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Research Article

Evaluation of multiple surgeries as therapeutic options for Obstructive Sleep Apnea Syndrome

Abstract

Obstructive Sleep Apnea Syndrome (OSAS) is a chronic disease characterized by repeated airflow obstruction in the upper airway. Location of obstructive site is essential for proper surgical planning.

Objective: To evaluate the success rate of multiple surgeries, in various combinations, in the treatment of Moderate and Severe OSAS.

Methods: Fifty patients with moderate and severe OSAS subjected to multiple surgeries for treatment were studied, and the laboratory values of pre- and postoperative polysomnography were analyzed.

Results: Considering the reduce AHI from an average of 47.9 events / hour (± 23.30) preoperatively to a mean postoperative value of 19.82 events / hour (± 21.16) in cases of moderate OSAS, AHI was reduced from 22.89 to 18.50 events / hour. In severe cases of OSAS, the AHI reduced from 58.62 to 20.38 events / hour.

Conclusion: Several combinations of multiple surgeries for OSAS are valid for the treatment-resistant patients using CPAP alternatives. The success rate is significantly better in severe cases than in mild ones. Among the surgeries, craniofacial surgery contributed to improve postoperative AHI and showed a greater reduction than in patients not undergoing this technique.

Introduction

Obstructive Sleep Apnea Syndrome (OSAS) consists of a chronic disturbance, characterized by repeated episodes of collapse of the upper airways that lead to fragmented sleep. It is directly related to arterial hypertension, cardiovascular diseases, excessive daytime sleepiness, and a decrease in the quality of life [1-3].

The pathogenesis of OSAS and its physiopathology are complex, and its primary aggression mechanism would depend on repetitive episodes of hypoxia during apnea events followed by Reoxygenation, causing inflammatory changes and atherosclerosis².

Some are the risk factors related to OSAS, such as: male gender, 40 years of age or over and, in particular, obesity [1,4,5]. These would be involved in the multi-factorial etiology related to a functional and structural reduction of the caliber of the upper airways (UA). Diagnosis is made through clinical history, by physical otolaryngologic examination, combined with fiberoptic nasopharyngolaryngoscopy (NPL) and polysomnography (PSG). PSG is the only objective way to

diagnose and quantify the severity of OSAS, its performance being essential not only for diagnostic, but also as an aid in the control of improvement and cure after therapeutic measures have been taken.

A variety of conservative therapeutic strategies and surgeries are available to manage OSAS and have been intensely studied over the last two decades. Many patients respond well to weight loss, behavioral measures, oral motor speech therapy, the use of intraoral devices, and to Continuous Positive Airway Pressure (CPAP). However, conservative treatment of OSAS requires willpower, long-term follow up, and compliance with proposed techniques, for which reason, it is oftentimes not therapeutically successful. CPAP, despite being a treatment with well-established efficacy, has a long-term compliance below 50% (using CPAP on average 4 hours nightly during 70% of nights) [6,7].

There are many surgical procedures to treat OSAS. The low success rate of approximately 40% of individual Uvulopalatopharyngoplasty in non-selected patients with mild to severe OSAS spread the idea that combinations of surgical procedures would be the best option treatment [8].

The precise identification of the anatomic location of the collapsed UA is essential for the planning of adequate surgical interventions, which in most cases are multiple. Therefore, there is a need for different levels of surgery in order to achieve therapeutic success. The object of this study is to objectively determine the efficiency of multiple surgeries in the treatment of moderate to severe OSAS.

Materials and Methods

A retrospective study was carried out in a large private medical institution, from January 2002 until March 2017, with patients reporting symptoms suggestive of OSAS. After reviewing medical records from our institution, 50 patients were selected, all diagnosed with moderate (Apnea and Hypopnea Index (AHI) greater than or equal to 15 and less than 30) and severe obstructive sleep apnea (AHI greater than 30), who underwent multiple surgeries to treat OSAS. Other inclusion criteria were: (1), no prior surgery to treat OSAS (2), patients 18 years of age or older, (3), pre and post-operative full night Polysomnography (4), refusal of CPAP use, opting for surgical procedure, and (5), height and weight registration.

Polysomnography were performed in several clinics, initially marking the stages of sleep according to criteria established by Rechtschaffen e Kales [9], Apnea was defined as absence of respiratory air flow with breathing effort at least 10 seconds, while hypopnea was defined as a decrease in the respiratory airflow greater than 50%, accompanied by oxygen desaturation greater than 3% and awakening. After 2007, polysomnography respected the criteria of the American Academy of Sleep Medicine (AASM), where apnea would consist of a decrease in the airflow of 90% using a thermal sensor for at least 10 seconds.

Nasal, nasopharynx, oropharynx, hypopharynx, base of tongue surgeries and facial skeletal surgeries in several associations. Septoplasty (SP), bilateral inferior turbinectomy (T), Pyriformoplasty (PP), Rhinosseptoplasty (RSP), when appropriate, were the nasal surgeries performed. Adenoidectomy (AD) was performed to treat nasopharyngeal obstruction. Oropharynx collapse was treated with palatal surgeries, such as: Uvulopalatopharyngoplasty (UPPP), Expansion Pharyngeal Sphincteroplasty (EPS) and Lateral pharyngoplasty (LP). Genioglossal Advancement (GGA), Midline Glossectomy (MLG) and Thyrohyoidopexy (THP) were the hypopharyngeal surgeries performed. Maxillomandibular Advancement (MMA) was the Craniofacial Surgery performed. In one of the cases, associated Mentoplasty was performed. All the procedures were performed in one single surgical period under general anesthesia, following the described techniques. The selection of the surgical technique to be performed was based on physical examinations, Friedman staging, Facial classification, Nasofibrolaryngoscopies, Cephalometry, and in selected cases, image studies and Drug Induce Sleep Endoscopy (DISE).

For a better data analysis, the surgical procedures were grouped in: Palatal Surgeries, Craniofacial surgery, Hypopharyngeal surgeries and Nasal surgeries (Figure 1). The

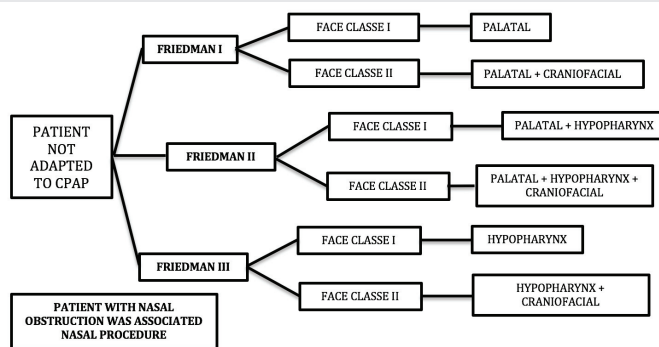


Figure 1: Indicator criteria for surgical procedures.

analysis of data included the body mass index (BMI), age, sex and pre and post-operative polysomnography parameters. Post-operative polysomnography was performed after 6 months of surgical procedures.

Statistical analysis was performed in SPSS (version 21.0 for Windows) and $p \leq 0,05$ was considered as statistically significantly. The Kolmogorov-Smirnov test was used to verify variable normality. The Levenne test was used to verify variable homogeneity among groups. When the distribution was normal, Student's t Test was for paired samples, and when the distribution was not normal, Wilcoxon's test. Linear regression was performed to verify the influence of each type of surgery to improve AHI, and ROC curves were performed to verify sensitivity and specificity of each type of surgery to improve AHI.

This study was approved by the ethic committee of the private entity, number 170.121.

Results

Of the 50 studied patients, 4 were female and 46 male. The average age was 44,6 years $\pm 10,12$, with a minimum age 18 and a maximum 65 years. 14 patients presented Friedman I, 34 Friedman II and 2 Friedman III. 43 patients presented facial classification I, and 7 were II. BMI medium was 28 kg/m² $\pm 3,4$, minimum BMI was 22,2 and maximum 37 kg/m². 15 patients (30%) presented moderate OSAS, 35 were severe (Table 1). AHI pre-operative oscillated from 25,13 until 115,10 events/hour with 47,9 $\pm 23,3$ on average, AHI Postoperative 0,2 to 81,36 on average 19,82 $\pm 21,16$. After evaluate the average

Table 1: Characteristics of the study population (n = 50).

	Total	Average	SD	Maximum	Minimum
Age (years)	n	44.6	10.12	65.0	18.0
BMI	n	28.0	3.4	37.0	22.20
Mild OSAS	0	-	-	-	-
Moderate OSAS	15	-	-	-	-
Severe OSAS	35	-	-	-	-
Friedman I	14	-	-	-	-
Friedman II	34	-	-	-	-
Friedman III	2	-	-	-	-
Facial Class I	43	-	-	-	-
Facial Class II	7	-	-	-	-

Abbreviations: BMI, body mass index; OSAS, Obstructive Sleep Apnea Syndrome; SD, standard deviation

difference of AHI pre and postoperative obtained 28,08 ±30,82, p < 0,001.

The combinations of the procedures were diversified (Table 2) and promoted AHI reduction.

Criteria for surgical success was defined as an AHI reduction greater than 50%, with an apnea index less than 208, therefore 33 patients (66%) were successful, while 17 (34%) cases failed. When considering an AHI < 5 events/hour, attempting to define a cure for OSAS, 15 (30%) patients presented with this value at the post-operative polysomnography.

Considering just moderate cases of OSAS the AHI average pre-operative was 22, 89 events/hour ±4, 95 and the post-operative was 18, 5 events/hour ±19, 64. The average reduction was 4, 39 ±19, 90 (p= 0,407). The average age was 44,4years ±9, 67. BMI pre-operative average was 26, 29 kg/m2 ±2, 3. The surgical success occurred in 8 patients (53, 33%) 6 of them (40%) had cure (IAH < 5events/hour). Failure of treatment occurred in 7 patients (46, 66%).

Considering only severe OSAS cases, AHI preoperative average was 58.62events/hour ±19,44 and post-operative average was 20,38 events/hour ±22,02. The average reduction of AIH was 40, 30 ±28, 97 (p< 0,001). The average age was 44, 65 years ±10, 44. The BMI preoperative was 28, 74 kg/m2 ±3, 55. The surgical success occurred in 28 (80%) patients, which 9 of them (25, 72%) were cured (AIH lower than 5 events/hour). The treatment failure occurred in 7 patients (20%).

Patients with severe OSAS had a significantly reduction in AHI after surgery than those patients with moderate OSAS, so much so that in our study, age and BMI did not contribute to the improvement of AHI after the surgery (p=0.069 e p=0.834, respectively).

Based on presented data, a linear regression was realized, searching an isolated analysis of each surgical group performance. In Facial Skeletal surgery the AIH preoperative presented average 61, 83 events/hour ±21, 09 turned into 6, 23 events/hour ±6, 52, an average difference 55, 90 ±26, 34. In the hypo pharynx surgeries the preoperative AIH presented average 52,94 events/hour ±24,68 turned to 19,34 events/hour ±21,64, an average difference 35,60 ±31,39. In palatal surgeries IAH preoperative presented average 48,45events/hour ±23, 28 became 20, 39 events/hour ±21, 40, an average difference 29, 56 ±31, 64. Nasal surgeries had IAH average preoperative 46, 29 ±24, 07 turned to 18, 98 ±20, 32, an average difference 27, 36 ±34, 31 (Table 3).

Patients who underwent craniofacial surgeries had a more significant reduction of the postoperative AHI than those not submitted to craniofacial surgery (p=0,014), regardless of OSAS severity. Performing nasal, palatal or hypo pharyngeal surgery did not significantly affect the postoperative AHI (p=0,432, p=0,561 and p=0,081) respectively.

However, when we abdicated linear regression and evaluated palatal surgery in conjunction with other surgeries, we observed that the UPPP and EPS obtained an important AHI

Table 2: Surgical combinations performed and resulting Mean AHI reduction.

	N	Mean	Standard Deviation	95% CI for average (lower limit)	Minimum	Maximum
Craniofacial, hypopharyngeal, palatal and nasal	5	65.63	23.05	37.01	38.7	96.10
Craniofacial, hypopharyngeal and palatal	1	17.75			17.75	17.75
Craniofacial and hypopharyngeal	1	45.40			45.40	45.40
Hypopharyngeal, palatal and nasal	18	27.20	35.97	9.31	-39.95	95.60
Hypopharyngeal and palatal	10	38.85	19.75	24.72	14.20	70
Hypopharyngeal (2 techniques)	1	12.13			12.13	12.13
Palatal and Nasal	14	13.91	25.41	-,76	-54.49	46.60

Abbreviations: CI, Confidence Interval

Table 3: Pre and Post-operative AHI comparison according to surgery type, with linear regression.

	Pre-operative AHI		Post-operative AHI		AHI reduction		Value of P
	SD	Average	SD	Average	SD		
Total	47.9	23.3	19.82	21.16	28.08	30.82	<0.0001 ^a
Moderate OSAS	22.89	4.95	18.5	19.64	4.39	19.9	0.407 ^a
Severe OSAS	58.62	19.44	20.38	22.02	40.3	28.97	<0.0001 ^a
Craniofacial	61.83	21.09	6.23	6.52	55.9	26.34	0.014 ^a
Hypopharyngeal	52.94	24.68	19.34	21.64	35.6	31.39	0.081 ^a
Palatal	48.45	23.28	20.39	21.4	29.56	31.64	0.561 ^a
Nasal	46.29	24.07	18.98	20.32	27.36	34.31	0.423 ^a

Abbreviations AHI, apnea and hypopnea index; SD, standard deviation; OSAS, Obstructive Sleep Apnea Syndrome

^at Test used.

reduction, 28, 56 ±33, 77 (p<0,001) and 19,81 ±17,01 (p=0,05) respectively. LP did not result in an important statistically representation (p=0,093).

In performing linear regression and ROC curve, we evaluated the chance of an AHI reduction after performing each type surgery. Therefore, we evaluated the best sensitivity and specificity point of each surgery performed. We observed that those submitted to craniofacial surgery upon analysis of sensitivity had 85, 7% chance of reducing chances preoperative AHI by 38,4 events/hour, and upon analysis of specificity, 69,8% chance of not presenting such a reduction (AUC 0,791). Those submitted to hypo pharynx surgery, upon analysis of sensibility, have a 72% chance of reducing preoperative AHI by 17, 42 events/hour, and upon analysis of specificity, 43% chance of not presenting such a reduction (AUC 0,681). Those submitted to palatal surgery have an 81,3% chance of reducing preoperative AHI by 12,31 events/hour, when evaluating sensitivity, and 50% chance of not presenting such a reduction when evaluating specificity (AUC 0,542). Nasal surgery, under the sensitivity analysis perspective, has a 62,2% chance of

reducing preoperative AHI by 18,42 events/hour, and when evaluating specificity, a 31% chance of not presenting this reduction (AUC 0,423) (Figure 2).

Discussion

OSAS is a relatively common illness, defined as repeated events of complete or partial obstruction of the upper airways, with a reduction or cessation of airflow during sleep. An epidemiologic study with the population of the city of São Paulo, the focus of this study, shows that 32.8% [10], of its resident present criteria for OSAS. There is a general consensus that the majority of patients present with multiple airway collapse areas. Taking this fact into consideration, an approach which would use a single surgical procedure is subject to failure or to a lower than expected result in most cases.

Success after multiple procedures on many levels of the airway has been demonstrated in many studies, especially when we compare single UPPF to procedures combining tongue base and hypo pharynx. A recent meta-analysis showed a success rate of 66.4% with multilevel sleep apnea surgeries involving two anatomical sites, which could be nose, oro- and hypo pharynx. This study involved 1,978 patients and had as success criteria an AHI reduction to less than 20 and a reduction greater than 50% of the value [11]. Other authors show favorable results using a combination of surgeries to treat apnea.

Riley et al. described positive surgical results after genioglossus advancement and hyoid myotomy, which varied from 75% success in patients with mild and moderate OSAS to 40% in patients with severe OSAS [12]. Dattilo et al. also observed that not only those patients submitted to THP, UPPP, MLG, and GGA, but also those submitted to MMA, showed therapeutic success according to analysis of pre- and post-operative AHI

in 78% and 93% of the cases, respectively [13]. Neruntarat described response to GGA combined with hyoid myotomy in 70% of the patients, with long-term success [14]. In addition, he states that performing single UPPF does not lead to absolute success, since the obstruction of the UA many times occurs in multiple sites, therefore all of these sites must be addressed [15]. Li et al. reported success after UPPP combined with MLG in 83.3% of the cases [16]. Zhang et al. evaluated answers after 6 months, 1 year, and 3 years as of the performance of UPPP and MLG in severe OSAS, achieving success in 100%, 84.6%, and 76.9% of the cases respectively [17]. Vilaseca et al. also demonstrated therapeutic success in 100% of the patients with mild OSAS and in 57% of those with moderate and multiple UA obstructions, after UPPP combined with GGA and THP [18]. D. Suh presented a success rate of 75.9% in Friedman III patients submitted to midline glossectomy in conjunction with UPPP, with an average AHI decrease of 28.4 [19]. Even though nasal surgery is considered adjuvant in the treatment of OSAS without positive influence on AHI when performed alone [20], Stow et al. demonstrated a reduction of more than 50% in the respiratory distress index (RDI) and a post-operative RDI lower than 20 in 85% of the patients submitted to nasal surgery and amygdlectomy [21].

In our study, even though the surgical success rate of the moderate OSAS group was only the severe OSAS group had a success rate of 80%, which resembles, and in some cases even exceeds those of the cited works. We noticed that many surgeries present positive results with greater frequency in severe OSAS cases.

It has difficult to determine a single decisive factor for the variation of the success rate by comparing severe and moderate OSAS. OSAS has multiple causes [22], and the anatomic contribution in patients with narrowing airways can have a more decisive role in some cases than in others, leading to a difference in results. Factors such as age and BMI, which are normally cited as being important for a result, show no interference in our study Analyzing data from linear regression we are able to determine the role of each surgery in the final result, as well as their individual performance.

The craniofacial surgery in our study showed an important role, with similar findings to those reported in worldwide studies. Confirming the importance of said procedure in the treatment of OSAS, Holty and Guilleminault [23], carried out a meta-analysis on MMA for treating OSAS in 2012, showing an average decrease of 63.9/h to 9.5, $p < 0.001$, with a therapeutic success rate of 86% and cure rate of 43.2%. This procedure, even individually, must be considered as a therapeutic option. In combination with surgeries, it can be maximized in cases of multiple UA obstructions. Pinto et al. [24], showed an average decrease of 45.79/h to 4.77/h when combining MMA and MLG, adding to the significance of this procedure.

Despite the fact that hypopharyngeal surgeries showed a decrease in AHI similar to that reported by Kezirin & Goldberg [25], which showed an AHI reduction from 60/h to 29/h with hypopharyngeal surgeries, the number shown does not present a statistical significance ($p = 0.081$) when we analyze solely the

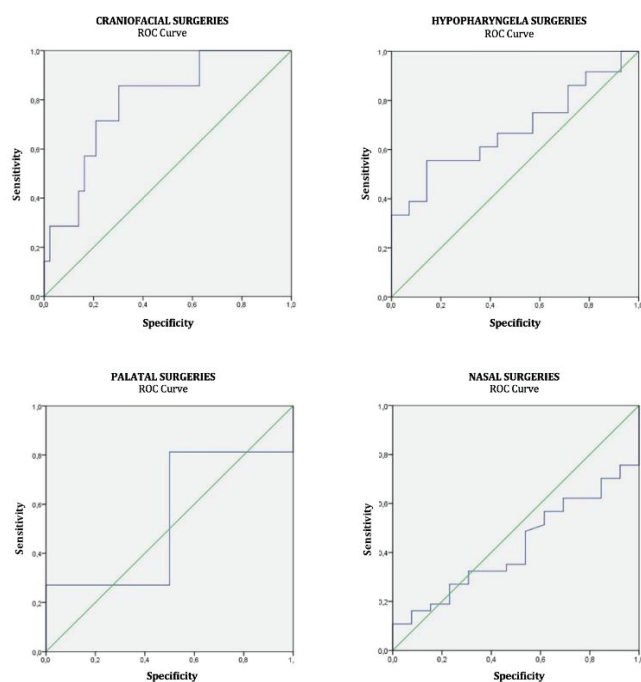


Figure 2: ROC curve of performed surgeries.

influence of this surgical technique. Similarly, nasal surgeries do not present significant influence, when performed alone, even with the average difference being close to the numbers reported by Li et al. [26], citing a decrease of 35.2 22.6/h to 33.5 23.8/h. Nevertheless, such procedures must be considered when we think of combinations on a multi-level basis.

Palatal surgeries also do not show significant influence when performed and analyzed as an individual procedure (p 0.561), however, the authors observed that failed cases, where palatal surgeries were present, were cases occurring in the beginning of the study and used the classic UPPP technique. It is hard to predict whether this fact happened due to the actual evolution of the surgical techniques, if it is related to the greater mastery of the authors' techniques, or if the selected cases did not have as favorable an anatomy as originally supposed. Cases that are very selected present good results only with palatal procedures, as shown in Friedman et al. [27], in which patients with stage Friedman I present a success rate of 80.6%. However, in the same study, patients submitted to UPPP alone with not so favorable palatal anatomy, present success rates of 37.9% and 8.1% in Friedman stages II and III, respectively. It is important to point out that when submitted to tongue-base reduction with coblation, combined with UPPP, the success rate in stage II increased to 74%, and in stage III to 36.8%.

Another fact worth pointing out in our study is that UPPP and EPS techniques show statistical value when performed as part of the treatment. In comparison with other studies, the decrease shown with UPPP as part of multiple surgeries (reduction of 28.56 +33.77) is greater than that presented by Caples et al. [28], which showed a pre-operative AHI of 40.3/h and post-operative AHI of 29.8/h. Even though the decrease did not show the same values presented by Pang & Woodson [29], the EPS also proved to be significant when combined with other techniques. LP in combination with another surgery, even with an AHI reduction of 44.35 ± 36.46, cannot be considered determinant, probably due to the low number of cases for such a procedure.

Several intra or post-operative complications are reported by the varied surgical techniques used in this study. In our group, there were 2 cases of bleeding after palatal surgeries, where one occurred after a UPPP and another after an LP, requiring surgical re-interventions. If we consider only the UPPPs, post-operative bleeding in 2.85% of all performed is a value discretely more elevated than others already presented by Riley [30] and Li [31], which show occurrences smaller than 1%. In skeletal surgery cases, we had 1 case (11.11%), among 9 patients submitted to MMA, with inferior lipparesthesia due to osteotomy close to the mandibular foramen. In the surgeries for hypopharynx, as a complication, we report a case of GGA fixation displacement with respiratory insufficiency by ptosis of the glossoepiglottic complex, in 10 cases performed.

A limitation of our work is that when grouping together a big number of surgical techniques performed, such as the palatal ones, associated with a limited number of patients, it becomes difficult to evaluate the efficacy of each technique individually. Nevertheless, the main objective of this study is

to determine the efficiency of multiple surgeries for treating OSAS, with no restriction to any particular approach. Even so, we observed important data when we selectively analyzed procedures at different levels, but as already reported due to the short n we can't use the isolated value of the efficacy from each procedure.

Conclusion

OSAS obstruction is a dynamic process. Patients who are offered surgical treatment must be informed that the results are difficult to predict. Contrary to the great difficulty in providing the patient with an objective measure (AHI<5) "cure", the improvement of sleep parameters after surgery is associated to the patient's satisfaction and the subjective improvement of diurnal somnolence. Furthermore, the AHI reduction can reduce future sequelae, in addition to helping patients comply with CPAP in those cases where there is a residual disease.

Multiple surgeries have shown a greater success rate in patients with severe OSAS than for those with moderate OSAS, according to polysomnography parameters.

There is a variety of possible procedures combinations to treat OSAS, depending on the levels of involvement. Multiple surgeries, when combined, have shown an important beneficial influence in surgical treatment. Among the surgeries performed, craniofacial surgeries contributed to the postoperative AHI improvement and showed a more significant reduction than in patients not submitted to this technique.

The majority of therapeutic failures happened due to the multilevel nature of the obstructions. The prior, precise, and physiological analysis of these sites is the prognostic key and focus of future research. The analysis of results is made difficult and obscured by the different and subjective definitions of success and by the heterogeneity of samples and proposed treatments for OSAS existing among different research groups.

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