Maxillo-Facial Surgical Considerations in the Management of Obstructive Sleep Apnoea

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Abstract

Obstructive sleep apnoea (OSA) represents an important public health issue affecting approximately 4% of the UK population. Maxillo-mandibular advancement (MMA) can be considered the most successful surgical procedure for the treatment of OSA. Despite the evidence of the efficacy of MMA, there have been no previously published studies from the UK in this area. This research was designed to investigate several key aspects relevant to the application of MMA in OSA.

The results from these studies shed light on both the effectiveness and role of maxillofacial orthognathic procedures in the treatment of selected patients with OSA who require alternative treatment options to first-line therapies. The potential applications of technical modifications to maxillofacial procedures in order to improve outcome is also discussed.

The research addresses the important consideration of optimising patient selection for MMA procedures through the utilisation of clinical tools, as well as considering important individual patient factors. In particular, these studies have demonstrated that the Malampatti airway classification does not have a predictive role in outcome following MMA, in contrast to other surgical modalities used to treat OSA. The Kushida morphometric model which incorporates cranio-facial dysmorphism, does not appear to correlate with surgical outcomes, but in spite of this, it retains a diagnostic value to maxillofacial surgeons treating OSA patients.

These research findings have shown that baseline OSA severity as well as duration of continuous positive airway pressure (CPAP) use prior to MMA surgery, would

appear to significantly correlate with a reduction in subjective outcome measures, however, this association was not seen with objective outcome measures. The lack of consistent correlation between these outcome variables perhaps highlights a complexity that has not been reflected in previously published surgical literature.

The important surgical consideration of patient acceptance of a permanently altered facial profile was investigated, with the findings demonstrating that the majority of patients subjectively rated their postoperative facial appearance positively following MMA. This was found to be independent of overall surgical outcome. Additionally, we examined cardiovascular risk factor modification after MMA demonstrating that this surgery has a potent beneficial effect on blood pressure reduction, particularly in those with established hypertension.

This body of research significantly contributes to the evidence base in support of this branch of maxillofacial surgery which is currently not widely practiced in the UK. The research demonstrates that surgery can be safely and efficaciously applied to treat selected patients with MMA procedures as an alternative treatment modality in OSA, when other first-line treatments are not tolerated or successful.

Background

The clinical problem of a diminishment in sleep quality and its variable clinical sequelae is recognised to be an increasing problem world-wide. The international classification of sleep disorders identifies approximately eighty different diagnoses potentially responsible for a reduction in sleep quality[1]. Of these an important group in terms of incidence and prevalence are the sleep disordered breathing (SDB) conditions. The SDB disorders may be associated with or without airway / air-flow obstruction. For example, Ondine's curse syndrome (primary alveolar hypoventilation) and central sleep apnoea have an underlying neurological aetiology with no component of airway / air-flow obstruction. There are a spectrum of SDBs which may be considered a continuum of related conditions with a similar underlying pathophysiology resulting from airway / air-flow obstruction. This group includes simple snoring at one end, moving through to upper airways resistance syndrome (UARS), and progressively onto mild, moderate and severe obstructive sleep apnoea syndrome.

Simple snoring may be defined as sound created through vibration of soft tissue in constricted segments of the upper airway, importantly it is not accompanied with impairment of breathing and does not disrupt sleep quality. In contrast to simple snoring, UARS is associated with a rise in respiratory resistance and a consequent increase in respiratory effort. However, the muscle tone of the upper airway is sufficient to maintain at least a partial lumen. The resulting effect is the occurrence of an abnormal frequency of respiratory arousals during sleep, without detectable apnoeas and has been shown to have a negative impact on sleep quality [2].

Obstructive sleep apnoea (OSA) is characterised by the periodic narrowing of the upper airway with associated reduction of airflow during sleep. This results from an imbalance between the forces dilating and occluding the upper airway during sleep. A reduction of

upper airway muscle tone together with inspiratory suction force and pressure from surrounding tissues produces this narrowing. A well-recognised classification system for identifying the level of upper airway obstruction was described by Fujita et al in 1981 [3]. These authors described three main areas of upper airway collapse in patients with OSA. Type I occurring at the level behind the soft palate (retro-palatal), Type II encompassing both soft palate and hypopharyngeal (base of tongue) obstruction and Type III at the level of the hypopharynx alone. The majority of OSA sufferers have multiple levels of upper airway narrowing. The precise diagnosis of the level of obstruction can be difficult and a number of techniques have been utilised, including sleep naso-endoscopy, lateral cephalometric analysis and more recently the use of ApneaGraph™ technology.

Recurrent apnoeas and hypopneas in OSA trigger episodic central arousals with disturbance of sleep physiology. The associated release of catecholamines places an increased burden on the cardiovascular system in particular, via recurrent sympathetic nervous system stimulation. In the UK, it is estimated that around 4% of men and 2% of women suffer from OSA [4]. The predominant symptoms associated with OSA are, intermittent snoring, daytime somnolence, diminished cognitive performance, together with other symptoms such as personality change, male impotence, morning headaches, and nocturnal enuresis[5]. In addition to their direct symptoms relating to reduced sleep quality, these individuals have an increased risk of adverse health outcomes. Conditions known to be associated with OSA include cardiovascular disease, type 2 diabetes, depression, cognitive impairment, premature death as well as increased road traffic accidents [5,6,7].

In excess of 94% of OSA patients have concomitant persistent snoring; diagnostically this highlights the importance for clinicians to be able to differentiate accurately those suffering from harmless simple snoring alone from those with OSA [8]. OSA is diagnosed through obtaining a comprehensive history and examination, including completed Epworth

sleepiness score (ESS) questionnaire, combined with appropriate additional diagnostic investigations. Conventionally this would entail polysomnographic assessment.

The ESS was first introduced by Johns in 1991 utilising a validated questionnaire designed to subjectively assess the daytime somnolence of a patient [9]. Eight questions involving 8 different situations are rated with a possible total score of 0-24. A score of <10 is considered to be within the normal range. The ESS has both a high specificity (100%) and high sensitivity (93.5%)[10]. Although validated for individuals with OSA, in recent years its application in other sleep disorders such as narcolepsy has been demonstrated. ESS is a useful tool to assess subjective response to therapy for OSA and has been used extensively in published literature in the context of continuous positive airway pressure (CPAP) therapy.

The diagnosis of OSA is confirmed through the demonstration of apnoeas and / or hypopneas following formal polysomnographic assessment (sleep study). The objective severity of OSA can be classified using the apnoea/hypopnoea index (AHI). This represents the number of apnoeas plus hypopnoeas per hour of sleep. There is some international variability in cut off scores in terms of OSA severity stratification. In the UK, mild OSA is classed as an AHI of 5-14/hr, moderate 15-30/hr, and severe OSA represented by an AHI >30/hr. Published literature has demonstrated an association between increased AHI and mortality risk[11]. Additionally, the AHI has been used to assess objective response to treatment for OSA in the context of surgical and non-surgical therapy.

Whilst both ESS and polysomnographic data provide accurate and robust diagnostic information, it is perhaps worth highlighting that these objective and subjective modalities do not always correlate and present the clinicians with a challenge in terms of screening patients and identifying the most appropriate treatment modality [12,13,14].

There are multiple treatment options for OSA and these can be broadly classified into conservative treatments, devices/appliances (including CPAP) and surgical methods. Conservative treatment encompasses lifestyle modification with a focus on weight reduction and optimisation of sleep hygiene. Several studies have shown that weight reduction improves OSA[15]. Maintaining good sleep hygiene, in particular an avoidance of alcohol, sedatives and nicotine, as well as establishing a regular sleep pattern is part of standard medical advice offered.

CPAP has been first line treatment world-wide since it was first described in 1981[16]. CPAP acts by providing a pneumatic splint to the upper airway and helps to prevent airway collapse. It is currently considered the most effective non-invasive treatment modality and the efficacy of all other therapies are therefore measured against it. The major problem with CPAP therapy for OSA is the issue of long-term adherence. Unfortunately, patients often find compliance difficult through the need to endure a tight-fitting mask each night. The adherence to CPAP varies and would appear to decline the younger patients are, as well as in those who experience a lesser improvement in their subjective symptoms with CPAP therapy[17]. The overall rate of compliance has been reported to be around 60%[18,19].

There are a variety of oral appliances that have been trialled in the treatment of OSA, including mandibular advancement devices, tongue retaining devices and soft-palate lifters. Of these the most successful has been the mandibular advancement device (MAD). Documented success rates in mild to moderate cases of OSA range between 50-70% [20, 21, 22]. Many patients prefer oral appliances when compared to CPAP, where both modalities are equally effective, and this may relate to the fact that MADs offer a more convenient and acceptable treatment for them [23]. Subjective compliance with MAD has been estimated at 40-80% [24,25]. Unfortunately adherence limiting side-effects have been reported in more than

two-thirds of patients and these include temporomandibular joint symptoms, dental discomfort, xerostomia and hypersalivation [26].

Historically, uvulopalatopharyngoplasty (UPPP) with or without nasal surgery has been the most commonly performed operative intervention in OSA patients and is the most researched form of surgical treatment for OSA. It typically involves enlargement of the retro-palatal airway by excision of any enlarged tonsils, trimming and reorientation of the posterior and anterior tonsillar pillars, and excision of the uvula and posterior portion of the palate. The success of UPPP is a little under 50%[27, 28]. However, a number of other surgical procedures have been employed in an attempt to correct the upper airway narrowing seen in OSA and these include tracheostomy, hyoid suspension, tongue base resection with variable published results[27]. Of note, in selected patients with morbid obesity there is evidence that undertaking bariatric surgical procedures can significantly improve their OSA [29].

Maxillofacial orthognathic surgery for the treatment of upper airway obstruction due to retrognathic mandible was first described by Kuo et al in 1979 [30]. These authors proposed maxillofacial surgery as an alternative to tracheostomy in the management of OSA. To date, tracheostomy remains the only intervention with a documented 100% cure rate for sleep disordered breathing, and has been described in the literature as far back as the 1960's [31,32]. It is also perhaps worth recalling that the work of Kuo et al[30] precedes Sullivan's[16] seminal paper on the use of CPAP by two years.

In the context of maxillofacial orthognathic surgery, jaw relations are commonly described in terms of the relationship between maxilla and mandible and are best demonstrated in profile. There are three classes of occlusion, with Class 1 representing a normal relationship between the maxilla and mandible. Class II represents mandibular retrognathism, in which

the maxilla lies in a more anterior position. This malocclusion can result from either a hypoplastic mandible, maxillary hyperplasia or a combination of both. Class III represents mandibular prognathism, in this situation the mandible is situated in a more anterior position relative to the maxilla. The underlying problem may be a hyperplastic mandible or maxillary hypoplasia and is often a combination. Conventional maxillofacial orthognathic surgery aims to correct skeletal class II and class III malocclusion in order to achieve a class I relationship postoperatively and a functional occlusion.

The usual method of MMA involves performing a Le Fort 1 osteotomy with maxillary advancement and internal fixation using mini-plates. The osteotomy line resembles the fracture line analogous to Le Fort 1 fracture. The mandibular advancement procedure is usually performed utilising the bilateral sagittal split osteotomy technique as described by Obswegeser and Dalpont[33,34,35]. After aligning the mandible to the correct occlusion, internal fixation of the mandible is performed with mini-plates or bicortical screws. The average advancement of the maxilla and mandible is 8-10mm.

Currently, maxillomandibular advancement (MMA) can be considered the most successful surgical procedure for the treatment of OSA after tracheostomy. The rationale of MMA is the simultaneous expansion of the naso, oro and hypopharyngeal airway through the stretching or advancement of soft palate, tongue and lateral pharyngeal walls. Given that the majority of OSA sufferers have multi-level airway narrowing (Fujita II), MMA offers a multi-level solution, to alleviate retropalatal and retrolingual obstruction with one surgical procedure. A number of previous studies have demonstrated a comparable efficacy in terms of reduction in AHI with MMA compared with CPAP, with sustained improvement observed with long term follow up[36,37]. Typically the published success rates with MMA range from 75-100%[36,37,38].

Despite the evidence of the efficacy of MMA, there have been no studies from the UK in this area. In 2005, The Cochrane collaboration reviewed seven studies which assessed the effectiveness of various surgical interventions in the management of OSA[39]. Regrettably, however, none of the studies included considered MMA procedures in OSA patients. The authors concluded that there was insufficient evidence overall to support the widespread use of surgical treatment in OSA. In contrast, a more recent European Respiratory Society (ERS) working group in 2011 reviewed the evidence base for alternative treatment options for OSA[40]. This group concluded that maxillomandibular advancement was as effective as CPAP in patients who refuse or fail to tolerate conservative treatments. Moreover, the ERS group felt that young patients with OSA, who lack lifestyle risk factors which can be readily modified, would potentially benefit from early maxillofacial intervention[40].

Despite the ERS working group advocating its role in selected patients, at present in the United Kingdom maxillofacial surgical techniques remain under-utilised in the management of OSA.

Overall objectives

This body of published works (9 peer reviewed papers), represents the first UK maxillofacial surgical unit's clinical research into operative outcomes in patients who have undergone MMA for the treatment of OSA. Surgical outcomes were considered utilising both objective and validated subjective measures. Additionally, this body of research examines a number of unexplored clinical questions relevant to the practice of maxillofacial surgery in OSA. The scope, content and contribution that each published paper makes to the advancement of the subject will now be discussed in turn.

Paper 1:

PUBLISHED: Ormiston IW, **Islam S**. The Role of Maxillomandibular Advancement Surgery in Obstructive Sleep Apnoea. *PMFA (plastics, maxillofacial and aesthetic surgery).* 2014;11(6):16-19.

Scope and content:

- To provide an overview of the role of the maxillofacial surgeon in OSA surgery.
- To consider the evolution of this area of surgical practice.
- Detailed description of the surgical technique for MMA.
- A review of the current literature of the area in relation to MMA in OSA

Summary and key findings:

Facial skeletal deformity surgery has been practiced for many decades by maxillofacial surgeons. This expertise has provided maxillofacial surgeons with an appreciation of the interaction between facial skeletal movements and the consequent alteration to soft tissues of the head and neck. There has been a growing recognition of the profound effects on the posterior airway space at both retropalatal and retrolingual levels following maxillofacial orthognathic surgery in patients who undergo facial skeletal advancement for retrognathic mandible or midfacial hypoplasia. This has led to the development of the cross-application of maxillofacial techniques to treat upper airway narrowing seen in subjects with OSA. This paper describes the concept and classification of facial skeletal disproportion in the context of orthognathic surgery. It also encompasses a description of operative technique employed for MMA which typically involves a bilateral saggital split osteotomy as well as Le fort 1 maxillary osteotomy. Furthermore, this paper offers an overview of the clinical considerations relevant to patient selection for operative management.

Contribution to the advancement of the subject:

This paper provides an accessible review of the role of MMA in OSA, which is likely to be of value to clinicians working in the area of sleep disordered breathing. In particular for practitioners who are perhaps less familiar with the application of maxillofacial techniques in OSA. In the UK this area of surgery remains underutilised. It would therefore seem important for information regarding this developing area of surgical practice to be available to clinicians and patients to promote greater awareness of MMA as a treatment modality in OSA.

Paper 2:

PUBLISHED: **Islam S,** Uwadiae N, Ormiston IW. Orthognathic surgery in the management of obstructive sleep apnoea: Experience from a maxillofacial surgery unit in the UK. *British Journal of Oral and Maxillofacial Surgery.* 2014 ;52(6):496-500.

Scope and content:

- To report on the operative experience from the maxillofacial unit in University Hospital Leicester.
- To record detailed baseline characteristics including preoperative skeletal profile and operative data of individuals undergoing MMA to develop a better understanding of this subgroup of OSA patients.
- To report on surgical outcomes using three measures: Apnoea/Hypopnoea Index (AHI), Epworth Sleepiness Scores (ESS) and lowest recorded oxygen saturation (SpO2).
- To review the surgical morbidity associated with MMA procedures in OSA patients.

Summary and key findings:

We identified 51 patients who met the eligibility criteria for inclusion in our study. These were predominantly male with a mean age of 44 yrs and a mean BMI of 29. When previous therapies for OSA were considered, 14% had been unable to trial or had declined CPAP therapy, with 41% having previously undergone nasal surgery, UPPP or a combination of these. The majority of the sample had a normal skeletal profile (Class 1 occlusion) with only one third of patients having a class 2 skeletal profile secondary to mandibular retrognathism. The principle study findings show that maxillofacial orthognathic procedures are very effective in the management of OSA patients when widely accepted objective outcome measures are utilised. Polysomnographic examination following MMA surgery demonstrated a statistically significant reduction in AHI ($p<0.001$), and improvement in the recorded lowest

oxygen saturation levels (p=0.006). Postoperatively subjective outcome measures (ESS) similarly demonstrated a significant reduction from baseline levels (p<0.001). 85% of patients met the criteria for surgical 'success' based on AHI <15 postoperatively.

The most frequent surgical complication was transient sensory nerve morbidity. Permanent partial sensory nerve deficit presenting as lip and or chin hypoaesthesia / paraesthesia was noted in 22% of patients but this appeared to be well tolerated.

Contribution to the advancement of the subject:

This paper constitutes the first published UK series of patients who have received MMA for OSA. The findings validate the surgical technique as a highly efficacious intervention for OSA, and importantly adds to the evidence base in the English medical literature. The data confirms a high rate of surgical success when outcomes are measured using three of the most common outcome variables, namely AHI, ESS and oxygen saturation. Conventionally, outcome measures in surgical studies have focused on the AHI. This study demonstrates important modifications to oxygen saturation which are achievable with MMA. It is noteworthy that patients in our study had a baseline mean nocturnal oxygen saturation nadir of 76% which improved to 83% postoperatively. Recent published research has reported a threshold oxygen saturation nadir of 78%, below which the risk of sudden adverse cardiovascular events increases significantly [41].

In clearly defining the characteristics of this subgroup of patients with OSA, the study contributes to the scientific literature in better informing clinicians about the patients who may benefit from maxillofacial surgical intervention, with particular reference to baseline facial skeletal profile. The original description of the application of orthognathic surgery for the treatment of OSA was based on patients with evidence of mandibular deficiency (Class

II). The perception that maxillofacial surgery is primarily indicated in OSA patients with a retrognathic mandible is still prevalent. This paper confirms that all patients, irrespective of their baseline skeletal profile, may undergo MMA procedures successfully. Moreover, in this study 65% of the patients had preoperative class 1 skeletal profile. These findings therefore refute the notion that MMA procedures should be restricted to individuals with Class II skeletal profiles.

There is currently some debate amongst surgeons as to whether patients who fail to adhere to non-invasive therapies, should undergo primary MMA surgery or undergo a perceived less invasive operative procedure first, such as UPPP. This paper highlights that a significant number of patients in our study population had undergone surgery to their upper airway for OSA prior to being referred for MMA. The data therefore supports the current view that the aforementioned procedures are only successful in a select group of patients, and in keeping with ERS working group recommendations that such single level interventions should be considered with a degree of caution [40].

Whilst the techniques involved in the MMA procedure are considered routine by maxillofacial surgeons, to many clinicians working in the area, there is perhaps a perception that this operation is unduly aggressive as a primary surgical intervention and potentially places the patient at risk of significant complications. The data from this study demonstrates that MMA was well tolerated with minimal postoperative morbidity, and therefore helps to inform and reassure sleep clinicians and patients. This aspect of the research is particularly important and relevant given the paucity of published material discussing the rates of postoperative morbidity in this patient group. Such individuals are appreciably older than the typical patient undergoing maxillofacial orthognathic surgery for facial skeletal deformity, with commonly quoted complications rates derived from younger patients. It is recognised however that the incidence of complication following MMA increases with patient age [42].

Paper 3:

PUBLISHED: **Islam S,** Selbong U, Taylor CJ, Ormiston IW. How well does a patient's Mallampati score predict the outcome following maxillomandibular advancement surgery for obstructive sleep apnoea? *British Journal of Oral and Maxillofacial Surgery.* 2015;53(1):23-7.

PRESENTED: XXII Congress of European Association of Cranio-maxillofacial Surgery (EACMFS), Prague, Czech Republic, October 2014

Scope and content:

- A review of the wider application of the Mallampati airway classification in OSA.
- A review of the utilisation of the Mallampati score in relation to upper airway surgical procedures in OSA.
- To assess the predictive value of the Mallampati score in patients undergoing MMA surgery for OSA

Summary and key findings:

The Mallampati airway classification provides a simple and practical method for assessing a patient's airway, and may be easily performed by any clinician evaluating a patient with OSA. It has been hypothesised that patients with high Mallampati scores have relatively narrow upper airways and are therefore at higher risk of suffering from sleep disordered breathing. Previously published literature has demonstrated an association between Mallampati score and the presence and severity of OSA [43,44]. It is perhaps not surprising that surgeons have attempted to utilise this tool in their patient selection for upper airway surgical procedures for OSA, such as UPPP. Researchers have demonstrated a predictive value for the Mallampati score in UPPP and also nasal surgery for OSA [45,46]. In this paper we studied the potential role of the Mallampati airway classification in predicting surgical

outcome in the context of MMA for OSA. We identified 50 patients who met the inclusion criteria for this study. We stratified this population into two groups based on the Mallampati airway classification at initial presentation: low score group (Mallampati class I/II) and high score group (Mallampati class III/IV). We explored the association between the preoperative Mallampati score and subjective and objective outcome measures, comprising ESS, AHI and lowest recorded oxygen saturation postoperatively. This study found that there is no statistically significant difference in the postoperative mean reduction of AHI and ESS following surgery when patients are stratified by their baseline Mallampati airway classification score.

Contribution to the advancement of the subject:

This study represents the first research to explore the possible association between Mallampati score and surgical outcome in MMA for OSA, and by extension its potential application as a preoperative predictive tool. This topic is highly relevant to surgeons as an adjunct in optimising patient selection and would be extremely valuable in clinical practice. Traditionally, the most common operation performed for OSA has been UPPP, with highly variable clinical results. In the light of this Friedman and colleagues developed a classification system incorporating the Mallampati scores as a key component. Poor surgical success (<10%), was described in patients with high scores utilising the Friedman classification system, with a consequent emphasis on identifying patients with low Mallampati scores as more suitable for UPPP procedures. This research paper demonstrates that these considerations need not apply in patients being considered for MMA surgery. Data derived from studies involving UPPP, cannot therefore be considered to be applicable in other upper airway procedures for the treatment of OSA. In this context our data constitutes an important negative finding, refuting the perception that patients with high Mallampati score do less well following surgery in general.

The traditional two-phased approach for the surgical treatment of OSA would entail a UPPP or variation, with assessment of clinical response, followed by definitive MMA if required. There is still some debate with regard to the appropriateness of this advocated two-phase model [42,47,48]. Surgeons who are competent to perform both UPPP as well as MMA could therefore use the Mallampati score to enable them to identify patients in whom a primary MMA is preferable.

Paper 4:

PUBLISHED: **Islam S,** Taylor CJ, Ormiston IW. The predictive value of obstructive sleep apnoea severity on clinical outcomes following maxillomandibular advancement surgery. *British Journal of Oral and Maxillofacial Surgery.* 2015; 53(3):263-7.

PRESENTED: XXII Congress of European Association of Cranio-maxillofacial Surgery (EACMFS), Prague, Czech Republic, October 2014

Scope and content:

- A review of the current literature covering the topic of severity of OSA as defined by AHI, and its impact on operative outcomes for sleep disordered breathing.
- To determine if the severity of OSA as defined by AHI has any predictive value in patients undergoing MMA surgery.
- To assess how well objective and subjective outcomes correlate after MMA and discuss the clinical implications.

Summary and key findings:

Currently there is no widely accepted treatment algorithm to assist the surgeon in identifying the most suitable operative modality for individuals with OSA who have failed first-line CPAP therapy. Previous research has attempted to stratify this subgroup of patients utilising the baseline AHI (OSA severity) to target appropriate operative interventions for individual patients. These upper airway operations could range from a single-level retropalatal procedure through to multi-level procedures, including MMA. It has been advocated that with increased severity of OSA there is an associated increase in the extent of upper airway narrowing [49] . In view of these observations, patients with moderate to severe OSA are felt to require a procedure which is capable of alleviating airway obstruction at multiple levels.

There is currently a paucity of clinical research exploring the association between OSA severity and surgical outcome. The possible relationship between OSA and surgical outcome has previously been studied in patients undergoing UPPP for OSA, with the findings suggesting that patients with mild OSA (AHI <20) typically have better outcomes [27].

In this paper we examined the potential predictive value of the preoperative OSA severity in 39 patients who underwent MMA for their OSA. Our sample was divided into two groups based upon the AHI score, with a mild-moderate OSA group (AHI<30) and a severe OSA group (AHI >30). The primary outcome measure was postoperative AHI derived from a repeat sleep study carried out 6-months following surgery. The secondary outcome measure was ESS scores after operation. We defined surgical success as a postoperative AHI <15.

The key findings of this study were that we observed no statistically significant difference in rates of surgical success and mean reduction in AHI from baseline values between the study groups. However, when subjective outcome measures were considered the severe OSA group were found to have greater reduction in ESS score 6 months after surgery ($p<0.05$). All subjects, except one, reported an improvement in their subjective symptoms after surgery. An additional finding of interest was that rate of previous upper airway surgery was significantly higher in the mild-moderate OSA group.

Contribution to the advancement of the subject:

There is a dearth of research investigating the possible relationship between preoperative OSA severity and surgical outcome following MMA for OSA. The results of this research demonstrated that preoperative OSA severity based on AHI criteria does not predict surgical outcome following MMA, with both OSA severity groups found to have comparable surgical outcomes. This study adds to the current evidence base as there is limited previous

published work evaluating the impact of disease severity in MMA surgery for sleep disordered breathing. The results of this study would be of interest to both surgeons and referring sleep clinicians as it validates the application of MMA across the OSA severity spectrum, and highlights the potential pitfalls in performing single level procedures even in those OSA patients deemed mild-moderate severity in the disease spectrum.

We noted a greater reduction in the ESS score in the severe OSA group when compared to the mild-moderate OSA group. The majority of surgical literature relating to outcomes in patients undergoing operative interventions for OSA has tended to focus on objective outcome measures (AHI and oxygen saturations), with the ESS score predominantly utilised in the diagnostic work-up of patients. It is not surprising that clinicians have preferred to use objective parameters in their clinical decision making, however, in our study baseline ESS scores between the severity groups were equivalent. This is an interesting observation given that patients were reporting equal subjective severity despite the disparity in disease severity when stratified by AHI. Previous published research has similarly reported a poor correlation between changes in objective measures and subjective symptoms[12,13]. Subjective symptoms are extremely important to patients, and it could be argued that the relief from these symptoms is the predominant consideration for a patient consenting to undergo operative intervention for their OSA.

Paper 5:

PUBLISHED: **Islam S,** Taylor CJ, Ormiston IW. Effect of preoperative continuous positive airway pressure duration on outcomes after maxillofacial Surgery for Obstructive Sleep Apnoea. *British Journal of Oral and Maxillofacial Surgery.* 2015 ;53(2):183-6.

PRESENTED: ACBID- BAOMS, Joint Congress, Istanbul, Turkey, November 2014

Scope and content:

- To evaluate the physiological implications of long-term CPAP therapy.
- To explore the potential relationship between the preoperative duration of CPAP therapy and surgical outcomes in MMA for OSA, utilising both objective and subjective variables.
- Examine the possible impact prior CPAP therapy may have in patient selection for operative intervention
- To consider the potential implications to patients of the abrupt cessation of long-term CPAP therapy following successful MMA surgery for OSA.

Summary and key findings:

CPAP therapy remains first line treatment for OSA and most patients with symptoms will be offered a trial of CPAP. Long-term adherence continues to be a major limitation. In individuals unable to tolerate long term CPAP, operative interventions are advocated. MMA is recognised to be the most effective of these with comparable efficacy to CPAP. The long-term term physiological effects of CPAP are increasingly being recognised with various

clinical manifestations described. There is currently no published data assessing the potential variation in response to surgical interventions in patients using CPAP for longer or shorter durations, or indeed those whom have never trialled CPAP. The aim of this study was to explore a possible association between the duration of preoperative CPAP therapy and surgical outcomes following MMA for OSA. Outcome parameters consisted of AHI, ESS and nocturnal oxygen saturation nadir. Forty-three patients met the inclusion criteria for this study. The patient group was stratified according to length of time on CPAP preoperatively. The short-term group was defined as a period of CPAP therapy up to 12 months with the long-term therapy group consisting of patients who had used CPAP for greater than 12 months prior to MMA surgery. This study demonstrated no significant difference between long term and short term CPAP groups in terms of objective outcome parameters (AHI and oxygen saturation). The research demonstrated a statistically significant difference in the subjective outcome measure between the two CPAP duration groups, with the mean postoperative ESS scores lower in the long-term group ($p<0.001$). This study highlights that in spite of the physiological modification known to occur with CPAP we found no adverse effects on objective surgical outcome. Additionally of note, the long-term CPAP patients appeared to derive a greater subjective benefit from surgical intervention.

Contribution to the advancement of the subject:

This study represents the first published paper to explore the area of preoperative CPAP duration and its possible association with surgical outcomes in patients undergoing operative procedures for OSA. The results add to the current evidence base and reassure sleep clinicians treating OSA sufferers that they may consider patients for MMA regardless of the duration of preoperative CPAP therapy. There is limited published literature which has discussed the issue of prescribing both pre and postoperative CPAP therapy in patients undergoing MMA for OSA [42]. It has been advocated that patients with severe OSA should

receive CPAP therapy continuously for a minimum of 1 month prior to surgery in order to stabilise their cardiovascular physiology as well as helping to reduce upper airway oedema[42]. Additionally, some have suggested that patients continue with CPAP therapy postoperative until a follow up sleep study confirms surgical success. This research study helps to shed some light on this underexplored area as many of the patients in our study were not able to tolerate CPAP or were not regularly using CPAP therapy in the run up to their surgery. Those patients in our group who were non-adherent to CPAP were not counselled to restart therapy prior to their surgery. Additionally, the patients in our series were not routinely advised to continue CPAP following their MMA procedure. The results of this study would suggest that it is perhaps unnecessary for patients to continue with their CPAP after MMA pending their 6 month postoperative polysomnographic examination.

Paper 6:

PUBLISHED: **Islam S,** Aleem F, Ormiston IW. Does the Kushida Morphometric Model Predict Outcomes following Maxillomandibular Advancement Surgery for Obstructive Sleep Apnoea? *Journal of Cranio- Maxillofacial Surgery,* 2014; 42(8):1675-8.

PRESENTED: ACBID- BAOMS, Joint Congress, Istanbul, Turkey, November 2014

Scope and content:

- To review the role of the Kushida morphometric model in the assessment and diagnosis of patients with OSA.
- To investigate how well the Kushida values of our OSA subgroup matched the morphometric models diagnostic thresholds.
- To evaluate the role of the overall Kushida index score in relation to surgical outcome following MMA for OSA.
- To analyse the component variables constituting the Kushida morphometric model and assess their individual relationships with our surgical outcome variables.

Summary and key findings:

The mainstay in the diagnosis of OSA remains the utilisation of polysomnography and the derivation of an AHI. Several previous research studies have explored the area of mathematical modelling to assist in the clinical diagnosis of OSA[50,51,52]. Of these, the Kushida morphometric model has proved to be the most useful, and previous published research has confirmed a high sensitivity (97.6%) and high specificity (100%) for the diagnosis of OSA [53]. This mathematical formula incorporates disproportionate cranio-facial

anatomy as an important factor in the development of OSA, thereby differentiating it from previously proposed models. This morphometric model has therefore two constituent parts. The first part of the equation takes into account the relative contribution from a patients cranio-facial anatomy whilst the second part accounts for the contribution of elevated BMI. The formula is shown below.

Kushida Formula: $\mathbf{P+(Mx-Mn)+3\times 0J+3\times[Max\ (BMI-25)]\times(NC\div BMI).}$

Where P = palatal height (in millimetres). Mx = maxillary intermolar distance (in millimetres) between the mesial surfaces of the crowns of the maxillary second molars. Mn = mandibular intermolar distance (in millimetres) between the mesial surfaces of the crowns of the mandibular second molars. OJ = overjet (in millimetres). BMI is the body mass index (kg/m2) and NC is neck circumference (in centimetres).

The primary objective of this research study was to investigate the possible relationship between preoperative Kushida index score and postoperative surgical outcome following MMA for OSA. We additionally looked at the diagnostic concordance between calculated Kushida index values derived from our patient subgroup and the documented diagnostic thresholds for this morphometric model. Multivariate regression analysis was undertaken to determine specific relationships between outcome variables and individual component variables which comprise the Kushida morphometric model. We identified 28 patients with complete data available for analysis. The mean overall Kushida index score in the studied group was 79, which lies above the morphometric model diagnostic cut-off score of 70 [53]. Interestingly, our analysis showed that approximately one third of our patient group had a score solely derived from the cranio-facial dysmorphism component of the equation. The results of the regression analysis showed no statistically significant relationship between individual variables constituting the model and overall score with either of two outcome

variables (AHI and ESS). This study found that the Kushida morphometric model does not correlate with surgical outcomes and does not have a potential predictive role for the operating surgeon in assessing potential patients. However, the data from this study supports the fact that this mathematical equation constitutes a valuable tool in ensuring accuracy of the diagnosis, especially given that the results derived from polysomnography can be equivocal.

Contribution to the advancement of the subject:

This research study is the first to examine the potential role of the Kushida morphometric model in the context of evaluating patients referred for maxillofacial surgical intervention. There is a paucity of research in the surgical literature regarding the use of reliable screening tools for optimal patient selection. The stereotypical symptomatic OSA patient has an elevated BMI and is often quickly established on CPAP therapy. This research study adds to the current medical literature by drawing attention to an important group of OSA sufferers in whom craniofacial dysmorphism significantly contributes to the aetiology of their condition. Our findings lend support to the view that selected patients may benefit from a primary surgical intervention instead of receiving conventional first-line therapies. Additionally, the Kushida morphometric model has the capacity to help identify those OSA patients with subtle abnormalities in their facial skeletal architecture, without overt phenotypical appearances of maxillofacial dysmorphism. These patients may in fact be candidates for consideration of early referral for surgical treatment of their OSA.

Paper 7:

PUBLISHED: **Islam S,** Aleem F, Ormiston IW. Subjective assessment of facial aesthetics following maxillofacial orthognathic surgery for obstructive sleep apnoea. *British Journal of Oral and Maxillofacial Surgery.* 2015 ;53(3):235-8.

Scope and content:

- To review the current medical literature on patient acceptance of alteration to their facial profile as a result of MMA for OSA.
- To evaluate subjective perception of facial aesthetics in OSA patients following MMA procedures.
- To explore the potential relationship between subjective satisfaction with postoperative facial aesthetics and overall surgical outcome.

Summary and key findings:

The traditional role of maxillofacial orthognathic surgery has involved the correction of congenital or acquired facial skeletal deformity. Similarly, patients who undergo MMA for OSA are likely to be aware of some alteration in their postoperative facial profile. It has been postulated that the potential changes to their facial profile may be an important consideration for patients in deciding whether or not to proceed with MMA. This research study aimed to explore the subjective perceptions of facial aesthetics by patients following MMA. We also analysed a range of demographic and clinical characteristics to assess if there was a relationship between these and subjective perception. Additionally, we considered the previously unexplored question of whether or not patient satisfaction with their postoperative

facial aesthetics correlates with recognised outcome measures of surgical success. The study included 26 patients who underwent MMA surgery for OSA. The group were predominantly male with a mean age of 45. Patients were asked to assess their facial appearance pre and postoperatively utilising a visual analogue scale (VAS). We examined subjective perceptions of patients through the comparison of VAS scores before and after surgery. Pearson's correlation coefficient was used to assess the relationship between subjective VAS scores and postoperative AHI and ESS. The results of this study showed that 54% of patients reported a higher subjective satisfaction score with their facial appearance following surgery and 15% of patients recorded a neutral score. The remaining patients (31%) recorded postoperative subjective VAS scores that were lower than those obtained before MMA. We found no significant variance between postoperative AHI and ESS scores in those who felt that their facial appearance was improved or unchanged versus those who were less satisfied with their postoperative facial aesthetics. Postoperative VAS scores for facial appearance did not correlate with either of the two surgical outcome measures used. This study demonstrates a high level of subjective satisfaction with postoperative facial appearance after MMA. Furthermore, this research highlights that the subjective perceptions of patients appeared to be independent of the overall surgical outcome.

Contribution to the advancement of the subject:

There is limited data specifically addressing the concern that patients undergoing MMA for OSA, who do not have an associated facial skeletal dysmorphism, may experience adverse effects in postoperative facial aesthetic outcome. This study adds to the current body of evidence in demonstrating that a majority of patients subjectively rated their postoperative facial appearance positively following MMA. It is noteworthy that 81% of the patients studied had a preoperative class 1 skeletal profile. It has been previously postulated that middle-

aged patients with features of facial ageing and laxity of the soft-tissues may experience a rejuvenating effect following MMA, and consequently may perceive themselves to have a more youthful appearance. This phenomenon has been termed ‘reverse face-lift’ in previous published literature [54].

The possible correlation between surgical success and patients’ perception of facial aesthetics after MMA for OSA has not been previously researched. This question would seem pertinent given that individuals with poor outcome in terms of AHI / ESS reduction may be more likely to also subjectively rate their facial appearance more negatively after surgery. This paper therefore adds to the understanding of this topic in demonstrating that subjective perception of facial aesthetics appears to be independent of surgical outcome.

Paper 8:

PUBLISHED: **Islam S,** Ormiston IW. Innovative use of anterior subapical setback combined with bilateral sagittal split osteotomy in patients with obstructive sleep apnoea. *British Journal of Oral and Maxillofacial Surgery*. 2015 ;53(1):89-91.

Scope and content:

- To describe a novel use of the mandibular subapical setback osteotomy in combination with bilateral saggital split osteotomy in the context of surgical management of OSA.
- To highlight the versatility of maxillofacial orthognathic techniques, and their capacity to help individualise surgical treatment plans.

Summary and key findings:

The alteration to facial appearance following a conventional MMA procedure may not be cosmetically acceptable to all patients. Historically, the subapical osteotomy has been used in the management of patients with dento-facial deformity in view of its versatility. The potential use of anterior subapical setback osteotomy combined with bilateral saggital split osteotomy of the mandible in the treatment of OSA has not been previously described in the maxillofacial literature. This paper describes in detail the steps involved in performing this operation and discusses the potential advantages in using such a modification in selected individuals. Importantly the use of this technique enables the surgeon to correct retrolingual narrowing in individuals with OSA, whilst minimising alteration to facial appearance.

Contribution to the advancement of the subject:

This paper discusses a novel application of a well described orthognathic technique. It serves to highlight that there are potential single jaw advancement procedures which can be performed to remedy the upper airway narrowing in OSA as well as conventional bi-maxillary advancement. It could be argued that in patients identified as having localised retrolingual narrowing a mandibular advancement procedure may be more appropriate than the traditional MMA. Additionally, patients who have experienced a resolution of their OSA with an MAD may also be candidates for such procedures. The risk of velopharyngeal incompetence in patients who have previously undergone a UPPP procedure and subsequently undergo MMA is an important consideration. In this situation it may be justifiable to tailor their orthognathic surgery accordingly. This paper adds to the body of maxillofacial literature by highlighting that modifications in operative techniques may be useful in selected OSA patients.

Paper 9:

PUBLISHED: **Islam S,** Taylor CJ, Ormiston IW. Effects of maxillomandibular advancement surgery on systemic blood pressure in patients with obstructive sleep apnoea. *British Journal of Oral and Maxillofacial Surgery.* 2015 ;53(1):34-8.

PRESENTED: The European Respiratory Society International Congress (ERS), Munich, Germany, September 2014

Scope and content:

- To review the cardiovascular complications of OSA and discuss potential long term clinical implications in patients who are unable to adhere to first line therapy.
- To consider the published evidence regarding the effectiveness of CPAP and mandibular advancement devices on systemic blood pressure improvement in OSA patients.
- To investigate to what extent MMA influences a patients systemic blood pressure following surgery.
- To explore the relationship between cardiovascular outcomes and conventional outcome measures of surgical success, in a group of patients undergoing MMA for OSA.

Summary and key findings:

OSA is a widespread disorder associated with adverse health consequences in afflicted individuals. There is a growing body of literature drawing attention to OSA being an independent risk factor for cardiovascular morbidity; including hypertension, stroke and

sudden cardiac death [5,6,7,41]. Untreated hypertension is recognised as an important risk factor in cardiovascular diseases and is known to be strongly associated with OSA[41,55,56]. We examined the extent to which MMA affected a patient's blood pressure after surgery, and additionally compared the recorded postoperative blood pressure with postoperative polysomnographic data. Subgroup analysis was performed stratifying the group according to the presence or absence of a documented pre-surgical diagnosis of hypertension. We identified 45 patients who met the inclusion criteria for this research study. We compared mean blood pressure values before and after operation in all subjects and additionally analysed data in those with known hypertension, to examine whether changes observed in blood pressure were different in this subgroup. The results indicated that the mean postoperative systolic blood pressure was significantly reduced in our sample after surgery ($p<0.001$). The overall values of systolic and diastolic blood pressure as well as mean arterial pressure were lowered by 3.8 mmHg, 2.5 mmHg and 3.5 mmHg respectively. Analysis of the data in the known hypertensive subgroup demonstrated a significantly greater reduction in all of the three blood pressure parameters when compared with the overall study group. We observed no significant difference in blood pressures between patients who met our study criteria for surgical success (AHI <15 postoperatively) and those who did not (AHI >15).

Contribution to the advancement of the subject:

Published research has shown that OSA patients treated with CPAP and mandibular advancement devices have derived beneficial effects on recorded blood pressure[56,57,58,59,60,61].This research study makes a major contribution to the overall evidence base in the area of surgery for sleep disordered breathing by exploring a subject on which there is a paucity of previously published data. Our results highlight the potentially potent effect of MMA on blood pressure modification in OSA patients. This is a highly

relevant finding as it provides further evidence that in addition to effectively treating the symptoms of OSA and reducing AHI, MMA can also be shown to positively modify cardiovascular risk in such patients.

In general, the barometer for success for surgical procedures to the upper airway in the management of OSA has centred on objective polysomnographic results. Whilst this clearly remains important in confirming the desired reduction in the number of apnoeas and hypopnoeas during sleep, it could be reasonably argued that blood pressure reduction following MMA represents a valid indicator of operative success in its own right. These research findings lend support to the argument that “surgical success” solely defined by postoperative AHI scores perhaps provides an incomplete picture of the overall clinical benefit that OSA patients derive from MMA surgery.

Discussion

Sleep disordered breathing is of increasing importance as a public health issue with previous estimates of prevalence in the region of 10% in middle-aged women and 25% in middle-aged men[1,4]. OSA represents the most important condition within this group of disorders. First-line therapy with CPAP remains the gold standard, however, in light of the fact that a significant proportion of patients fail to tolerate CPAP long term, many patients are in need of alternative treatment options. A number of upper airway surgical interventions have been used, and of these MMA is widely recognised to be the most effective. In spite of the efficacy of MMA, only a handful of units in the UK currently provide a service to patients with OSA. This contrasts with the situation in North America, Continental Europe and Asia.

The published research works discussed explore a broad range of clinical considerations relating to the practice of MMA surgery in OSA patients. Furthermore, as a collective body of work it will serve to increase the general awareness of this important surgical modality for patients unable to tolerate conservative therapies.

The research studies were designed to assess several key aspects relevant to the application of MMA in OSA. The results from these studies discussed shed light on both the role and effectiveness of maxillofacial orthognathic procedures in the treatment of OSA. The potential of technical modifications of maxillofacial procedures to improve surgical outcome is also discussed. We address the concept of optimising patient selection for MMA procedures through the utilisation of clinical tools, as well as considering important individual patient factors, such as OSA severity. Surgical outcomes were assessed using objective and subjective measures. Additionally, we considered cardiovascular modification and patients' subjective perception of their facial aesthetics after MMA. The lack of consistent correlation

between these outcomes variables perhaps highlights a complexity that has not been reflected in previously published surgical literature.

The combination of both a paucity of scientific literature together with a relative lack of familiarity with MMA procedures amongst many clinicians working in the field of sleep medicine, may have led to the perception that MMA is unduly invasive and exposes patients to the risk of surgical morbidity. This body of work would be of interest to sleep clinicians of all designations, and refutes a number of the traditionally held views on the role of surgery and the risks and benefits to patients. Additionally, for a surgeon operating on OSA patients much of this research would be of value in assisting in their practice through providing a relevant clinical evidence base.

Recommendations for future research.

From the studies presented in this thesis, it is clear that MMA is a consistently effective treatment modality for OSA. Maxillofacial surgery for OSA has a crucial role as “salvage therapy” in those who have failed to tolerate CPAP and oral appliances, however, there are a limited number of maxillofacial surgeons performing this procedure for OSA. There is a need to raise the profile of maxillofacial operative techniques amongst sleep physicians in the UK.

It would be beneficial to conduct further research to demonstrate the cost effectiveness of maxillofacial surgical procedures for OSA in adults

There is growing evidence that the pathophysiology of OSA and metabolic syndrome overlap considerably. An interesting future study would be to investigate the effects of maxillofacial surgery on other constituent features of the metabolic syndrome in OSA patients using outcome measures such as insulin resistance and blood glucose/glycated haemoglobin measured pre and postoperatively.

Depression and anxiety are prevalent amongst patients diagnosed with OSA. A valuable future study would be to explore the impact of OSA surgery on depressive symptoms. Similarly, a study looking at health related quality of life in OSA patients before and after maxillofacial surgery would be a notable addition to the surgical literature.

As surgical techniques and technology continue to evolve new and exciting therapies for OSA are emerging. One such example is a hypoglossal nerve stimulator to provide electrical stimulation of the genioglossus muscle. A prospective study comparing the safety and efficacy of hypoglossal nerve stimulation with conventional maxillofacial orthognathic surgery for the management of OSA would be of considerable interest in evolving evidence for surgery in patient with sleep disordered breathing.

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