase PAV for chin advancements and posterior maxillary displacement of the PNS (*blue arrows*).*B*, Nonfavorable surgical movements (total maxillary downward and setback mandibular movements) which jeopardize the upper airway (*red arrows*). Abbreviations: CCW, counterclockwise; PAV, pharyngeal airway volume.

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should be considered part of the first-line armamentarium for OSA treatment in selected patients.

To summarize, taking into account the different variables analyzed, the surgical movements and upper airway gain correlated beyond the sample size with short- and long-term relapse, we suggest a basic surgical protocol when the main concern is the upper airway. We believe that all the surgical planning should begin with the idea that bimaxillary advancement with CCW rotation is necessary, and whenever possible, chin advancement and CCW rotation with posterior maxillary downward displacement must be considered to allow further airway improvement (Fig 4).

In conclusion, the results of this study suggest that orthognathic surgery, when planned and executed using soft tissue–nasion plane as an absolute reference, induces 3D increments at all levels of the pharyngeal airway in the long-term, regardless the surgical technique involved, with bimaxillary advancement and MOP changes by CCW rotation being the most significant contributors. Conversely, total maxillary downward displacement without rotation and mandibular setback movements penalized PAV gain in the different groups ($P < .05$, $P < .01$). However, a 10% skeletal and volumetric relapse should be expected at the 12-month follow-up. A continued research effort into the study of the diverse anatomic and nonanatomic factors that affect skeletal and airway size relapse after orthognathic surgery will allow a better match between personalized surgery-induced movements and a defined protocol to achieve a long-lasting success of the surgical treatment.

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References

1. Christovam IO, Lisboa CO, Ferreira DMTP, et al: Upper airway dimensions in patients undergoing orthognathic surgery: A systematic review and meta-analysis. Int J Oral Maxillofac Surg 45:460, 2016
2. Hernandez-Alfaro F, Guijarro-Martinez R, Mareque-Bueno J: Effect of mono- and bimaxillary advancement on pharyngeal airway volume: Cone-beam computed tomography evaluation. J Oral Maxillofac Surg 69:e395, 2011
3. Giralt-Hernando M, Valls-Ontañón A, Guijarro-Martínez R, et al: Impact of surgical maxillomandibular advancement upon pharyngeal airway volume and the apnoea-hypopnoea index in the treatment of obstructive sleep apnoea: Systematic review and meta-analysis. BMJ Open Respir Res 6:1, 2019
4. Mattos CT, Vilani GNL, Sant'Anna EF, et al: Effects of orthognathic surgery on oropharyngeal airway: A meta-analysis. Int J Oral Maxillofac Surg 40:1347, 2011
5. von Elm E, Altman DG, Egger M, et al: The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. Int J Surg 12:1495, 2014
6. Dodson TB: Writing a Scientific Paper is not Rocket Science!. J Oral Maxillofac Surg 73:S160, 2015
7. Obwegeser H: The indications for surgical correction of mandibular deformity by the sagittal splitting technique. Br J Oral Surg 1:157, 1963
8. Hernandez-Alfaro F, Guijarro-Martinez R: "Twist technique" for pterygomaxillary dysjunction in minimally invasive Le Fort I osteotomy. J Oral Maxillofac Surg 71:389, 2013

9. Raffaini M, Hern F, Paredes-de-sousa-gil A, et al: Three-dimensional analysis of long-term stability after bilateral sagittal split Ramus osteotomy fixed with a single miniplate with 4 monocortical screws and 1 bicortical Screw: A retrospective 2-Center study. J Oral Maxillofac Surg 75:1036, 2017
10. Hernández-Alfaro F: Upper incisor to soft tissue plane (UI-STP): A new reference for diagnosis and planning in dentofacial deformities. Med Oral Patol Oral Cir Bucal 15:8, 2010
11. Aboul-Hosn Centenero S, Hernandez-Alfaro F: 3D planning in orthognathic surgery: CAD/CAM surgical splints and prediction of the soft and hard tissues results - our experience in 16 cases. J Craniomaxillofac Surg 40:162, 2012
12. Haas Junior OL, Guijarro-Martínez R, Sousa Gil AP de, et al: Cranial base superimposition of cone-beam computed tomography images. J Craniofac Surg 30:1809, 2019
13. Solow B, Sandham A: Cranio-cervical posture: A factor in the development and function of the dentofacial structures. Eur J Orthod 24:447, 2002
14. Lin X, Edwards SP: Changes in natural head position in response to mandibular advancement. Br J Oral Maxillofac Surg 55:471, 2017
15. dos Santos RMG, De Martino JM, Haiter Neto F, Passeri LA: Influence of different setups of the Frankfort horizontal plane on 3-dimensional cephalometric measurements. Am J Orthod Dentofac Orthop 152:242, 2017
16. Guijarro-Martínez R, Swennen GRJ: Three-dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: A validation study. Int J Oral Maxillofac Surg 42(9):1140, 2013
17. Rubio-Bueno P, Landete P, Ardanza B, et al: Maxillomandibular advancement as the initial treatment of obstructive sleep apnoea: Is the mandibular occlusal plane the key? Int J Oral Maxillofac Surg 46:1363, 2017
18. Veys B, Pottel L, Mollemans W, et al: Three-dimensional volumetric changes in the upper airway after maxillomandibular advancement in obstructive sleep apnoea patients and the impact on quality of life. Int J Oral Maxillofac Surg 46:1525, 2017
19. Camacho M, Noller MW, Del Do M, et al: Long-term results for maxillomandibular advancement to Treat obstructive sleep apnea: A meta-analysis. Otolaryngol Neck Surg 160:580, 2019
20. Dicus Brookes CC, Boyd SB: Controversies in obstructive sleep apnea surgery. Oral Maxillofac Surg Clin North Am 29:503, 2017
21. Ayappa I, Rapoport DM: The upper airway in sleep: Physiology of the pharynx. Sleep Med Rev 7:9, 2003
22. Iwasaki T, Sato H, Suga H, et al: Relationships among nasal resistance, adenoids, tonsils, and tongue posture and maxillofacial form in Class II and Class III children. Am J Orthod Dentofac Orthop 151:929, 2017
23. Prinsell JR: Primary and secondary telegnathic maxillomandibular advancement, with or without adjunctive procedures, for obstructive sleep apnea in adults: A literature review and treatment recommendations. J Oral Maxillofac Surg 70:1659, 2012
24. Schendel SA, Jacobson R, Khalessi S: Airway growth and development: A computerized 3-dimensional analysis. J Oral Maxillofac Surg 70:2174, 2012
25. Yang Y, Yang K, Zhao Y: Three-dimensional changes in the upper airway of skeletal class III patients after different orthognathic surgical procedures. J Oral Maxillofac Surg 76:155, 2018
26. Gandedkar NH, Chng CK, Por YC, et al: Influence of bimaxillary surgery on pharyngeal airway in class III deformities and effect on sleep apnea: A STOP-BANG Questionnaire and cone-beam computed tomography study. J Oral Maxillofac Surg 75:2411, 2017
27. Lee JY, Kim Y Il, Hwang DS, Park SB: Effect of maxillary setback movement on upper airway in patients with class III skeletal deformities: Cone beam computed tomographic evaluation. J Craniofac Surg 24:387, 2013
28. Haas Junior OL, Guijarro-Martínez R, de Sousa Gil AP, et al: Hierarchy of surgical stability in orthognathic surgery: Overview of systematic reviews. Int J Oral Maxillofac Surg 48:1415, 2019
29. Haas Junior OL, Guijarro-Martínez R, de Sousa Gil AP, et al: Stability and surgical complications in segmental Le Fort I osteotomy: A systematic review. Int J Oral Maxillofac Sur 46:1071, 2017

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HSOA Journal of Otolaryngology, Head and Neck Surgery
Research Article

Airway Volume Changes after Orthognathic Surgery in Patients with Down Syndrome: A Diagnostic-Therapeutic Algorithm

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Abstract

Background: Down syndrome (DS) patients tend to suffer severe dentofacial and skeletal deformities leading to severe occlusal, speech and respiratory problems. The increase in life expectancy of these subjects opens new horizons for improvement of their oral, dental and facial functions, among others. However, no surgical treatment protocol is described elsewhere in the literature. Then, the present study proposes a protocol for the surgical management of orodental and facial deformities in DS patients based on a series of three cases and a review of the literature.

Methods: The protocol contemplates dentofacial deformity diagnostic work-up, obstructive sleep apnoea diagnosis and follow-up, pre-admission medical and anaesthetic evaluation, treatment plan, and perioperative management.

Results: All patients presented with midface retrusion due to underlying severe maxillary hypoplasia and dental crowding. A mean maxillary advancement of 4.53 mm and a mean maxillary descent of 3.6 mm were obtained. A mean pharyngeal airway volume gain of 10,954.33 mm3 (50%) was recorded at the one-month follow-up visit. Non-relevant skeletal and airway relapses were noted. Stable occlusion was achieved in all cases after postoperative orthodontic treatment, with proper chewing function, and the parents referred decreased snoring.

Conclusion: In selected DS patients with specific dysmorphic orofacial features, orthognathic surgery constitutes the first line treatment to improve the occlusion disorders and associated feeding, respiratory and sleep-disorder problems. Therefore, the use of this algorithm represents the first line surgical treatment for DS patients with dentofacial deformities and allows the clinician to tailor the surgical treatment to each patient's needs.

Keywords: Down syndrome; Orthognathic surgery; Obstructive sleep apnoea; Pharyngeal airway volume

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Abbreviations

DS: Down Syndrome
OSA: Obstructive Sleep Apnea
OS: orthognathic surgery
CBCT: Cone-Beam Computed Tomography
PSG: Polysomnography
3D: Three-Dimensional
PAV: Pharyngeal Airway Volume
SD: Standard Deviation
EDS: Excessive Daytime Sleepiness

Introduction

Down syndrome (DS) is the most frequent chromosomal disorder, occurring in one out of every 700 births [1]. Since 1866, when the British physician John Langdon Down first described the disorder, trisomy 21 has gained scientific relevance and is currently one of the most extensively studied genetic alterations. Apart from intellectual disabilities of varying degrees, these patients may suffer a broad range of organic defects - the most common being cardiac abnormalities, gastroesophageal reflux, celiac disease, hypothyroidism, hearing and vision problems, leukemia and early Alzheimer's disease [2]. Dysmorphic cranial and orofacial features have also been widely described in DS patients, particularly a small cranium, a flat nose and flat malar bones with slanted eyes, severe maxillary hypoplasia with a high-arched and constricted palate, and mandibular hypoplasia although seemingly prognathic mandible because of the previous issue, hypodontia, relative macroglossia because of the small maxillo-mandibular framework with the tongue resting inactively between the lips due to muscle hypotonia in the orofacial region and, ultimately, a flattened face with anterior open bite and Class III dental and skeletal relationships [3]. These anatomical features may lead to speech, swallowing and masticatory functional impairments, as well as to an increased predisposition to obstructive sleep apnoea (OSA) and mouth breathing [4]. Medical advances and the multidisciplinary management of DS patient's have doubled the life expectancy of these patients in the last decade, from 30-40 to 60-70 years, with increased quality of life and more community-involved and productive lives [5]. This in turn opens new horizons for improvement of their oral, dental and facial functions, among others.

The present study describes a protocol for the surgical management of orodental and facial deformities in DS patients based on a series of three cases and a review of the literature.

Patients and Methods

Three consecutive patients with DS were referred to our Department for dentofacial deformity treatment with orthognathic surgery (OS). A retrospective evaluation was made of the treatment applied in all three cases, and a review of the literature was carried out in order to validate the proposed management algorithm (Figure 1).

The guidelines of the Declaration of Helsinki were followed in all the treatment phases. Consent was requested from the legal guardians of the patients. As this was a retrospective analysis, Institutional Review Board approval of the study was not considered necessary.

Diagnostic work-up

The diagnostic work-up comprised three phases, which were also used to concomitantly evaluate patient and parent collaboration: a) physical intraoral and facial examination, with intraoral and facial photographic records and the study of plaster dental casts and wax bites; b) periodontal evaluation and a follow-up visit to check patient and parent capacity to maintain proper periodontal health; and c) cone-beam computed tomography (CBCT) (i-CAT, Imaging Sciences International, Inc., Hatfield, USA) study to complete the facial analysis.

Obstructive sleep apnoea diagnosis and follow-up

A thorough anamnesis is required, with quality of life evaluation in children with OSA [6,7]. When OSA is suspected, polysomnography (PSG) should be requested. In addition, three-dimensional (3D) pharyngeal airway volume (PAV) should be measured with CBCT (T0).

The three tests (quality of life evaluation, PSG and CBCT) should be repeated after one month and one year of follow-up in order to assess the clinical and radiological changes and their long-term stability in relation to the OS procedure.

Pre-admission medical and anaesthetic evaluation

The anaesthetic management of patients with DS constitutes a challenge for the anesthetist, due to the difficulty of the airway, the possible associated comorbidities they may present, and behavioral and communication problems [8].

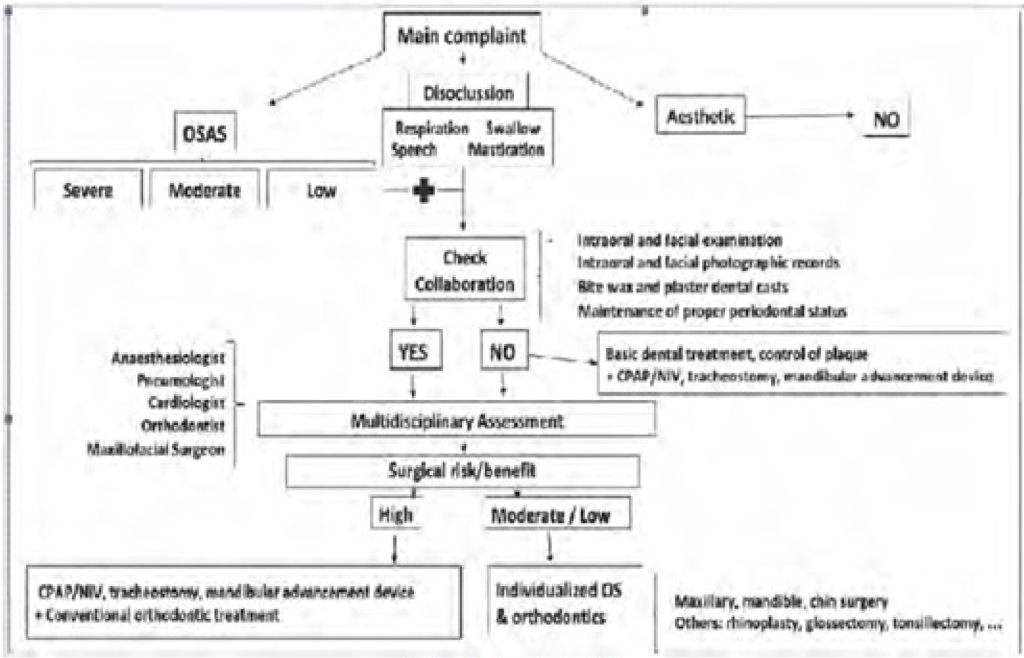


Figure 1: Captions to Illustrations.

Decision making algorithm in Down syndrome patients with disocclusion and obstructive sleep apnoea: selection of suitable candidates for orthognathic surgery. OSA: Obstructive sleep apnea; OS: orthognathic surgery; CPAP: continuous positive airway pressure; NIV: non-invasive ventilation.

The airway may prove difficult due to the following DS-related issues: a) small airway size secondary to maxillary hypoplasia, micrognathia, macroglossia, tonsillar hypertrophy, short neck, glottic and subglottic stenosis and tracheomalacia; b) atlanto-axial/atlanto-occipital instability with a high risk of spinal cord injury; and c) OSA secondary to central apnoea, low muscle tone in the mouth and upper airway, poor coordination of airway movements, and the abovementioned small airway size [4,9,10]. On the other hand, associated comorbidities may develop in any body system11. The most frequent and relevant conditions are congenital cardiac alterations (40-50% of all patients), such as interatrial / interventricular communications, transposition of large vessels and tetralogy of Fallot, which are generally diagnosed in advance. However, there are also other cardiac diseases such as valve defects or arrhythmias (with increased susceptibility to bradycardia) that typically are not diagnosed and should be evaluated preoperatively. Other alterations that are also often seen in this population comprise gastroesophageal reflux disease (with an increased risk of bronchoaspiration), obesity, diabetes, hypotonia, immune suppression with susceptibility to pulmonary infections, autoimmune alterations such as hypothyroidism, and moderate to severe mental retardation. Thus, potential disease conditions require in depth evaluation, as well as the management of potential complications planned beforehand, in order to ensure a safe anaesthetic procedure [8,11].

Treatment plan

If both patient and parent collaboration proved good enough in all phases, the orthodontic-surgical treatment plan was established and orthodontic treatment was started. Once again, provided cooperation with the orthodontic treatment was adequate, surgery was virtually planned using specific software (Dolphin® 3D Orthognathic Surgery Planning Software Version 11.8) [12,13].

Perioperative management

In order to increase comfort and relaxation of the patients, a caregiver accompanied them to the anaesthetic induction area, and to the recovery room. The patients were operated upon under general anesthesia and with endotracheal intubation, as in conventional orthognathic surgery procedures. However, a smaller tube than expected for the age of the patient was chosen in all cases in order to reduce the incidence of subglottic oedema and post-intubation stridor. As mentioned above, airway management of DS patients is considered to be highly complex, so trained anaesthesia personnel and a difficult airway cart were ready for both induction and eduction procedures [8].

There are no perioperative drug contraindications or medications specifically recommended for patients with DS; nevertheless, perioperative treatment was patient-tailored according to the comorbidity present in each case.

Surgery

A bilateral mandibular sagittal split osteotomy was performed using the Dal Pont-Obwegeser technique, with a maxillary LeFort I osteotomy using the "twist technique" [14]. All patients were extubated in the operating room, and all wore a closed-circuit cold mask (17°C) during hospital admission. Standard antibiotic and anti-inflammatory medication for OS was prescribed. Functional training with light guiding elastics was followed for one month, together with a soft diet during the same period of time.

Postoperative evaluation

Eventual surgical complications were recorded at one week and 1, 6 and 12 months of follow-up. In addition, two control CBCT scans were performed at one month (T1) and one year of follow-up (T2) in order to assess both airway and bony surgical enlargement (T1-baseline [T0]) and its long-term stability after surgery(T2-T1). CBCT scans were obtained in DICOM (Dental Imaging Communication) format and processed with specific third-party software (Dolphin® 3D Orthognathic Surgery Planning Software Version 11.8). A 3D volume was created with hard tissue reconstruction for the T0, T1 and T2 databases. Three-dimensional superimposition and dimensional comparisons were performed by means of surface matching between different datasets [15].

In order to evaluate surgical bony enlargement and stability, the following linear measurements were obtained at the maxillary midline in all three spatial planes:

- Sagittal plane: projected distance from A-point to nasion perpendicular (A-Nper) for the maxilla; and projected distance from B-point to nasion perpendicular (B-Nper) for the mandible.
- Transverse plane: distance between both greater palatine foramina (PFR-PFL) for the maxilla; and distance between both gonions (GoR-GoL) for the mandible.
- Vertical plane: perpendicular distance from A-point to the Frankfort horizontal plane through the nasion (A-FHN) for the maxilla; and distance from B-point to the Frankfort horizontal plane through the nasion (B-FHN) for the mandible.

Lastly, PAV enlargement and its stability were assessed by measuring enlargement three-dimensionally (3D) at three different levels with respect to the limits of the pharyngeal airway sub regions: nasopharynx, oropharynx and hypopharynx, following a previously validated protocol described in detail elsewhere [16].

Statistical Analysis

A descriptive analysis was made of the study variables, with calculation of the mean, standard deviation (SD), minimum and maximum values, and median for continuous variables. Absolute and relative frequencies (percentages) were reported in the case of qualitative variables. The statistical analysis was carried out using the SPSS version 15.0.1 statistical package (SPSSInc., Chicago, IL, USA). Descriptive statistics were used for quantitative analysis. Percentage variation referred to maxillary or mandibular surgical movements (relapse) for each patient was calculated as follows: one-year postoperative A/B-point position • 100 / one-month postoperative A/B-point position. Similarly, percentage variation referred to PAV (relapse) for each patient was calculated as follows: one-year postoperative PAV • 100 / one-month postoperative PAV.

Results

The clinical cases are summarized in (Table 1). The study sample comprised two men and a woman with a median age of 26.7 years (range 20-37). The main reason for consultation was the presence of patient chewing difficulties, though thorough anamnesis also evidenced snoring and excessive daytime sleepiness (EDS) in all patients. None of them were diagnosed of OSA or used night time continuous positive airway pressure (CPAP). No multi organ alterations were observed at the pre-admission medical evaluation.

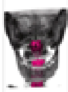
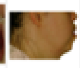
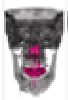
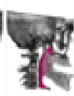
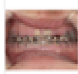
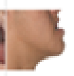
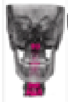
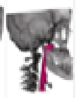
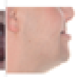
PATIENT	SEX	AGE	MAIN COMPLAINT	OTHER PATHOLOGIES	FACIAL PROFILE	OCCLUSION	OSA	PRE-OPERATIVE PAV (mm^3)	ANTERIOR VIEW	LATERAL VIEW	PA 3D	OCCLUSAL VIEW	PROFILE
1	F	37	• Difficulty in chewing • Snoring	• Maxillary hypoplasia • Anteroposterior mandibular hyperplasia • Hypoplasic nasal bone • Hypothyroidism • Scoliosis	• Concave • Brachycephalic	• Class III • Anterior open bite • Superior and inferior dental crowding	Symptoms but not diagnosed	15681					
2 (JL)	M	20	• Difficulty in chewing	• Sagital maxillary hypoplasia • Sagital mandibular hypoplasia • Right mandibular deviation • Macroglossia • Nasal hypoplasia	• Concave • Dolichofacial	• Class III • Anterior open bite • Superior and inferior dental crowding • Bilateral crossbite • Microdontia • Supernumeray tooth	Symptoms but not diagnosed	42204					
3	M	23	• Difficulty in chewing • Snoring	• Anteroposterior maxillary hypoplasia • Right mandibular deviation	• Concave • Brachycephalic	• Class III • Anterior Crossbite • Superior dental crowding	Symptoms but not diagnosed	19467					

Table 1: Preoperative facial, occlusal and airway features and images.

a F: female; M: male; OSA: obstructive sleep apnea; PAV: pharyngeal airway volume; PA: pharyngeal airway

The salient feature in the facial analysis was midface retrusion due to underlying severe maxillary hypoplasia, and dental crowding in all cases. These findings are consistent with the characteristic orofacial dysmorphic features of DS that contribute to OSA. Basal PAV was quantified (3D) based on the preoperative CBTC study, with a mean value of 25.784 mm^3 (range 15.681-42.204). Cases 1 and 3 presented an underlying constricted upper airway (15.681 mm3 and 19.467 mm^3, respectively). Specifically, narrowing was observed in all airway sub regions: naso-, oro- and hypopharynx (Table 1). On the other hand, case 2 presented a normal initial PAV (42.204 mm^3).

All patients received pre- and postoperative orthodontic treatment and were operated upon under general anesthesia by the same surgeon (FHA). All underwent maxillary surgery using the minimally invasive "twist technique"14, but only case 2 was subjected to mandibular surgery for backward movement (Table 2).

There were no surgical complications in the form of dental, nerve or vascular injuries, or poor split osteotomy. All patients were extubated in the operating room, and anaesthetic perioperative management proved uneventful. All patients wore a closed-circuit cold mask (17ºC) during hospital admission and were discharged 24 hours after surgery, with pain control using common analgesics. Standard antibiotic and anti-inflammatory medication for OS was prescribed. Functional training with light guiding elastics was followed for one month, together with a soft diet during the same period of time. The immediate and long-term (one year of follow-up) postoperative courses were uneventful. Surgical skeletal movement and PAV gain was assessed through CBCT superimposition (comparison between T0 and T1). A mean maxillary advancement of 4.53 mm and a mean maxillary descent of 3.6 mm were obtained. Consequently, a mean PAV gain of 10.954.33 mm^3 (50%) was recorded at the one-month follow-up visit (Table 2). Stable occlusion was achieved in all cases after postoperative orthodontic treatment, with proper chewing function and decreased snoring as reported by the parents. The stability of both bony and PAV gain was assessed based on two postoperative CBCT evaluations (T1 and T2). Regarding skeletal stability, a non-relevant relapse was observed in maxillary bone: a mean relapse of 1.2 mm in the sagittal dimension, 0.6 mm vertically, and none in the transverse dimension. On the other hand, in relation to PAV stability, we recorded a mild mean relapse at one year of follow-up of -2.712 mm^3 (5%), though the final mean PAV gain was notorious 35.834 mm^3 (45%) (Table 3).

Lastly, the degree of satisfaction with the functional outcome and quality according to the patients, family and surgeon was excellent, with a very good professional-patient relationship.

Discussion

The main reasons why patients seek OS and related surgical orthodontic treatments are occlusal and aesthetic problems, and OSA. Although DS is associated to altered facial dimensions, and some authors advocate cosmetic facial surgery to avoid stigmatization and ensure better social acceptance [17], in our opinion aesthetics should not be the sole indication of OS in DS patients, in view of its unfavorable benefit/risk balance. This means that when orthodontic treatment suffices to correct the malocclusion, or when OSA is well controlled with CPAP in DS patients with balanced occlusion, surgery should be ruled out even though cosmetic skeletal disharmony may persist.

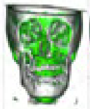
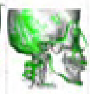
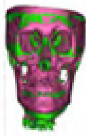
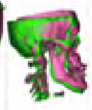
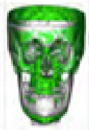
PATIENT	SURGERY				VIRTUAL SURGICAL PLAN ANTERIOR VIEW	VIRTUAL SURGICAL PLAN LATERAL VIEW	INTRAOPERATIVE COMPLICATIONS	1-MONTH PAV (mm³)	PAV GAIN (%) (T1-T0)	CBCT SUPERIMPOSITION (T1-T0) ANTERIOR VIEW	CBCT SUPERIMPOSITION (T1-T0) LATERAL VIEW
	Maxillary	Mandible	Chin	Others							
1	LefortI • Forward (5 mm)	None	Genioplasty • Forward (6 mm) • Downward (4 mm)	• Rhinoplasty (pyramid augmentation) • Septoplasty			None	27420	74%		
2	Segmented LefortI • Forward (5mm) • Downward (3mm) • Expansion (5mm)	Mandibular retrusion (4.2 mm)	None	• Rhinoplasty • Septoplasty			None	54143	28%		
3	LefortI • Forward (3.6 mm) • Downward (3.8 mm)	None	None	None			None	28652	47%		

Table 2: Surgical virtual plan, procedures and complications. Postoperative PAV gain and skeletal movement through CBCT superimposition after one month of follow-up.

a PAV: pharyngeal airway volume; CBCT: cone-beam computerized tomography.

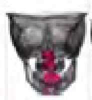
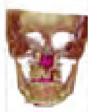
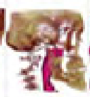
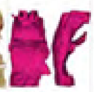
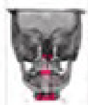
PATIENT	POSTOPERATIVE COMPLICATIONS	SKELETAL RELAPSE	1-YEAR PAV (mm³)	PAV GAIN (%) (T2-T0)	SATISFACTION PATIENT-FAMILY-SURGEON-ORTHODONTIST	ANTERIOR VIEW	LATERALVIEW	PA 3D	FOLLOW UP
1	Osteosynthesis plate removal due to repetitive inflammation	None	25859	64%	10-10-10-10				10 years
2	None	None	52992	25%	10-10-10-10				24 months
3	None	None	28652	47%	10-10-10-10				18 months

Table 3: Final outcome after one year of follow-up: skeletal and airway stability and degree of satisfaction with the overall procedure.

a PAV: pharyngeal airway volume; PA: pharyngeal airway.

Nevertheless, OS may be the best management option in other carefully selected patients (Figure 1). On one hand, occlusal disharmonies with anterior open bite, dental Class III and a lack of inter-arch contacts are common in patients with DS, due to their abovementioned skeletal cranial and orofacial dysmorphic features. Moreover, other dental anomalies such as oligodontia, periodontal disease, tooth agenesis, taurodontism, microdontia and altered eruption of primary and permanent dentition are often present in this population [3,18]. In the attempt to create more dental contacts these individuals protrude the mandible, which in the end can jeopardize temporomandibular joint function [19]. Besides, such malocclusion involves speech and feeding problems, which are aggravated by their inherent neuro-motor disability for articulation and chewing/swallowing, respectively. Moreover, this severe malocclusion may have respiratory consequences such as OSA or the aspiration of food or fluids into the lungs [20]. Thus, it is evident that DS patients are in need of treatment for their malocclusions. On the other hand, persons with DS are prone to develop OSA due to a series of associated anatomical and physiological features [21]: a) a small airway size because of underlying maxillary hypoplasia, micrognathia, relative macroglossia, adeno- and lingual- tonsillar hypertrophy, fat deposits in the lateral wall of the pharynx, glottic and subglottic stenosis and tracheomalacia; and b) low muscle tone in the mouth and upper airway, poor coordination of airway movements, and gastroesophageal reflux disease that leads to inflammation and obstruction of the upper airway4,9. Some studies suggest that the prevalence of OSA in children with DS is 30-50%, and that approximately 90% of the adults will develop OSA, which in such cases moreover tends to be severe [9,11,22]. Apart from the typical comorbidities associated to OSA, such as arterial hypertension, altered blood glucose homeostasis, cardiovascular and cerebrovascular diseases, pulmonary hypertension, cognitive deficits and even death, individuals with DS specifically suffer worsening of overall cognitive function - starting with weakening of neurocognitive development in early ages, and followed later on by deteriorated communication ability, behavior, functional outcomes and quality of life [23].In this regard, several management strategies have been described: a) positive airway support in the form of noninvasive ventilation (NIV) or CPAP, though this is associated to high dropout and non-adherence rates [24]; b) weight loss, which does not cure OSA, but is recommended in addition to other therapies in patients who are overweight [25]; c) airway soft tissue surgery, such as adeno- and lingual-tonsillectomy, which are associated to high OSA persistence rates4 (adeno- and lingual-tonsillectomy therefore should be indicated only when hypertrophy is clearly evidenced) [4,26]; d) partial glossectomy, which should only be indicated when true excessive enlargement of the tongue results in insufficient space for the organ [27]; e) hypoglossal nerve stimulation, which is a promising and minimally invasive technique, though further studies are needed to optimize patient selection and better assess the long-term efficacy of the technique [28]; and f) tracheostomy, which is linked to severe short- and long-term complications, including decannulation, bleeding or infection among others, and may be required only in cases of severe OSA not amenable to other forms of treatment.

These poor outcomes point to OS as the first line treatment option, considering the characteristic orofacial dysmorphic features of individuals with DS and that contribute to airway narrowing, such as retrusion or shortening of the mandible and maxillary hypoplasia [29]. Although recommending OS in this population is controversial, it has been demonstrated that OS procedures can be carried out with success rates (predictability, complications during and after the operation, and overall treatment stability) as high as in mentally healthy individuals [30]. Nonetheless, the overall complexity of patients with DS calls for a multidisciplinary team comprising primary care physicians, maxillofacial surgeons, orthodontists and other dental professionals, anesthetists, medical rehabilitators, physiotherapists, speech therapists, pulmonologists and neurophysiologists, among others. Once the patient reports for maxillofacial consultation due to occlusal problems or OSA, a number of aspects must be taken into account. Firstly, regarding the craniofacial features, patients with DS have reduced head and facial dimensions with a brachiocephalic cranium, a shorter and flatter cranial base, reduced or absent frontal sinus and nasal bone, small ears, and hypertelorism with slanted eyes. Thus, cephalometric landmarks such as the nasion or porion for facial analysis and head orientation purposes may be altered, making it difficult to properly classify the underlying dentofacial anomaly [31]. For this reason, it is highly advisable to use 3D CBCT for facial analysis instead of 2D X-rays. On the other hand, the diagnosis of OSA in children is based on an association of PSG parameters when the apnoea-hypopnea index is > 5 episodes/hour, though the SpO2 and PtcCO2 levels are also taken into account [32,33] and on clinical symptoms based on a specific OSA quality of life test for children (the OSA-18 survey) [6,7,34]. Apart from the cardinal manifestations of OSA, such as snoring, fatigue and restless sleep, children with DS specifically may also present with failure to thrive, hyperactivity, behavioral disruptions and poor school performance, whereas adults with DS may present with mood dysregulation and depression [22]. Although the cases in our study did not undergo PSG, because their main complaint was malocclusion, it is advisable to systematically perform PSG in all patients presenting OSA symptoms. Besides, diagnostic CBCT for facial analysis may also be used to detect upper airway constrictions. In our study, cases 1 and 3 showed basal upper airway constriction (15.681 mm3 and 19.467 mm3), respectively (Table 1), compared to reference normal PAV values of 23.400mm [35,36]. Specifically, a narrowed airway was observed in all upper airway sub regions: naso- oro- and hypopharynx. Conversely, mandibular advancement devices, apart from being an option for treating mild to moderate OSA with better patient compliance than when CPAP is used 22, are also useful in deciding which patients may benefit from surgical mandibular advancement in the context of OSA. Unfortunately, similar maxillary devices for predicting the impact of maxillary advancement upon OSA are not available. On the other hand, it is essential to detect as far as possible central origin OSA cases through PSG, since OS would not be worthwhile in such situations.

Thus, correct screening referred to patient eligibility for orthodontic-surgical treatment is essential. We thus propose the above described diagnostic work-up in order to evaluate patient and parent collaboration (examination - periodontal status and maintenance - CBCT) regardless of the patient intelligence quotient (IQ) and thus to refine the selection of suitable candidates for OS (Figure 1). Equally important is the establishment of a good and trusting professional-patient relationship. In this regard it is useful to explain the planned procedures in depth and indicate the expected results and eventual complications to the patient and his/her relatives. Keeping close contact through telephone support and more frequent follow-up visits is also useful.

Surgical planning differs from the regular scenario where aesthetics constitute a key element, and instead priority is placed on minimal surgery in terms of mono- rather than bi maxillary operations, with reduction of the amount of skeletal movements, while always ensuring proper occlusion and sufficient PAV enlargement. Thus, in general, in the presence of a typical midface deficiency with high palate, reduction of its length, together with a narrowed oropharynx, usually implies advancement, widening and antero-posterior leveling/upward maxillary movements. Then, the mandible may be adjusted to maxillary positioning. Regarding the specific surgical management of OSA, a maxilla-mandibular advancement of 1cm is considered the gold standard in OS [37]. Nevertheless, there is not enough evidence to establish the magnitude and direction of maxillary and/or mandibular movements required in order to cure OSA, which additionally should be individualized for each patient. Our sample of patients underwent a mean maxillary advancement of 4.53 mm, which was enough to correct both occlusal and narrowed airway problems. Although one patient required mandibular setback for occlusal purposes, it did not adversely affect overall PAV enlargement. Occasionally, where required, procedures concomitant to OS are recommended to optimize airway permeability and prevent open bite relapse, such as tongue reduction [27] or adeno- and lingual-tonsillectomy [4,26]. Although it has been widely demonstrated that OS is the most consistent and predictable surgical treatment option for adult patients diagnosed with moderate to severe OSA [38,39], its outcomes are less predictable in the DS population because, as previously mentioned, the causes of OSA in these patients are multiple and additive. Thus, a systematic sleep study based on PSG is strongly recommended prior to and after OS in order to check surgical effectiveness and determine whether further treatments are necessary. In cases where OSA persists after upper airway surgery, CPAP or NIV in the case of alveolar hypoventilation are indicated [4].

Postoperative discomfort should be reduced as far as possible, adopting minimally invasive approaches such as the "twist technique"14, the shortening of surgery time, the use of apiezoelectric saw when possible [40], the prescription of standard anti-inflammatory medication, manual lymphatic drainage for OS [41], and the wearing of a closed-circuit cold mask during the postoperative period [42]. Furthermore, whenever possible, light guiding elastics for functional training should be used instead of rigid intermaxillary fixation [30].

Regarding patient age at surgery, the standards advise waiting until cessation of mandibular growth. In the meantime, a two-phase or multiphase orthodontic treatment program is beneficial to assist correction of misalignment and maxillary transverse deficiency by means of palatal expansion or surgically assisted rapid palatal expansion, before and after closure of the palatal suture, respectively [19,43]. Similarly, myofunctional therapy or orofacial rehabilitation should be started during the growth period in order to favorn proper maxilla-mandibular growth, establish an adequate resting position of the tongue behind the upper incisors, reinforce orofacial tonicity, encourage nasal respiration and improve swallowing and speech functionality [44]. Besides, it also may reduce the inherent muscular imbalance that predisposes to an increased prevalence of relapse after OS [30]. Likewise, dentofacial harmonization by means of orthodontic treatment and OS have shown significant improvement in oral motor function, including mouth closure, inactive protrusion and positioning of the tongue in DS patients.

Conclusion

In selected patients with DS presenting specific orofacial dysmorphic features, orthognathic surgery is an effective and secure treatment to address both occlusion (and its consequent feeding-respiratory- and communication-related problems) and OSA. The implementation of this algorithm, together with minimally invasive surgery and cutting-edge technologies, allows OS to be safely performed in patients with DS. This algorithm allows clinicians to tailor the surgical treatment to each patient" s needs, consider in gage, comorbidities and barriers to treatment adherence. However, further clinical studies are needed to determine whether OS in DS patients with OSA is able to reduce cardiovascular risks, mortality and long-term outcomes after surgery.

References

1. Sherman SL, Allen EG, Bean LH, Freeman SB (2007) Epidemiology of Down syndrome. Ment Retard Dev Disabil Res Rev 13: 221-227.
2. Potter H (2016) Beyond Trisomy 21: Phenotypic Variability in People with Down Syndrome Explained by Further Chromosome Mis-segregation and Mosaic Aneuploidy. Journal of Down Syndrome & Chromosome Abnormalities 2: 1-4.
3. Bauer D, Evans CA, Begole EA, Salzmann L (2012) Severity of occlusal disharmonies in down syndrome. Int J Dent 872367: 1-7.
4. Dudoignon B, Amaddeo A, Frapin A, Thierry B, Sanctis LD, et al. (2017) Obstructive sleep apnea in Down syndrome: Benefits of surgery and non-invasive respiratory support. Am J Med Genet A 173: 2074-2080.
5. Gupta NA, Kabra M (2014) Diagnosis and Management of Down Syndrome. Indian J Pediatr 81: 560-567.
6. Chiner E, Landete P, Sancho-Chust JN, Perez Ferrer P, Pastoret E, et al. (2016) Adaptation and Validation of the Spanish Version of OSA-18, a Quality of Life Questionnaire for Evaluation of Children with Sleep Apnea-Hypopnea Syndrome. Arch Bronconeumol 52: 553-559.
7. Franco RA, Rosenfeld RM, Rao M (2000) Quality of life for children with obstructive sleep apnea. Otolaryngol Head Neck Surg 123: 9-16.
8. Borland LM, Colligan J, Brandom BW (2004) Frequency of anesthesia-related complications in children with Down syndrome under general anesthesia for noncardiac procedures. Paediatr Anaesth. 14: 733-738.
9. Bassell JL, Phan H, Leu R, Kronk R, Visootsak J, et al. (2015) Sleep profiles in children with Down syndrome. Am J Med Genet A 167A: 1830-1835.
10. Waage NS, Baker S, Sedano HO (2009) Pediatric conditions associated with compromised airway. Int J Paediatr Dent 31: 236-248.
11. Alexander M, Petri H, Ding Y, Wandel C, Khwaja O, et al. (2016) Morbidity and medication in a large population of individuals with Down syndrome compared to the general population. Dev Med Child Neurol 58: 246-254.
12. Centenero SAH, Alfaro FH (2012) 3D planning in orthognathic surgery: CAD/CAM surgical splints and prediction of the soft and hard tissues results - our experience in 16 cases. J Craniomaxillofac Surg. 40: 162-168.
13. Alfaro FH, Martinez RG (2013) New protocol for three-dimensional surgical planning and CAD/CAM splint generation in orthognathic surgery: an in vitro and in vivo study. Int J Oral Maxillofac Surg 42: 1547-1556.
14. Alfaro FH, Martinez RG (2013) "Twist Technique" for Pterygomaxillary Dysjunction in Minimally Invasive Le Fort I Osteotomy. J Oral Maxillofac Surg 71: 389-392.

15. Junior OL, Martinez RG, Gil AP, Meirelles LS, Oliveira RB, et al. (2017) Stability and surgical complications in segmental Le Fort I osteotomy: a systematic review. Int J Oral Maxillofac Surg 46: 1071-1087.

16. Martinez RG, Swennen GRJ (2013) Three-dimensional cone beam computed tomography definition of the anatomical subregions of the upper airway: a validation study. Int J Oral Maxillofac Surg 42: 1140-1149.

17. Olbrisch RR (1982) Plastic surgical management of children with Down's syndrome: indications and results. Br J Plast Surg 35: 195-200.

18. Trias MA, Perez JL, Perez AP (2016) Comparative study of dental anomalies assessed with panoramic radiographs of Down syndrome and non-Down syndrome patients. Eur J Paediatr Dent. 17: 65-69.

19. Javed F, Akram Z, Barillas AP, Kellesarian SV, Ahmed HB (2018) Outcome of orthodontic palatal plate therapy for orofacial dysfunction in children with Down syndrome: A systematic review. Orthodontics & Craniofacial Research 21: 20-26.

20. Hennequin M, Faulks D, Veyrune JL, Bourdiol P (2007) Significance of oral health in persons with Down syndrome: a literature review. Dev Med Child Neurol 41: 275-283.

21. Fung E, Witmans M, Ghosh M, Cave D, El-Hakim H, et al. (2012) Upper airway findings in children with Down syndrome on sleep nasopharyngoscopy: case-control study. J Otolaryngol Head Neck Surg 41: 138-144.

22. Lal C, White DR, Joseph JE, Bakergem KV, LaRosa A, et al. (2015) Sleep-disordered breathing in Down syndrome. Chest 147: 570-579.

23. Skotko BG, Macklin EA, Muselli M, Voelz L, McDonough ME, et al. (2017) A predictive model for obstructive sleep apnea and Down syndrome. Am J Med Genet A 173: 889-896.

24. Brooks LJ, Olsen MN, Bacevice AM, Beebe A, Konstantinopoulou S, et al. (2015) Relationship between sleep, sleep apnea, and neuropsychological function in children with Down syndrome. Sleep Breath 19: 197-204.

25. Corral AR, Caples SM, Jimenez FL, Somers VK (2010) Interactions between obesity and obstructive sleep apnea: implications for treatment. Chest 137: 711-719.

26. Prosser JD, Shott SR, Rodriguez O, Simakajornboon N, Meinzen-Derr J, et al. (2017) Polysomnographic outcomes following lingual tonsillectomy for persistent obstructive sleep apnea in down syndrome: PSG Outcomes of Lingual Tonsillectomy in DS. The Laryngoscope 127: 520-524.

27. Salmen F, Dedivitis R (2013) Partial glossectomy as an auxiliary method to orthodontic treatment of dentofacial deformity. International Archives of Otorhinolaryngology 16: 414-417.

28. Diercks GR, Wentland C, Keamy D (2018) Hypoglossal Nerve Stimulation in Adolescents With Down Syndrome and Obstructive Sleep Apnea. JAMA Otolaryngol Head Neck Surg 144: 37-42.

29. Lee RWW, Chan ASL, Grunstein RR, Cistulli PA (2009) Craniofacial phenotyping in obstructive sleep apnea a novel quantitative photographic approach. Sleep 32: 37-45.

30. Bock JJ, Maurer P, Otto C, Fuhrmann RAW, Schubert J, et al. (2006) Complications of orthodontic orthognathic surgery treatment in mentally handicapped patients. Journal of Cranio-Maxillofacial Surgery 34: 156-161.

31. Suri S, Tompson BD, Cornfoot L (2010) Cranial base, maxillary and mandibular morphology in Down syndrome. The Angle Orthodontist 80: 861-869.

32. Bull MJ (2011) Health supervision for children with Down syndrome. Pediatrics 128: 393-406.

33. Amaddeo A, Frapin A, Fauroux B (2016) Long-term non-invasive ventilation in children. Lancet Respir Med 4: 999-1008.

34. Marcus CL, Brooks LJ, Draper KA, Gozal D, Halbower AC, et al (2012) Diagnosis and management of childhood obstructive sleep apnea syndrome. Pediatrics 130: e714-755.

35. Shahidi S, Danaie SM, Omidi M (2016) Comparison of the Pharyngeal Airway Volume between Non-Syndromic Unilateral Cleft Palate and Normal Individuals Using Cone Beam Computed Tomography. J Dent (Shiraz) 17: 268-275.

36. Chousangsuntorn K, Bhongmakapat T, Apirakkittikul N, Sungkarat W, Supakul N, et al. (2018) Upper Airway Areas, Volumes, and Linear Measurements Determined on Computed Tomography During Different Phases of Respiration Predict the Presence of Severe Obstructive Sleep Apnea. J Oral Maxillofac Surg 76: 1524-1531.

37. Bartolucci ML, Bortolotti F, Raffaelli E, Anto VD, Michelotti A, et al. (2016) The effectiveness of different mandibular advancement amounts in OSA patients: a systematic review and meta-regression analysis. Sleep Breath 20: 911-919.

38. Zaghi S, Holty JEC, Certal V, Abdullatif J, Guilleminault C, et al (2016) Maxillomandibular Advancement for Treatment of Obstructive Sleep Apnea: A Meta-analysis. JAMA Otolaryngol Head Neck Surg 142: 58-66.

39. Caples SM, Rowley JA, Prinsell JR, Pallanch JF, Elamin MB (2010) Surgical modifications of the upper airway for obstructive sleep apnea in adults: a systematic review and meta-analysis. Sleep 33: 1396-1407.

40. Bussolaro CT, Galvan JG, Pereira CP, Mir CF (2019) Maxillary osteotomy complications in piezoelectric surgery compared to conventional surgical techniques: a systematic review. Int J Oral Maxillofac Surg 48: 720-731.

41. Yaedu RYF, Mello MDAB, Tucunduva RA, Silveira JSZ, Takahashi MPMS, et al. (2017) Postoperative Orthognathic Surgery Edema Assessment With and Without Manual Lymphatic Drainage. J Craniofac Surg 28: 1816-1820.

42. Lateef TA, Al-Anee AM, Agha MTF (2018) Evaluation the Efficacy of Hilotherm Cooling System in Reducing Postoperative Pain and Edema in Maxillofacial Traumatized Patients and Orthognathic Surgeries. J Craniofac Surg 29: e697-e706.

43. Musich DR (2006) Orthodontic intervention and patients with Down syndrome. Angle Orthod 76: 734-735.

44. Faulks D, Mazille MN, Collado V, Veyrune JL, Hennequin M, et al. (2008) Masticatory dysfunction in persons with Down's syndrome. Part 2: management. J Oral Rehabil 35: 863-869.

08

APPENDIX II

8.1 Approval of the PhD Thesis Project by the UIC

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ESCUELA DE DOCTORADO

PROGRAMA DE DOCTORADO EN CIENCIAS DE LA SALUD

EVALUACIÓN CURSO ACADÉMICO 17-18

Barcelona, 14 de noviembre de 2018

Apreciada María

Por la presente le comunico que la Comisión Académica del programa de Doctorado en Ciencias de la Salud (CAD) en relación al siguiente proyecto de tesis:

Título: Impacto de la cirugía ortognática en la vía aérea superior (VAS) y el índice de apnea-hipopnea (IAH)
Doctorando: María Giralt Hernando
Directores: Dr. Federico José Hernández Alfaro y Dra. Adaia Valls Ontañón

Resuelve que el trabajo desarrollado por el doctorando durante el curso académico 17-18 de acuerdo al Documento de Actividades (DAD) presentado, ha sido evaluado FAVORABLEMENTE.

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Sònia Soriano
Secretaría Escuela de Doctorado

8.2 Approval and concession of the competitive predoctoral fellowship ID: FI_B200134 by the AGAUR *(Agencia de Gestió d'ajudes Universitàries i d'investigació) of the Generalitat de Catalunya.*

Agència de Gestió d'Ajuts Universitaris i de Recerca AGAUR

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CREDENCIAL

Per Resolució de 8 de febrer de 2018 feta pública el 9 de febrer de 2018, de la Comissió Executiva d'Ajuts de Recerca de l'Agència de Gestió d'Ajuts Universitaris i de Recerca de la Generalitat de Catalunya i d'acord amb la Resolució EMC/2199/2017 de 14 de setembre (DOGC núm. 7459 de 21.9.2017) de convocatòria; l'AGAUR ha atorgat a les Universitats, Centres de Recerca i Fundacions Hospitalàries els fons necessaris per a contractar personal investigador novell, segons la legislació vigent, i entre d'altres la persona que es detalla a continuació,

DADES PERSONA BENEFICIÀRIA	
COGNOMS: Giralt Hernando	
NOM: Maria	
NIF: [redacted]	**NÚM. EXPEDIENT:** 2018FI_B_00383

CENTRE DE DESTINACIÓ	
CENTRE/UNIVERSITAT:	Universitat Internacional de Catalunya

8.3 Approval of the PhD thesis project by the health Health Sciences Doctoral Academic Committee (Comisión Académica de Doctorado, CAD).

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ESCUELA DE DOCTORADO
PROGRAMA DE DOCTORADO EN CIENCIAS DE LA SALUD

APROBACIÓN DEL PROYECTO DE TESIS POR LA CAD

Barcelona, 18 de octubre de 2018

Apreciado doctorando

Te comunico que la Comisión Académica del Doctorado en Ciencias de la Salud ha aprobado el siguiente proyecto de tesis:

Línea de Investigación: Investigación básica y aplicada en odontología

Doctorando: Maria Giralt Hernando

Directores: Dr. Federico José Hernández Alfaro
Dra. Adaia Valls Ontañón

Titulo del plan proyecto de tesis: Impacto de la cirugía ortognática en la vía aérea superior (VAS) y el índice de apnea-hipopnea (IAH). (Impact of orthognathic surgery on the upper airway and the apnea-hypopnea index (AHI))

Dedicación: tiempo completo

Idioma: castellano

Cualquier cambio debe ser solicitado a la CAD.

Atentamente,

Universitat Internacional de Catalunya
Escola de Doctorat
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Sònia Soriano
Secretaría Escuela de Doctorado

8.4 Approval of the PhD Thesis project by the Ethics in Research Committee (Comité d'Ética de Recerca, CER).

CER Comitè d'Ètica de Recerca | Universitat Internacional de Catalunya

APROVACIÓ PROJECTE PEL CER/ APROBACIÓN PROYECTO POR EL CER

Codi de l'estudi / *Código del estudio*: CIR-ECL-2018-07
Versió del protocol / *Versión del protocolo*: 1.0
Data de la versió / *Fecha de la versión*: 01/10/18
Títol / *Título*: Impact of orthognathic surgery on the upper airway (UA) and the apnea-hypopnea index (AHI)

Sant Cugat del Vallès, 30 d'octubre de 2018

Doctorand/o: Maria Giralt-Hernando

Dicrectors/es: Federico Hernández-Alfaro, Adaia Valls-Ontañón

Títol de l'estudi / *Título del estudio*: Impact of orthognathic surgery on the upper airway (UA) and the apnea-hypopnea index (AHI)

Benvolgut/da,

Valorat el projecte presentat, el CER de la Universitat Internacional de Catalunya, considera que, el contingut de la investigació, no implica cap inconvenient relacionat amb la dignitat humana, tracte ètic per als animals ni atempta contra el medi ambient, ni té implicacions econòmiques ni conflicte d'interessos, **però no s'han valorat els aspectes metodològics del projecte de recerca degut a que tal anàlisis correspon a d'altres instàncies.**

Per aquests motius, el Comitè d'Ètica de Recerca, RESOLT FAVORABLEMENT, emetre aquest CERTIFICAT D'APROVACIÓ, per que pugui ser presentat a les instàncies que així ho requereixin.

Em permeto recordar-li que si en el procés d'execució es produís algun canvi significatiu en els seus plantejaments, hauria de ser sotmès novament a la revisió i aprovació del CER.

Atentament,

Apreciado/a,

*Valorado el proyecto presentado, el CER de la Universidad Internacional de Catalunya, considera que, el contenido de la investigación, no implica ningún inconveniente relacionado con la dignidad humana, trato ético para los animales, ni atenta contra el medio ambiente, ni tiene implicaciones económicas ni conflicto de intereses, **pero no se han valorado aspectos metodológicos del proyecto de investigación debido a que tal análisis corresponde a otras instancias.***

Por estos motivos, el Comitè d'Ètica de Recerca, RESUELVE FAVORABLEMENTE, emitir este CERTIFICADO DE APROBACIÓN, para que pueda ser presentado a las instancias que así lo requieran.

Me permito recordarle que si el proceso de ejecución se produjera algún cambio significativo en sus planteamientos, debería ser sometido nuevamente a la revisión y aprobación del CER.

Atentamente,

Dr. Josep Argemí
President CER-UIC

8.5 Approval of the PhD Thesis project by the Teknon Medical Center Ethics Committee of Clinical Investigation (Comité Ético de Investigación Clínica, CEIC).

quirónsalud
La salud persona a persona

APROBACIÓN DEL COMITÉ ÉTICO DE LA INVESTIGACIÓN

Dr. José Luis Simón Riazuelo, Presidente del Comité Ético de la Investigación del Grupo Hospitalario Quirón en Barcelona,

CERTIFICA

Que este Comité ha evaluado la propuesta realizada por el promotor: **Servicio Maxilofacial Centro Médico Teknon – Grupo Quirónsalud** código de protocolo: **OSAS-OS** titulado: "Impacto de la cirugía ortognática sobre el síndrome de apnea-hipopnea obstructiva del sueño (SAHOS)". Protocolo Versión 1.0 de fecha 30 de octubre de 2017 y considera que:

Se cumplen los requisitos necesarios de idoneidad del protocolo en relación con los objetivos del estudio y están justificados los riesgos y molestias previsibles para el sujeto.

La capacidad del investigador y los medios disponibles son apropiados para llevar a cabo el estudio.

Son adecuados los procedimientos previstos para obtener el Consentimiento Informado.

El alcance de las compensaciones económicas previstas no interfiere con el respeto a los postulados éticos.

Y que este Comité acepta que dicho estudio sea realizado por la **Dra. Adaia Valls como Investigador Principal del Centro Médico Teknon - Grupo Quirónsalud**

En Barcelona, a 30 de noviembre de 2017.

Fdo.: Dr. José Luis Simón Riazuelo

8.6 International PhD mention approval certificate by the Pontifical Catholic University of Rio Grande do Sul (PUCRS), coordinated by the tutor prof. Dr.Rogerio Belle de Oliveira

PUCRS | ESCOLA DE CIÊNCIAS DA SAÚDE E DA VIDA

Pontifícia Universidade Católica do Rio Grande do Sul
Curso de Odontologia

International University of Catalonia
San Cugat del Valles
Post-graduation Program Ph.D – International Ph.D

Dear Coordinator,

I hope to find you and all your staff safe and well. During all this period of COVID-19 pandemic, Maria Giralt Hernando [redacted], started on January of 2020 until now, has been working on-line in a multicentric study about the tridimensional effects of Orthognatic Surgery over the superior airway and facial soft tissues. Title in Spanish:" *Impacto de la cirugía ortognática en las vías aéreas en 3D."*

As the Coordinator of this multicentric study in the Oral and Maxillofacial Department at the Pontifical Catholic University of Rio Grande do Sul (PUCRS), I`m affirming that she is achieving high skills of critical thinking and research in our field of interest. As soon as possible Giralt-Hernando's effort will pay off with papers in the best indexed Oral and Maxillofacial Surgery journals.

Best regards,

Rogerio Belle de Oliveira, DDS, MsC, Ph.D
Pontifical Catholic University of Rio Grande do Sul (PUCRS)
School of Health and Life Sciences (SHLS)
Professor of Oral and Maxillofacial Surgery (SHLS/PUCRS)
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